

Enantioselective Synthesis of γ -Oxycarbonyl Motifs by Conjugate Addition of Photogenerated α -Alkoxy Radicals

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Cite This: *Org. Lett.* 2021, 23, 5703–5708



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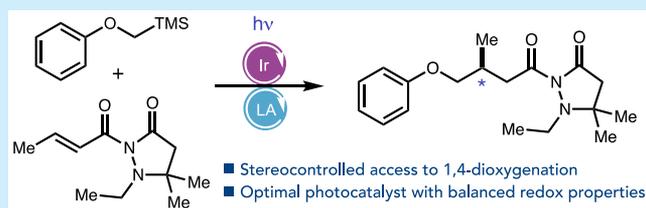


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Supporting Information

ABSTRACT: Enantioselective catalytic Giese addition of photogenerated α -alkoxy radicals to acyl pyrazolidinones can be accomplished using a tandem Sc(III) Lewis acid/photoredox catalyst system. Surprisingly, the excited-state oxidation potential was not the only important variable, and the optimal photocatalyst was not the strongest oxidant screened. Our results show that both the oxidation and reduction potentials of the photocatalyst can be important for the reaction outcome, highlighting the importance of holistic considerations in designing photochemical reactions.



Retrosynthetic disconnections are often defined by the relative disposition of oxygen-containing functional groups.¹ The 1,3-dioxygenation pattern is perhaps the most iconic of these retrons, suggestive of aldol or Claisen disconnections, and the development of stereocontrolled aldol reactions has figured prominently in the history of asymmetric synthesis.² Similarly, 1,5- and 1,2-dioxygenation patterns, suggestive of Michael addition or Rubottom oxidation retrons, respectively, have also been targeted by enantioselective catalytic methods (Figure 1A).³ The enantiocontrolled catalytic synthesis of 1,4-dioxygenation patterns, however, has remained a conspicuous challenge with few highly effective solutions,⁴ despite their presence in many medicinal lead compounds.⁵

Our laboratory has a long-standing interest in stereocontrolled reactions of photogenerated radicals. We demonstrated that Giese addition of α -silyl amines to Michael acceptors, a classical photoreaction studied in detail by Mariano,⁶ could be made highly enantioselective using a dual catalyst protocol.⁷ This method utilizes a Ru(II) photoredox catalyst that initiates the oxidative desilylation of an α -silyl amine pronucleophile and a chiral Lewis acid cocatalyst that activates the Michael acceptor and dictates the facial selectivity of the radical addition (Figure 1B). We reasoned that the use of α -silyl ether pronucleophiles might offer an analogous strategy for the generation of chiral γ -alkoxycarbonyl adducts. While this modification is conceptually straightforward, it presents a significant tactical challenge because oxygen functionalities are substantially harder to oxidize than their nitrogen counterparts (Figure 1B).⁸ The use of α -silyl ethers in racemic conjugate additions has previously been reported by Steckhan⁹ and Woo,¹⁰ but these reactions have been limited to highly electron-deficient Michael acceptors. Recently, Melchiorre described enantioselective Giese additions to enals using organophotoredox/chiral amine dual catalysis.¹¹ A single

example using a photogenerated α -alkoxy radical was described, but the generality of this process was not studied. We hypothesized that a Lewis acid cocatalyst might expand the scope of this reaction to include less electrophilic acceptors and provide an opportunity for stereocontrol in the Giese addition of oxyfunctionalized organoradical intermediates.

Subjecting α -silyl ether **1a** and pyrazolidinone **2a** to conditions optimized for radical conjugate addition of α -silyl amines gave only returned reactants (Table 1, entry 2), indicating that the excited-state photocatalyst $[\text{Ru}^*(\text{bpy})_3]^{2+}$ is unable to oxidize **1a** to produce the requisite radical intermediate. We hypothesized that a more oxidizing photocatalyst might be able to initiate the reaction and conducted a screen of several candidates commonly utilized in oxidative photoredox catalysis. Surprisingly, there was no correlation between the excited-state oxidation potential of the photocatalyst and the yield of **3a** (Table 1, entries 3–5); the most oxidizing transition-metal and organic photocatalysts in our screen afforded poor conversions after 12 h. The Fukuzumi acridinium salt, a common oxidizing photocatalyst,¹² produced somewhat better results (entry 4). The highest yield, however, was obtained using $[\text{Ir}(\text{dFCF}_3\text{ppy})_2(\text{dtbbpy})]\text{PF}_6$ (**Ir**), which possesses a comparatively modest excited-state oxidation potential.¹³ Lowering the reaction temperature improved the mass balance and enantioselectivity of the reaction (entry 6). Control experiments (entries 7–9) showed that no product is formed in the absence of light, photocatalyst, or Lewis acid.

