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Electrochemistry Broadens the Scope of Flavin Photocatalysis: Photoelectrocatalytic Oxidation of Unactivated Alcohols

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Abstract

Riboflavin-derived photocatalysts have been extensively studied in the context of alcohol oxidation. However, to date, the scope of this catalytic methodology has been limited to benzyl alcohols. In this work, we gained further mechanistic understanding of flavin-catalyzed oxidation reactions in the absence or presence of thiourea as a cocatalyst. The mechanistic insights enabled us to develop an electrochemically driven photochemical oxidation of primary and secondary aliphatic alcohols using a pair of flavin and dialkylthiourea catalysts. Electrochemistry makes it possible to avoid using O_2 oxidant and generating H_2O_2 byproduct, both of which oxidatively degrade thiourea under the reaction conditions. This modification unlocks a new mechanistic pathway in which the oxidation of unactivated alcohols is achieved via thiyl radical-mediated hydrogen-atom abstraction

Graphical abstract

Abstract

The combination of electrochemistry and photochemistry allows for the generation of highly reactive catalytic intermediates without the need for a chemical oxidant. This photoelectrocatalytic strategy thus turns on the elusive reactivity of flavins of oxidizing unactivated aliphatic alcohols

Keywords

Electrochemistry; Flavin; Photoelectrocatalysis; Thiourea; Alcohol oxidation; Thiyl radical

Introduction

Oxidation and reduction reactions are among the most important and frequently executed processes in organic synthesis.¹ In recent decades, the discovery and development of new redox reactions—including catalytic hydrogenations, epoxidations, and C–H oxidations—have fundamentally changed how molecules are made.² Recently, the emergence of new catalytic strategies that cleverly adopt concepts and techniques from areas such as photochemistry³ and electrochemistry⁴ has provided chemists with new tools for solving contemporary synthetic problems.

Photoredox chemistry⁵ and electrochemistry⁶ have both proven to be disruptive technologies in organic synthesis, displaying complementary characteristics in synthetic contexts. Photoredox catalysis offers access to unique chemical reactivities at the excited states of organic molecules (Scheme 1A). This mode of catalysis is particularly suited to overall redox-neutral transformations. To achieve net-oxidation or reduction reactions, however, would require the use of a terminal redox agent and would generate byproducts,^{5e} both of which could complicate the reaction. Electrochemistry offers a solution to this issue by using electricity as the traceless redox agent, in combination with either an innocuous oxidant/reductant (e.g., H⁺) or one that can be separated in an independent compartment (i.e., using a divided cell) (Scheme 1B). In principle, electrochemistry can also grant access to highly reactive intermediates at extreme electrode potentials without relying on excited states.⁷ Nonetheless, the constant application of such highly biased potentials will likely lead to uncontrolled reactions due to accumulation of reactive intermediates near the electrode surface as well as compromised chemoselectivity in complex reaction systems.

We envision that the merger of electrochemistry and photochemistry has the potential to expand the scope of single-electron redox chemistry into new territories (Scheme 1C).⁸ Specifically, the combination of electrochemical catalyst activation and photo-excitation will grant access to reactive intermediates with high redox potential in a transient fashion in the absence of an oxidant or reductant. In this report, we demonstrate the generation of a highly reactive thiourea radical by means of flavin photoelectrocatalysis and its application in the oxidation of unactivated alcohols.⁹ The additive features granted by photoelectrochemistry proved critical, as neither photoredox catalysis nor electrocatalysis alone can provide the same reactivity in this catalytic system.