Received: June 2, 2021

Published: July 23, 2021



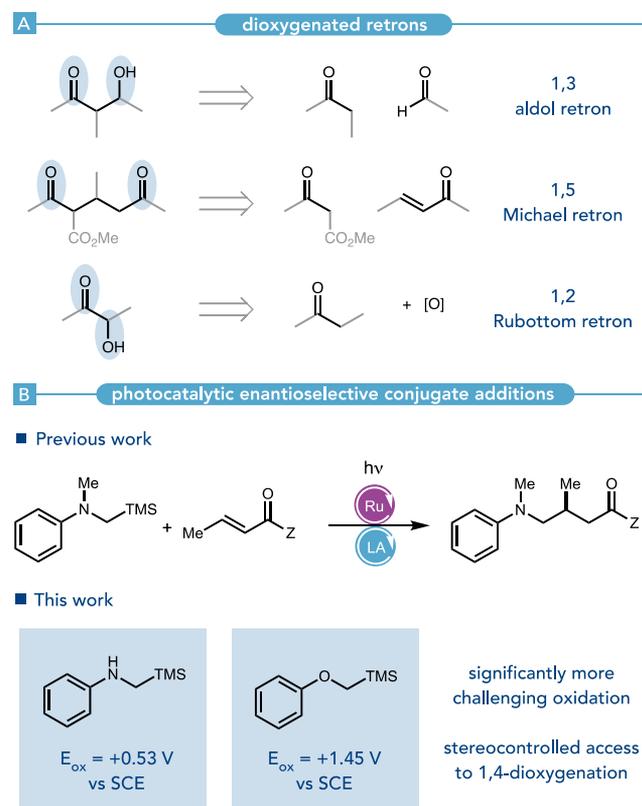


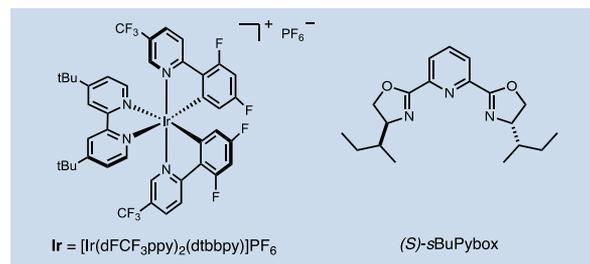
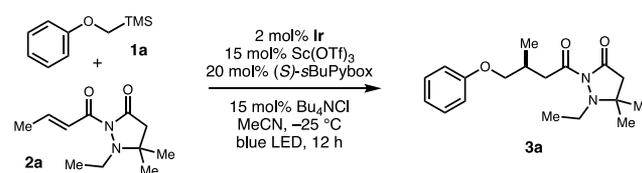
Figure 1. (A) Retrosynthetic disconnections defined by dioxxygenation patterns. (B) Stereocontrolled access to 1,4-dioxygenation patterns via asymmetric photoredox conjugate addition.

The addition of a soluble chloride salt (Bu_4NCl) increased the yield and enantiometric excess (e.e.) of the conjugate addition, but the effect was less pronounced than in the α -silyl amine reaction (entry 10).⁷ Finally, no product was formed when insoluble ScCl_3 was used in place of $\text{Sc}(\text{OTf})_3$ (entry 11).

Figure 2 summarizes studies exploring the scope of the enantioselective photocatalytic Giese addition. With respect to the α -silyl ether pronucleophiles, functional groups such as halogens and boronic acids are well-tolerated under the reaction conditions, providing handles for further synthetic manipulation. Steric hindrance led to a lower yield (**3ia**), while both mildly electron-donating groups and electron-withdrawing groups provided good yields and excellent e.e. values. However, highly electron-rich and electron-deficient pronucleophiles did not yield the desired conjugate addition products. In the case of highly electron-rich substrates, we observed decomposition, while for highly electron-deficient substrates, we recovered the starting pronucleophiles in good yield.

With respect to the Michael acceptor, we noticed a sensitivity toward the nature of the β -substituent, while α -substituents shut down the reactivity. Increasing steric bulk leads to diminished yields. On the other hand, we were pleased to see that synthetic handles such as chlorine and a terminal alkene remained intact during the reaction. Polar functional groups, including Boc-protected amine, ether, and amino acid derivatives, are also tolerated. Lewis basic functionalities such as esters result in decreased e.e. values. Unexpectedly, aromatic substituents, which were well-tolerated in our previously reported α -amino radical addition, did not lead to the desired products. Rather, we observed no further reaction after enone *E/Z* isomerization, suggesting that access to the triplet enone is