Results and Discussion

Flavins, a family of most versatile redox cofactors in nature,¹⁰ have recently been studied as organic photoredox catalysts for oxidative organic transformations.¹¹ For examples, riboflavin tetraacetate (RFT) is a readily available compound with an oxidation potential of +1.67 V (vs SCE) upon photo-irradiation ($\nu_{\text{max}} = 440 \text{ nm}$). This characteristic has allowed RFT and its derivatives to function as photocatalysts in the aerobic oxidation of benzylic C–H bonds,¹² benzyl alcohols,¹³ benzyl amines,¹⁴ sulfides,¹⁵ and carboxylic acids¹⁶ using O₂ as the terminal oxidant. Nonetheless, the scope of flavin catalysis is limited by the oxidation potential of the photoexcited state. The substrates suitable for this reaction system are thus confined primarily to those with electron-releasing substituents that can stabilize the key

radical or radical cation intermediates (Scheme 2). For example, flavin-catalyzed aerobic oxidation of alcohols is only applicable to electron-neutral and -rich benzyl alcohols.¹² Recent advances in catalyst development have led to cationic flavin analogs that can oxidize electron-deficient benzyl alcohols.¹⁷ However, aliphatic alcohols have not been successfully engaged in flavin-promoted oxidation reactions. This limitation significantly hampers the broad use of flavins in organic synthesis.¹⁸

Reports have shown that the addition of a Lewis acid^{11b,19} or thiourea^{12c} co-catalyst may enhance the catalytic efficiency of flavin but does not improve the reaction scope. Among these strategies, the use of thiourea as an additive is appealing from a mechanistic point of view. The mechanism of synergistic flavin/thiourea catalysis in the context of benzyl alcohol oxidation is not well understood. Initially thought to function as a H-bond donor that activates the flavin catalyst, thiourea has also been postulated to promote alcohol oxidation as a redox mediator between the substrate and flavin.^{12c} However, the reduction potential of thiourea is relatively low ($E \approx 0.8\text{--}1.0$ V vs SCE) and neither it nor its corresponding radical cation absorbs light in the visible region to reach the photoexcited state. As such, it is very unlikely that thiourea acts purely as an outer-sphere electron transfer agent. König postulated that thiourea could form highly reactive radical intermediates by means of flavin oxidation, which could then promote the oxidation of alcohols.^{12c} We hypothesize that the S-centered radical derived from single-electron oxidation of thiourea could serve to abstract a hydrogen-atom adjacent to the alcohol, thus resulting in the generation of a ketyl radical en route to carbonyl formation.

Computed bond dissociation energy (BDE; Scheme 3) supports this hypothesis. The S–H BDEs in isothiuronium (**TU-1•H⁺**) and its neutral form, isothiurea (*iso*-**TU-1**), are 93 and 91 kcal/mol, respectively; both of these values are higher than the C–H BDE in benzyl alcohol (88 kcal/mol)²⁰ and close to that of isopropanol (95 kcal/mol).²¹ These data suggest that, in theory, thiourea could promote the oxidation of both benzylic and unactivated aliphatic alcohols on thermodynamic grounds.

We reason that understanding the behavior of thiourea in the existing alcohol oxidation systems could facilitate a critical expansion of the scope of flavin photocatalysis to substrates beyond benzylic compounds.

Elucidating the fate of thiourea in flavin-catalyzed alcohols oxidation.

We set out to study both the effect of thiourea on the oxidation of alcohols and the fate of this mediator following reaction. Under conditions developed by König *et al.*, 4-methoxybenzyl alcohol (**1a**) was oxidized to 4-methoxybenzaldehyde (**2a**) in 40% yield (Scheme 4, entry 1) in the presence of RFT as the sole catalyst in 1 atm O₂ under blue light irradiation. In stark contrast, under the same reaction conditions, 4-*tert*-butylcyclohexanol (**1b**) substrate was completely recovered with no observed formation of the ketone product (entry 3). These results are not surprising given the oxidation potential of **1b** ($E > 1.9$ V vs SCE; Figure 1A) is much higher than that of **1a** ($E \sim 1.5$ V) and excited RFT (RFT*; $E \sim 1.67$ V). In fact, photo-quenching experiments (Figure 1B) showed that RFT* is efficiently quenched by **1a** but not by **1b**.

Analogous to previous reports, the reaction yield with **1a** could be improved to 85% in the presence of 10 mol% thiourea (**TU-1**; Scheme 4, entry 3). Encouragingly, addition of 10 mol % **TU-1** to the reaction of substrate **1b** led to formation of a minute amount of ketone product **2b** (entry 4), providing proof-of-concept that thiourea can in fact promote the oxidation of unactivated secondary alcohols. However, extending the reaction time did not lead to an increase in reaction yield in this case.