Table 1. Variations of the Reaction Conditions^a



entry	deviation from the standard conditions	E_{ox}^* (V vs SCE)	yield	e.e.
1	none	+1.21	82%	95%
2	$[\text{Ru}(\text{bpy})_3]\text{Cl}_2$ instead of Ir, rt	+0.77	0%	—
3	$[\text{Ru}(\text{bpz})_3]\text{Cl}_2$ instead of Ir, rt	+1.45	0%	—
4	MesAcrMe ⁺ instead of Ir, rt	+2.06	45%	83%
5	TPPT instead of Ir, rt	+2.30	16%	85%
6	rt instead of $-25 \text{ }^\circ\text{C}$	+1.21	71%	87%
7	no light	+1.21	0%	—
8	no photocatalyst	—	0%	—
9	no $\text{Sc}(\text{OTf})_3$	+1.21	0%	—
10	no Bu_4NCl	+1.21	72%	90%
11	ScCl_3 instead of $\text{Sc}(\text{OTf})_3$	+1.21	0%	—

^aReaction conditions: **1a** (0.15 mmol, 1 equiv), **2a** (0.225 mmol, 1.5 equiv), photocatalyst (3×10^{-3} mmol, 2 mol %), $\text{Sc}(\text{OTf})_3$ and Bu_4NCl (0.0225 mmol, 15 mol %), (*S,S*)-sBuPybox (0.03 mmol, 20 mol %), MeCN (3.0 mL, 0.05 M), 34 W blue LEDs. Yields were determined by ¹H NMR analysis of the crude reaction mixtures using mesitylene as an internal standard.

feasible under the reaction conditions. Nevertheless, the current system enabled functionalization of moderately electrophilic Michael acceptors, overcoming a major limitation in the previous reports by Steckhan⁹ and Woo.¹⁰ The absolute configuration of **3a** was confirmed by X-ray crystallographic analysis of the corresponding carboxylate salt (see the **Supporting Information**).

The most intriguing feature of our optimization studies was that the yield of the reaction did not correlate with the excited-state oxidation potential of the photocatalyst. Moreover, the excited-state oxidation potential of the optimal Ir photocatalyst (+1.21 V) seems insufficient to directly oxidize the α -silyl ether nucleophile (+1.45 V), suggesting that the initiation mechanism of this process is different from that of the α -silyl amine reaction we reported previously.⁷ We thus elected to study the mechanism of this process in greater detail.

We first conducted a Stern–Volmer study to interrogate the abilities of the two reactants to quench the excited state of the photocatalyst, either alone or in the presence of added Lewis acid (**Figure S1**).¹³ The photoluminescence of the photocatalyst does not change significantly with varying concentrations of the α -silyl ether either with or without added $\text{Sc}(\text{OTf})_3$. These results indicate that one-electron photooxidation of the α -silyl ether does not initiate this photo-reaction. In contrast, we observed a concentration-dependent increase in photoluminescence quenching in the presence of