In the reactions with **TU-1**, the thiourea catalyst was not detected by HPLC following the reaction, but a white precipitate formed during the course of the reaction, which was identified as thiourea dioxide (**TU-1•O₂**) through comparison with an authentic sample (Figure 2). We hypothesize that **TU-1•O₂** arises from the oxidative degradation of **TU-1**, by either O₂ or H₂O₂ – a byproduct arising from the catalytic turnover of flavin by O₂ (Scheme 5A). Indeed, H₂O₂ was detected in 34 mM (0.63 equiv with respect to **1a**) in the reaction with **1a** and in a smaller but still significant amount (2.6 mM, 0.05 equiv) with **1b** (Scheme 4, entries 2 and 4).

Further experiments lend support to our hypothesis. In these experiments, 1,3-diisopropylthiourea (**TU-2**) was employed instead of **TU-1** to allow for the facile determination of the remaining thiourea by ¹H NMR. Upon treatment of **TU-2** with 1 equiv of H₂O₂ in the presence or absence of RFT, approximately 60% of the thiourea was consumed and the corresponding thiourea dioxide (**TU-2•O₂**) was observed (Scheme 5B, entries 1 and 2).

Under conditions analogous to the photochemical oxidation of benzyl alcohol **1a**, singlet O₂ – a strong oxidant – was detected using the furfural test²² (Scheme 5C). ¹O₂ is presumably generated through photoirradiation of ³O₂ in the presence of RFT as the sensitizer. Under photolytic conditions with O₂, **TU-2** was fully consumed to form **TU-2•O₂** in the presence RFT (Scheme 5B, entry 3) but fully recovered in the absence of RFT (entry 4). These findings suggest that RFT can promote the photodecomposition of thiourea via two pathways, by means of singlet O₂ and byproduct H₂O₂.²³ In the reaction with simple alcohol **1b**, it is likely that the singlet O₂ pathway is predominant because the formation of H₂O₂ needs at least one turnover of the flavin catalyst and is thus slow, given the small amount of product generated.

To explain the moderate rate acceleration effect of thiourea on the oxidation of **1a**, we reason that thiourea decomposition is slower than or comparable to the oxidation of reactive benzyl alcohols. However, this decomposition pathway out-competes the oxidation of more challenging unactivated alcohols such as **1b**.

Solving the thiourea degradation problem using electrochemistry.

Based on this discovery, we hypothesize that the decomposition of thiourea, which mediates the oxidation of alcohol by photoexcited flavin, plagues the catalytic system and is likely the cause for its narrow substrate scope. We aimed to further substantiate this theory and find a solution that would allow us to expand the reaction to the transformation of unactivated alcohols. Intuitively, replacing O₂ with another oxidant could resolve this problem. However, O₂ represents one of the mildest and most atom-economic oxidizing agents and is uniquely

suited for flavin photocatalysis. The use of another oxidant could lead to oxidative decomposition of flavin and/or thiourea (as in the case with H_2O_2) and generate side products that could complicate the reaction by reacting with the alcohol substrate or other reactive intermediates. Mindful of the electrochemical activity of flavin derivatives,²⁴ we reasoned that using electricity to replace O_2 with H^+ as the innocuous terminal oxidant might provide an effective solution.

Our initial explorations revealed that the oxidation of **1b** could be achieved in significantly improved yield (up to 67%) in an electrolysis cell (cell voltage $U_{\text{cell}} = 2.5$ V, initial anodic potential $E_{\text{anode}} \approx 0.8$ V vs SCE) in the presence of RFT and 10 mol% **TU-1** using carbon foam as the anode, Pt coil as the cathode, LiClO_4 in MeCN as the electrolyte solution, and H_2O as the proton source (Scheme 6A, entry 1). To further optimize the oxidation and probe the role of thiourea in the reaction, we surveyed several substituted thioureas (entries 2-4). Among the *N,N*-dialkylthioureas tested, the isopropyl version proved optimal, providing **2b** in improved 78% yield (entry 2). Fully substituted thiourea **TU-7** was incompetent in promoting the oxidation reaction (entry 5), while acetylthiourea (**TU-8**) gave the product in a diminished 21% yield (entry 6). Various electrolytes were also investigated. While commonly used tetraalkylammonium salts did not increase the reaction efficiency (entries 7, 8), LiOTf proved superior, furnishing the ketone nearly quantitatively (entry 9). Finally, control experiments suggest that electrical potential, blue LED, RFT, and the thiourea are all essential to this transformation, as exclusion of any of these components led to no formation of **2b** (entries 10–13). Finally, controlled potential electrolysis showed that alcohol oxidation could be observed at an anodic potential as low as 0.58 V, albeit at a much slower rate as expected (entry 14).

These optimized reaction conditions were applied to several other secondary alcohols and provided the desired ketones (**2c–i**) in satisfactory yields (Scheme 6B). An unactivated primary alcohol was also found to be compatible, affording carboxylic acid **2j** in 53% yield.

Probing the role of thiourea.

As previously discussed, in König's reaction system with benzyl alcohols, thiourea was proposed as a redox mediator. However, the role of thiourea in promoting the alcohol oxidation is not well understood. In particular, the reduction potential of thiourea is relatively low ($E \approx 0.8$ – 1.0 V vs SCE) and neither it nor its corresponding radical cation absorbs light in the visible region. As such, it is very unlikely that thiourea serves purely as an outersphere electron mediator.

Fluorescence quenching experiments suggest that RFT* could be quenched by a thiourea (Figure 3). We propose that thiourea is oxidized by RFT* to a thiyl radical cation **3**, which can be deprotonated to form neutral thiyl radical **4** (Scheme 7A). The formation of thiyl radicals is supported by alkene isomerization experiments (Scheme 7B).²⁵ Thus, when β -methylstyrene **6** in predominantly *Z*-configuration (*Z/E* = 6:1) was added to the standard photoelectrochemical reaction, in the absence of any thiourea, 71% of **6** was recovered with a *Z/E* ratio of 10:1. This result suggests that the radical induced isomerization did not occur. The marginal enrichment of the major *Z*-isomer was likely due to the fact that the *E*-isomer

undergoes preferential RFT*-mediated isomerization or decomposition.^{11a,26} By contrast, when subjected to **TU-2**, **6** was essentially completely isomerized to the more stable *E* configuration (*Z/E* = 1:100). This isomerization is most likely induced by thiourea-derived radicals **3** or **4**.

The formation of thiyl radicals was also supported by the formation of disulfide-like dimer **7** during the alcohol oxidation. In particular, when we increase the thiourea loading from 10 mol% to 20 mol% and 40 mol%, the generation of H₂S is evident from the distinct odor of the completed reaction. Thiourea-derived radicals have been reported to first dimerize and then decompose to the corresponding urea and H₂S in the presence of H₂O.^{25,27} Increasing the loading of **TU-2** led to a *decrease* in reaction rate (Figure 4), a phenomenon that we can also attribute to the catalyst decomposition pathway. In fact, an apparent induction period was observed in the presence of 40 mol% **TU-2** (blue triangles, Figure 4). Product **2b** only began to form after 4 h reaction time when the concentration of **TU-2** reached a sufficiently low level due to decomposition so that the catalytic reaction outcompeted the unproductive dimerization.

The ability of thiourea-based radicals to promote alcohol oxidation was investigated using cyclic voltammetry (Figure 5A). **TU-2** alone showed an oxidative wave with an onset potential of ca. 0.58 V vs SCE. This broad wave appears to encompass at least two features, peaking at 1.0 and 1.2 V. The second peak may correspond to oxidation of the thiourea dimer but we have not carried out further experiments to support this hypothesis. The addition of alcohol **1b** to the system led to the observation of a catalytic current, which increased in intensity as the amount of **1b** was increased. This current enhancement is indicative of the fact that **TU-2** is capable of catalytically oxidizing the alcohol substrate. This catalytic activity is likely promoted by thiourea-based radicals **3** or **4**. Control experiments excluded the role of thiourea dimer (cf. **7**) in the alcohol oxidation activity: (1) using commercial available dimer of **TU-1** as the catalyst instead of **TU-1** or **TU-2** under optimal photoelectrochemical conditions, only a trace amount of ketone product was observed (~7%, vs 76% using **TU-1**); (2) cyclic voltammetry study of **TU-1** dimer did not show catalytic current upon addition of alcohol **1b**.