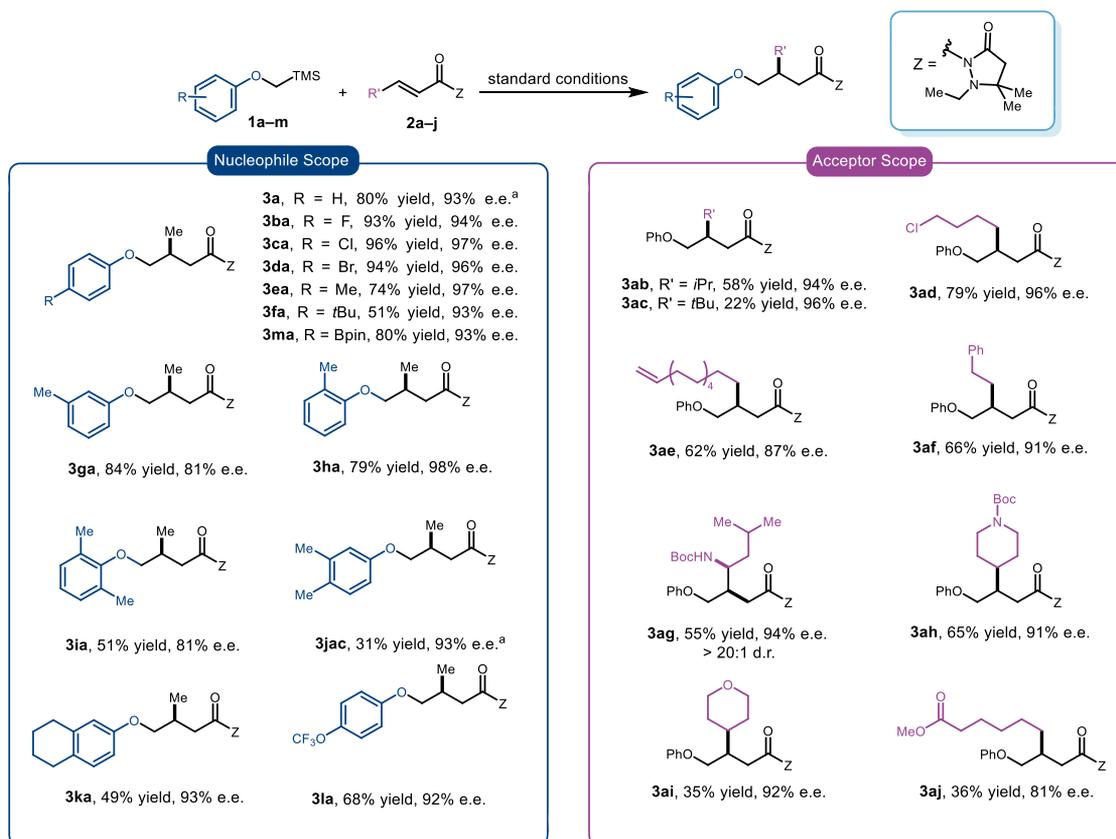


Figure 2. Reaction scope studies. Standard conditions: **1** (0.50 mmol, 1 equiv), **2** (0.75 mmol, 1.5 equiv), Ir (0.01 mmol, 2 mol %), Sc(OTf)₃ and Bu₄NCl (0.075 mmol, 15 mol %), (*S,S*)-sBuPybox (0.10 mmol, 20 mol %), MeCN (10.0 mL, 0.05 M), 34 W blue LEDs, 24 h. ^a18 h.

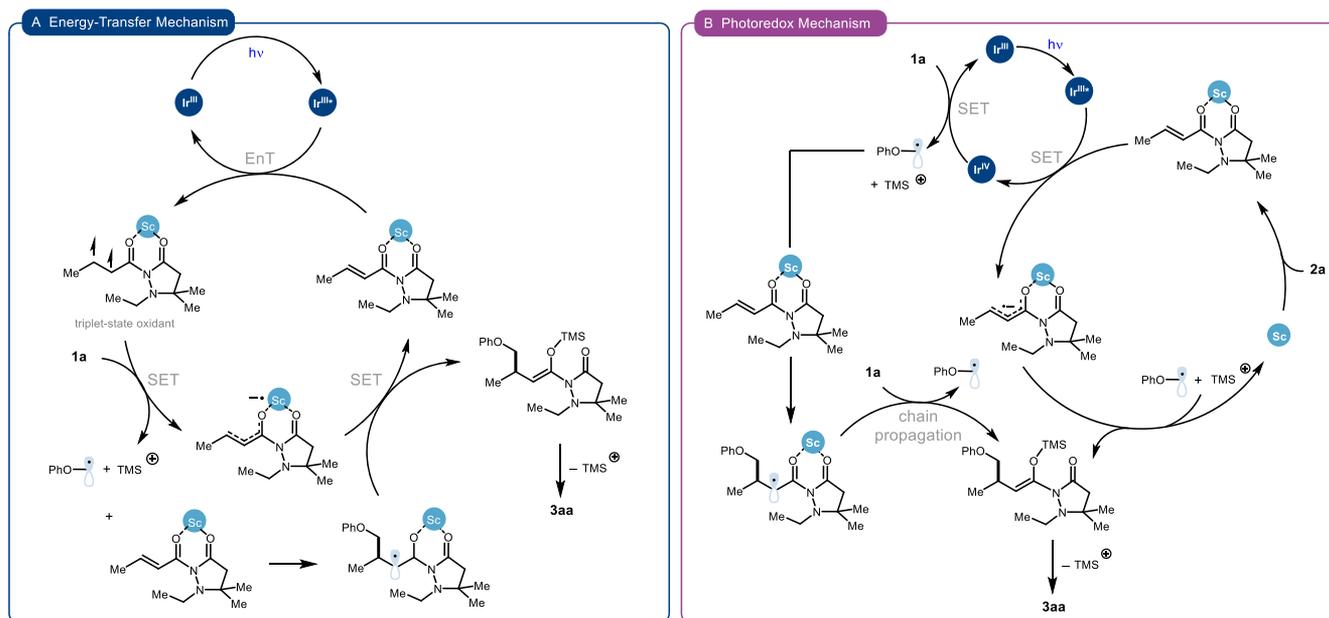


Figure 3. Possible (A) energy-transfer and (B) photoredox mechanisms for asymmetric photocatalysis.