We propose that thiourea-derived radicals promote the oxidation of unactivated alcohols through abstraction of the H atom α- to the hydroxy group (see Scheme 7A).²⁸ The resultant ketyl radical **5** then readily loses the O-bound H-atom (BDE_{O-H} = 20–30 kcal/mol)²⁹ to furnish the ketone. The intermediacy of a ketyl radical was suggested by a radical probe experiment with alcohol **8**, which bears a cyclopropyl group (Figure 5B). Thus, when **8** was exposed to standard conditions, a number of products were isolated, including ketone **10** (2% yield) and a mixture of products **11–13** (combined 14% yield). The latter products arose from radical-triggered ring opening of the cyclopropane unit in intermediate **9**. DFT data (see Scheme 3) suggest that the hypothesized H-atom abstraction mechanism is thermodynamically plausible.

Understanding the role of RFT.

This mechanistic proposal supposes that flavin plays the role of a pure photooxidant and does not have a discrete function in the alcohol oxidation process. Indeed, when we used Ir and pyrrilium-based photocatalysts in lieu of RFT, we observed the formation of desired product **2b**, albeit in lower yield (Table 1, entries 2 & 4 vs entry 1). These photocatalysts alone without thiourea are ineffective in promoting the alcohol oxidation (entries 3 & 5).

The cyclic voltammetry data suggested that a photocatalyst might not be necessary at all and that the thiourea could potentially serve as an electrocatalyst to effect alcohol oxidation under dark conditions. However, direct electrolysis *in the absence of RFT* under conditions otherwise identical to the optimal conditions did not give appreciable amounts of ketone (entry 6). We also conducted a controlled potential electrolysis experiment at 1.09 V (vs SCE) anodic potential in the absence of RFT or light irradiation, but did not observe any desired oxidation product (entry 7). In this reaction, the distinct odor of H₂S was detected. We reason that under pure electrolytic conditions, the thiourea-based radicals are generated directly on the anode, resulting in a high concentration of the reactive intermediates within the diffusion layer. Thus, undesired dimerization of these key catalytic species predominates. This issue was not readily addressed by lowering the rate of anodic oxidation, as electrolysis at a very low constant current of 0.5 mA (6–10 times lower than the typical current under optimal conditions) with **TU-1** alone without RFT or blue light also did not provide any desired ketone product (entry 8). In contrast, under photoelectrochemical conditions, the thiourea radicals are generated in small quantities by the transient photoexcited state of RFT, which will preferentially react with the alcohol substrate to promote the desired reaction pathway.

Based on the above studies, we propose the reaction mechanism depicted in Scheme 8. Upon irradiation, electron transfer followed by proton transfer between excited **RFT*** and **TU-2** results in **4** and semiquinone form (**RFT***)–H. The thiyl radical **4** abstracts the α -position hydrogen from alcohol **1** to produce the corresponding ketyl radical **5**, which can further react with (**RFT***)–H via hydrogen-atom transfer (HAT) to afford the desired ketone product **2**. Finally, the dihydroquinone form of catalyst (**RFT**)–H₂ is oxidized at the anode surface to regenerate the ground-state catalyst **RFT**. An alternative mechanism in which thiyl radical cation **3** functions as the H atom abstractor is also plausible (see Supporting Information). Given the fact that tetraalkyl thiourea (e.g., **TU-7**) is ineffective in catalyzing the oxidation reaction, we currently favor the proposed mechanism in Scheme 8. However, the current level of evidence does not allow us to fully distinguish between these two pathways, and it is possible that both are operating in the reaction system.

Under the photoelectrocatalytic conditions, we did not observe appreciable amounts of **TU-1•O₂**. The major side reaction is the dimerization of thiyl radical **4** to produce dimer **7**, which then undergoes irreversible decomposition to H₂S and urea **14**, the former of which may be detected by odor.