Michael acceptor **2a**, and the degree of quenching is significantly greater in the presence of added Sc(OTf)₃ (Figure S1). Thus, the principal photocatalytic quenching process in this reaction is between the excited-state photocatalyst and the Sc-bound complex of Michael acceptor **2a**.

Because Stern–Volmer analysis does not distinguish between energy- and electron-transfer mechanisms, we

considered both possibilities (Figure 3). First, we recently discovered that Lewis acid cocatalysts can accelerate energy transfer from excited-state Ru(II) and Ir(III) photocatalysts to enone acceptors, producing Lewis acid-bound triplet-state enones that undergo enantioselective [2 + 2] cycloadditions.¹⁴ Mariano¹⁵ and Melchiorre¹⁶ reported desilylative conjugate additions initiated by excited-state Michael acceptors. We

Table 2. Reaction Outcomes with Photocatalysts Having Similar Triplet Energies^a

entry	photocatalyst	E_T (kcal/mol)	$E_{1/2}(M^*/M^+)$ (V vs SCE)	$E_{1/2}(M^+/M)$ (V vs SCE)	yield (e.e.)
1	$[\text{Ir}(\text{dFCF}_3\text{ppy})_2(\text{dtbbpy})]\text{PF}_6$	60.1	-0.89	+1.69	82% (95%)
2	$\text{Ir}(4\text{-F},4'\text{-tBuppy})_3$	59.4	-1.27	+0.98	0%
3	$\text{Ir}(\text{ppy})_3$	55.2	-1.97	+0.78	4%
4	$[\text{Ir}(\text{dFppy})_2(\text{bpy})]\text{PF}_6$	54.7	-0.80	+1.49	68% (80%)
5	$[\text{Ru}(\text{bpz})_3](\text{PF}_6)_2$	48.4	-0.26	+1.86	0%

^aReaction conditions: **1a** (0.15 mmol, 1 equiv), **2a** (0.225 mmol, 1.5 equiv), photocatalyst (3×10^{-3} mmol, 2 mol %), $\text{Sc}(\text{OTf})_3$ and Bu_4NCl (0.0225 mmol, 15 mol %), (*S,S*)-*sBuPybox* (0.03 mmol, 20 mol %), MeCN (3.0 mL, 0.05 M), 34 W blue LEDs. Yields were determined by ¹H NMR analysis of the crude reaction mixtures using mesitylene as an internal standard.

wondered whether this reaction might proceed via initial Lewis acid-catalyzed energy transfer (Figure 3A). The key activation step would be the formation of the Lewis acid-bound triplet-state **2a**, which might oxidize α -silyl ether **1a** to the requisite α -alkoxy radical. However, we quickly determined that this electron-transfer step would be endergonic. The excited-state redox potential of a compound can be estimated using the ground-state reduction potential and the energy of the triplet excited state. Cyclic voltammetry experiments using **2a** gave irreversible reduction features with estimated E_p values of -1.1 and -1.2 V vs SCE in the absence and presence of $\text{Sc}(\text{OTf})_3$, respectively (see the Supporting Information). Unfortunately, we were not able to ascertain the triplet-excited-state energies of **2a** either experimentally or computationally. Because efficient energy transfer depends on the thermodynamics in the exchange event, however, the maximum value for the triplet energies cannot be substantially higher than the triplet energy of the Ir sensitizer (2.6 eV).¹² Given this limiting condition, the maximum excited-state reduction potential available from the Sc-bound complex of **2a** cannot be significantly more positive than +1.4 V. One-electron oxidation of the α -silyl ether pronucleophile by excited-state **2a** is thus thermodynamically unfavorable by at least 370 mV and potentially more.

We therefore conclude that product formation in this reaction is initiated by electron-transfer quenching of the photocatalyst excited state. A plausible mechanism consistent with the available data is depicted in Figure 3B. The excited-state photocatalyst is oxidatively quenched by the Lewis acid-bound Michael acceptor **2a**. While it does not seem reasonable to expect the radical anion of **2a** to be capable of oxidizing α -silyl ether **1a**, the photoinduced electron-transfer event also generates a ground-state Ir(IV) species with a reported redox potential of +1.7 V vs SCE,¹² from which the oxidative desilylation of **1a** should be thermodynamically feasible. The addition of the resulting α -alkoxy radical to Michael acceptor **2a** would be accelerated by the chiral Lewis acid, which also determines the facial selectivity. This proposal is consistent with experiments examining the effect of the photocatalyst identity on the outcome of the desilylative conjugate addition (Table 2). Significant product formation was observed using only the optimal $[\text{Ir}(\text{dFCF}_3\text{ppy})_2(\text{dtbbpy})]\text{PF}_6$ photocatalyst and $[\text{Ir}(\text{dFppy})_2(\text{bpy})]\text{PF}_6$, a photocatalyst with similar excited-state reduction and ground-state oxidation abilities¹⁷ (entries 1 and 4). Both of these electrochemical characteristics