This thiourea-mediated, photoelectrochemically driven reaction mechanism is fundamentally different from that of photochemical oxidation of benzyl alcohols catalyzed by flavin alone (Scheme 2B).^{12e} In the latter, the photoexcited flavin directly removes an electron from the

substrate aromatic group to form a radical cation, which then loses H^+ to form the corresponding ketyl radical prior to conversion to the aldehyde product. The scope of the flavin-catalyzed reaction is thus limited by the oxidation potential of the flavin excited state and its ability to effect single-electron oxidation of the organic substrate. Such a limitation is overcome in the thiourea-mediated photoelectrocatalytic protocol, as the key catalyst-substrate reaction relies on H atom abstraction by the thiourea-based radicals generated by means of flavin oxidation.

Conclusion

In summary, we developed a new approach, namely molecular photoelectrocatalysis, for the oxidation of unactivated secondary alcohols. This catalytic strategy combines the attractive features of both photoredox chemistry and electrocatalysis, allowing efficient access to highly reactive excited states and radical intermediates in the absence of a stoichiometric oxidant. This merger critically expands the scope of flavin-catalyzed alcohol oxidation from electron-neutral and -rich benzyl alcohols to unactivated aliphatic alcohols. Future work will be directed toward further understanding the mechanism of molecular photoelectrocatalysis and applying this new strategy in new organic reactions.

Experimental Section

An oven-dried, 10 mL two-neck glass tube was equipped with a magnetic stir bar, a vacuum adapter with glass stopcock, a Teflon cap fitted with electrical feed-throughs, a carbon foam anode ($1.0 \times 0.5 \text{ cm}^2$, connected to the electrical feedthrough via a 9 cm in length, 2 mm in diameter graphite rod), and a platinum coil cathode. To this reaction vessel, RFT (5.4 mg, 0.01 mmol, 5 mol%), TU-2 (3.2 mg, 0.02 mmol, 10 mol%), alcohol (0.2 mmol, 1.0 equiv), 3.5 mL of electrolyte solution (0.10 M LiOTf in acetonitrile) and H_2O (0.2 mL) were added. The cell was sealed and subjected to three freeze-pump-thaw cycles. The resulting solution was stirred at room temperature under the irradiation from two 7W blue LEDs, and electrolysis was initiated at a constant voltage of 2.5 V for 24 hours. After that, the entire reaction mixture was filtered through a short silica gel column (3 cm in length, ca. 5 g) and flushed through with 60 mL of 1:1 mixture of hexanes and ethyl acetate to eliminate the inorganic salts, and the filtrate was concentrated under vacuum. The residue was purified by flash column chromatography on silica gel (eluted with hexanes/ethyl acetate) to afford the pure product.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

(A) Cyclic voltammetry of **1a** and **1b**. Conditions: alcohol (5.71 mM), LiOTf (0.1 M in MeCN), scan rate = 100 mV/s. (B) Fluorescence quenching of RFT with **1a**, **1b**.

Figure 2.
 ^{13}C -NMR spectrum of A) thiourea dioxide (**TU-1**• O_2); B) white precipitate in reaction system; C) thiourea, all in D_2O with MeCN as internal standard.

Figure 3.
Photo-quenching of RFT by thiourea **TU-2**.

Figure 4.
Reaction time course data with different concentrations of **TU-2**.

(A) Cyclic voltammetry of **TU-2** in the absence and presence of **1b**

(B) Radical probe experiment

Figure 5.

(A) Cyclic voltammetry of **TU-2** in the presence and absence of **1b**; (B) Radical probe experiment. Standard conditions: see Scheme 6A, entry 9.

Scheme 1.

General mechanistic depiction of photoredox catalysis, electrocatalysis, and molecular photoelectrocatalysis for oxidative transformations.