appear to be critical. $\text{Ir}(\text{ppy})_3$ features an excited state that can easily reduce **2a** but an Ir(IV) ground-state oxidation potential insufficient to oxidize **1a**, and it gives negligible product (entry 3). $[\text{Ru}(\text{bpz})_3](\text{PF}_6)_2$ has an oxidized Ru(III) ground state capable of oxidizing **1a** but an excited state that is unable to reduce **2a**,¹⁸ and it is similarly ineffective in this reaction. Finally, we observe no correlation between the triplet-excited-state energy of the photocatalyst and the yield of the conjugate addition product. For example, $\text{Ir}(4\text{-F},4'\text{-tBuppy})_3$ features an excited-state energy¹⁷ similar to that of $[\text{Ir}(\text{dFCF}_3\text{ppy})_2(\text{dtbbpy})]\text{PF}_6$ but results in the formation of no conjugate addition product (entry 2), consistent with the conclusion that triplet sensitization of Michael acceptor **2a** is not part of the product-forming reaction pathway.

In summary, we have developed a highly enantioselective method for the synthesis of γ -aryloxy carbonyl structures for which there are limited existing retrosynthetic disconnects. This transformation is accomplished using a dual chiral Lewis acid/photoredox catalyst system. An analysis of the energetics of the possible electron-transfer steps suggests a mechanism in which oxidative quenching results in an Ir(IV) complex, initiating an enantioselective radical chain process. An important feature of this study is the observation that the most effective catalyst is not the species with the most strongly oxidizing excited state but rather one with balanced electrochemical properties. In view of the range of activation mechanisms available using photoredox catalysis and the widely differing photophysical properties of excited-state compounds in different classes, it seems reasonable to conclude that no single thermodynamic parameter is likely to be sufficient to predict the optimal photocatalyst for a given application. A complete understanding of photoredox mechanisms requires a holistic appreciation of many potentially relevant thermodynamic parameters.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.orglett.1c01790>.

Detailed experimental procedures, full spectroscopic data for all new compounds, electrochemical data, and X-ray crystallographic data (PDF)

FAIR data, including the primary NMR FID files, for compounds **1a–m**, **2d–j**, **3aa–aj**, **3ba–ma**, **4ea**, and **5ea** (ZIP)

Accession Codes

CCDC 2044306 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank Ilia A. Guzei for X-ray structure determination and Shane D. Lies for measuring the cyclic voltammogram for *N*-methyl-*N*-((trimethylsilyl)methyl)aniline. Funding for this project was provided by the NIH (GM095666). NMR and MS facilities at UW—Madison are funded by the NIH (1S10 OD020022-1) and a generous gift from the Paul J. and Margaret M. Bender Fund. X-ray instrumentation was made possible by funds from the NSF (CHE-1919350) and the UW—Madison Department of Chemistry.

REFERENCES

- (1) Corey, E. J.; Cheng, X.-M. *The Logic of Chemical Synthesis*; John Wiley & Sons: New York, 1989.
- (2) (a) Geary, L. M.; Hultin, P. G. The State of the Art in Asymmetric Induction: The Aldol Reaction as a Case Study. *Tetrahedron: Asymmetry* **2009**, *20*, 131–173. (b) Matsuo, J.; Murakami, M. The Mukaiyama Aldol Reaction: 40 Years of Continuous Development. *Angew. Chem., Int. Ed.* **2013**, *52*, 9109–9118. (c) Yamashita, Y.; Yasukawa, T.; Yoo, W.-J.; Kitanosono, T.; Kobayashi, S. Catalytic Enantioselective Aldol Reactions. *Chem. Soc. Rev.* **2018**, *47*, 4388–4480.
- (3) (a) Krause, N.; Hoffmann-Röder, A. Recent Advances in Catalytic Enantioselective Michael Additions. *Synthesis* **2001**, 0171–0196. (b) Chen, B.-C.; Zhou, P.; Davis, F. A.; Ciganek, E. α -Hydroxylation of Enolates and Silyl Enol Ethers. In *Organic Reactions*; John Wiley & Sons: Hoboken, NJ, 2003; pp 1–356.
- (4) (a) Burke, E. D.; Lim, N. K.; Gleason, J. L. Catalytic Enantioselective Homoaldol Reactions Using BINOL Titanium(IV) Fluoride Catalysts. *Synlett* **2003**, 2003, 390–392. (b) Jang, H.-Y.; Hong, J.-B.; MacMillan, D. W. C. Enantioselective Organocatalytic Singly Occupied Molecular Orbital Activation: The Enantioselective α -Enolization of Aldehydes. *J. Am. Chem. Soc.* **2007**, *129*, 7004–7005. (c) Liang, T.; Zhang, W.; Chen, T.-Y.; Nguyen, K. D.; Krische, M. J. Ruthenium Catalyzed Diastereo- and Enantioselective Coupling of Propargyl Ethers with Alcohols: Siloxy-Crotylation via Hydride Shift

Enabled Conversion of Alkynes to π -Allyls. *J. Am. Chem. Soc.* **2015**, *137*, 13066–13071. (d) Enders, D.; Han, J.; Henseler, A. Asymmetric Intermolecular Stetter Reactions Catalyzed by a Novel Triazolium Derived *N*-Heterocyclic Carbene. *Chem. Commun.* **2008**, 3989–3991. (e) Liu, Q.; Perreault, S.; Rovis, T. Catalytic Asymmetric Intermolecular Stetter Reaction of Glyoxamides with Alkylidenemalonates. *J. Am. Chem. Soc.* **2008**, *130*, 14066–14067. (f) Jousseau, T.; Wurz, N. E.; Glorius, F. Highly Enantioselective Synthesis of α -Amino Acid Derivatives by an NHC-Catalyzed Intermolecular Stetter Reaction. *Angew. Chem., Int. Ed.* **2011**, *50*, 1410–1414. (g) Goti, G.; Bieszczad, B.; Vega-Peñaloza, A.; Melchiorre, P. Stereocontrolled Synthesis of 1,4-Dicarbonyl Compounds by Photochemical Organocatalytic Acyl Radical Addition to Enals. *Angew. Chem., Int. Ed.* **2019**, *58*, 1213–1217. (h) Kuang, Y.; Wang, K.; Shi, X.; Huang, X.; Meggers, E.; Wu, J. Asymmetric Synthesis of 1,4-Dicarbonyl Compounds from Aldehydes by Hydrogen Atom Transfer Photocatalysis and Chiral Lewis Acid Catalysis. *Angew. Chem., Int. Ed.* **2019**, *58*, 16859–16863. (i) Horibe, T.; Hazeyama, T.; Nakata, Y.; Takeda, K.; Ishihara, K. Enantioselective 1,4-Addition Reaction of α,β -Unsaturated Carboxylic Acids with Cycloalkanones Using Cooperative Chiral Amine–Boronic Acid Catalysts. *Angew. Chem., Int. Ed.* **2020**, *59*, 17256–17260.

(5) (a) Johnstone, C.; Large, M. S. Urea Compounds as Inhibitors for VLA-4. US 2003087956 A1, May 8, 2003. (b) Bonfanti, J.-F.; Kesteleyn, B. R. R.; Bardiou, D. A. M.-E.; Marchand, A. D. M.; Coesemans, E.; Forin, J. M. C.; Mercey, G. J. M.; Raboisson, P. J.-M. B. Substituted Indoline Derivatives as Dengue Viral Replication Inhibitors. WO 2018215315 A1, November 29, 2018. (c) Johnstone, C.; Large, M. S. Urea Compounds as Inhibitors for VLA-4. WO 0153279 A1, July 26, 2001. (d) Brittain, D. R.; Johnstone, C.; Davis, G. M.; Large, M. S. Chemical Compounds. WO 0005223, February 3, 2000.

(6) (a) Brumfield, M. A.; Quillen, S. L.; Yoon, U. C.; Mariano, P. S. A Novel Method for Heteroatom-Substituted Free Radical Generation by Photochemical Electron Transfer Induced Desilylation of $\text{RXCH}_2\text{SiMe}_3$ Systems. *J. Am. Chem. Soc.* **1984**, *106*, 6855–6856. (b) Hasegawa, E.; Xu, W.; Mariano, P. S.; Yoon, U. C.; Kim, J. U. Electron-Transfer-Induced Photoadditions of the Silyl Amine, $\text{Et}_2\text{NCH}_2\text{SiMe}_3$, to α,β -Unsaturated Cyclohexenones. Dual Reaction Pathways Based on Ion Pair-Selective Cation-Radical Chemistry. *J. Am. Chem. Soc.* **1988**, *110*, 8099–8111. (c) Zhang, X.; Yeh, S.-R.; Hong, S.; Freccero, M.; Albin, A.; Falvey, D. E.; Mariano, P. S. Dynamics of α -CH Deprotonation and α -Desilylation Reactions of Tertiary Amine Cation Radicals. *J. Am. Chem. Soc.* **1994**, *116*, 4211–4220.