(A) Flavin-catalyzed alcohol oxidation: substrate limitations

Ideal substrates: e-neutral and -rich benzyl alcohols

Examples: $\text{R}^1 = \text{Ph}$, $p\text{-MeO-Ph}$; $\text{R}^2 = \text{H}$, Me

Challenging substrates: unactivated aliphatic alcohols

Examples: $\text{R}^1 = \text{alkyl}$, $\text{R}^2 = \text{H}$, alkyl

(B) Proposed reaction mechanism

Scheme 2.

RFT-catalyzed photochemical oxidation of alcohols.

Scheme 3.

Computed bond dissociation energy of isothiuronium and isothioureia [M06-2x/6-311+G(d,p)/CPCM(CH₃CN)//B3LYP/6-31G(d)].

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(A) Proposed thiourea decomposition pathways

(B) Decomposition of thiourea by H₂O₂ and ¹O₂

Entry	RFT	oxidant	TU-2 recovered
1	5 mol%	H ₂ O ₂ (1 equiv)	40%
2	none	H ₂ O ₂ (1 equiv)	37%
3	5 mol%	O ₂ + blue LED	0%
4	none	O ₂ + blue LED	100%

(C) Trapping experiment showing RFT promotes ¹O₂ generation **Scheme 5.**

Decomposition of thiourea under RFT-promoted photooxidation conditions.

(A) Reaction optimization^a

Entry	Thiourea	Electrolyte	1b Conversion	2b Yield ^b
1	TU-1	LiClO ₄	75%	67%
2	TU-2	LiClO ₄	85%	78%
3	TU-3, -4, or -5	LiClO ₄	27–30%	20–26%
4	TU-6	LiClO ₄	7%	<5%
5	TU-7	LiClO ₄	5%	<5%
6	TU-8	LiClO ₄	27%	21%
7	TU-2	TBAPF ₆	24%	18%
8	TU-2	TBAPF ₆	95%	56%
9	TU-2	LiOTf	>95%	96% (91% ^c)
10 ^d	TU-2	LiOTf	8%	<5%
11 ^e	TU-2	LiOTf	8%	<5%
12 ^f	TU-2	LiOTf	6%	<5%
13	none	LiOTf	11%	6%
14 ^g	TU-2	LiOTf	12%	9%

(B) Oxidation of several other alcohols^{a,c} **Scheme 6.**

Photoelectrocatalytic oxidation of alcohols. ^aConditions: alcohol (0.2 mmol, 1 equiv), RFT (5 mol%), TU (10 mol%), electrolyte (3.5 mL, 0.1 M in MeCN), H₂O (0.2 mL), cell voltage $U_{\text{cell}} = 2.5$ V (initial anodic potential $E_{\text{anode}} \approx 0.8$ V vs SCE), blue LED. ^bYield determined by ¹H NMR. ^cIsolated yield. ^dWithout blue LED. ^eWithout RFT. ^fWithout electricity.

^gElectrolysis at a constant anodic potential of 0.58 V. ^hReaction time 36 h.

(A) Proposed key reaction intermediates

(B) Detecting thiyl radicals in photoelectrocatalytic reactions

Scheme 7.

Formation and role of thiyl radicals in the photoelectrocatalytic alcohol oxidation.

Scheme 8.

Proposed catalytic cycles for the photoelectrocatalytic oxidation.

Table 1.

Photoelectrocatalysis control experiments.

Entry	Photocatalyst	Thiourea	1b Conversion ^a	2b Yield ^a
1	RFT	yes	75%	67%
2	[Ir(dF(CF ₃)ppy) ₂ (dtbpy)]PF ₆	yes	32%	31%
3	[Ir(dF(CF ₃)ppy) ₂ (dtbpy)]PF ₆	no	5%	<5%
4	[Mes-Acr-Me] ⁺ ClO ₄ ⁻	yes	10%	8%
5	[Mes-Acr-Me] ⁺ ClO ₄ ⁻	no	<5%	<5%
6	None	yes	13%	<5%
7 ^b	None	yes	7%	<5%
8 ^c	None	yes	8%	<5%

^aDetermined by ¹H NMR.^bControlled potential electrolysis at $E_{\text{anode}} = 1.09 \text{ V}$ vs SCE without light irradiation.^cControlled current electrolysis at $i = 0.5 \text{ mA}$ without light irradiation.