(7) Ruiz Espelt, L.; McPherson, I. S.; Wiensch, E. M.; Yoon, T. P. Enantioselective Conjugate Additions of α -Amino Radicals via Cooperative Photoredox and Lewis Acid Catalysis. *J. Am. Chem. Soc.* **2015**, *137*, 2452–2455.

(8) See the [Supporting Information](#) for electrochemical data.

(9) Gutenberger, G.; Steckhan, E.; Blechert, S. α -Silyl Ethers as Hydroxymethyl Anion Equivalents in Photoinduced Radical Electron Transfer Additions. *Angew. Chem., Int. Ed.* **1998**, *37*, 660–662.

(10) Khatun, N.; Kim, M. J.; Woo, S. K. Visible-Light Photoredox-Catalyzed Hydroalkoxymethylation of Activated Alkenes Using α -Silyl Ethers as Alkoxyethyl Radical Equivalents. *Org. Lett.* **2018**, *20*, 6239–6243.

(11) Le Saux, E.; Ma, D.; Bonilla, P.; Holden, C. M.; Lustosa, D.; Melchiorre, P. A General Organocatalytic System for Enantioselective Radical Conjugate Additions to Enals. *Angew. Chem., Int. Ed.* **2021**, *60*, 5357–5362.

(12) (a) Ohkubo, K.; Mizushima, K.; Iwata, R.; Fukuzumi, S. Selective photocatalytic aerobic bromination with hydrogen bromide via an electron-transfer state of 9-mesityl-10-methylacridinium ion. *Chem. Sci.* **2011**, *2*, 715–722. (b) Tay, N. E. S.; Nicewicz, D. A. Cation Radical Accelerated Nucleophilic Aromatic Substitution via Organic Photoredox Catalysis. *J. Am. Chem. Soc.* **2017**, *139*, 16100–16104. (c) Tlili, A.; Lakhdar, S. Acridinium Salts and Cyanoarenes as

Powerful Photocatalysts: Opportunities in Organic Synthesis. *Angew. Chem., Int. Ed.* **2021**, DOI: 10.1002/anie.202102262.

(13) Lowry, M. S.; Goldsmith, J. I.; Slinker, J. D.; Rohl, R.; Pascal, R. A.; Malliaras, G. G.; Bernhard, S. Single-Layer Electroluminescent Devices and Photoinduced Hydrogen Production from an Ionic Iridium(III) Complex. *Chem. Mater.* **2005**, *17*, 5712–5719.

(14) (a) Blum, T. R.; Miller, Z. D.; Bates, D. M.; Guzei, I. A.; Yoon, T. P. Enantioselective Photochemistry Through Lewis Acid-Catalyzed Triplet Energy Transfer. *Science* **2016**, *354*, 1391–1395. (b) Miller, Z. D.; Lee, B. J.; Yoon, T. P. Enantioselective Crossed Photocycloadditions of Styrenic Olefins by Lewis Acid Catalyzed Triplet Sensitization. *Angew. Chem., Int. Ed.* **2017**, *56*, 11891–11895. (c) Daub, M. E.; Jung, H.; Lee, B. J.; Won, J.; Baik, M. H.; Yoon, T. P. Enantioselective [2 + 2] Cycloadditions of Cinnamate Esters: Generalizing Lewis Acid Catalysis of Triplet Energy Transfer. *J. Am. Chem. Soc.* **2019**, *141*, 9543–9547.

(15) Yoon, U. C.; Mariano, P. S. Mechanistic and synthetic aspects of amine-enone single electron transfer photochemistry. *Acc. Chem. Res.* **1992**, *25* (5), 233–240.

(16) Silvi, M.; Verrier, C.; Rey, Y. P.; Buzzetti, L.; Melchiorre, P. Visible-light excitation of iminium ions enables the enantioselective catalytic β -alkylation of enals. *Nat. Chem.* **2017**, *9*, 868–873.

(17) Singh, A.; Teegardin, K.; Kelly, M.; Prasad, K. S.; Krishnan, S.; Weaver, J. D. Facile Synthesis and Complete Characterization of Homoleptic and Heteroleptic Cyclometalated Iridium(III) Complexes for Photocatalysis. *J. Organomet. Chem.* **2015**, *776*, 51–59.

(18) (a) Crutchley, R. J.; Lever, A. B. P. Ruthenium(II) Tris(bipyrazyl) Dication-A New Photocatalyst. *J. Am. Chem. Soc.* **1980**, *102*, 7128–7129. (b) Haga, M.; Dodsworth, E. S.; Eryavec, G.; Seymour, P.; Lever, A. B. P. Luminescence Quenching of the Tris(2,2'-bipyrazine)ruthenium(II) Cation and its Monoprotonated Complex. *Inorg. Chem.* **1985**, *24*, 1901–1906.