

Enantioselective Paternò–Büchi Reactions: Strategic Application of a Triplet Rebound Mechanism for Asymmetric Photocatalysis

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ABSTRACT: The Paternò–Büchi reaction is the [2+2] photocycloaddition of a carbonyl with an alkene to afford oxetane products. Enantioselective catalysis of this classical photoreaction, however, has proven to be a long-standing challenge. Many of the best-developed strategies for asymmetric photochemistry are not suitable to address this problem because the interaction of carbonyls with Brønsted or Lewis acidic catalysts can alter the electronic structure of their excited state and divert their reactivity towards alternate photoproducts. We show herein that an alternative triplet rebound strategy enables the stereocontrolled reaction of an excited-state carbonyl compound in its native, unbound state. These studies have resulted in the development of the first highly enantioselective catalytic Paternò–Büchi reaction, catalyzed by a novel hydrogen-bonding chiral Ir photocatalyst.

INTRODUCTION

The [2+2] photocycloaddition of carbonyls with alkenes ranks among the most important reactions in classical organic photochemistry (Figure 1A).¹ Commonly referred to as the Paternò–Büchi reaction, it was among the earliest photoreactions to be reported,² and it has served as a model system for mechanistic interrogation of photochemical reactivity for many decades.³ Current research on the Paternò–Büchi reaction has been motivated by the recognition that oxetanes and other small-ring saturated heterocycles represent a promising and underexplored region of chemical diversity space for medicinal chemistry applications.⁴ Despite significant historical and contemporary interest in this reaction, there have been no examples of highly enantioselective catalytic Paternò–Büchi reactions reported to date. This is surprising, both because many early examples of successful asymmetric photoreactions were chiral-auxiliary-controlled Paternò–Büchi reactions⁵ and because many general strategies for the highly enantioselective catalytic [2+2] photocycloaddition between two alkenes have emerged over the past decade.⁶ The difficulty of extending these strategies to the excited-state cycloadditions of carbonyls represents a conspicuous unsolved challenge.

An underappreciated complication in the development of asymmetric Paternò–Büchi reactions appears to be that the binding of a carbonyl to an exogenous catalyst can alter the electronic structure and reactivity of its excited state (Figure 1B). Normally, the reactive configuration of an aromatic ketone is a low-lying (n,π^*) triplet state arising from promotion of an electron from an oxygen lone pair to a $C=O$ π^* orbital. The (n,π^*) state has significant oxyl radical character, which is responsible for the typical photoreactivity of these compounds, including the Paternò–Büchi reaction. Coordination of the

carbonyl to a Brønsted or Lewis acid, however, results in a destabilization of the (n,π^*) state and the population of a (π,π^*) state that lacks oxyl radical character and participates in very different chemistry.⁷ For instance, Bach recently reported that the chemoselectivity of 2-naphthaldehyde photochemistry is altered by Lewis acid coordination: in its unbound form, the (n,π^*) excited state undergoes smooth Paternò–Büchi reaction, but addition of $AlBr_3$, inhibits the [2+2] cycloaddition and diverts the reaction towards a dearomative cycloaddition of the aromatic ring via naphthaldehyde's (π,π^*) state.⁸ We have made analogous observations regarding the divergent photocatalytic activation of benzoylformate esters in the presence and absence of Lewis acids.^{9,10} Unfortunately for the prospect of developing an enantioselective catalytic Paternò–Büchi reaction, most established strategies for controlling excited-state stereochemistry require pre-coordination of a carbonyl compound to a Lewis or Brønsted acidic catalyst and thus seem unlikely to be easily applicable to an enantioselective Paternò–Büchi reaction.

Our laboratory has investigated a family of hydrogen-bonding chiral Ir photosensitizers that are excellent, highly enantioselective catalysts for excited-state [2+2] cycloaddition reactions.¹¹ The general design of these photocatalysts was inspired by hydrogen-bonding chiral-at-metal catalysts reported by Meggers and Gladys.¹² In mechanistic studies probing the intermolecular photocycloaddition of quinolones with maleimides, we recently discovered that this reaction proceeds via an unusual mechanism we refer to as a “triplet rebound” (Figure 1C).^{11bc} In the ground state, the catalyst exclusively engages in a binding interaction between the catalyst pyrazole N–H and the quinoline substrate, but unexpectedly, energy transfer occurs selectively to unbound maleimide, which then reacts with the bound quinolone with high ee. We refer to this mechanism as a

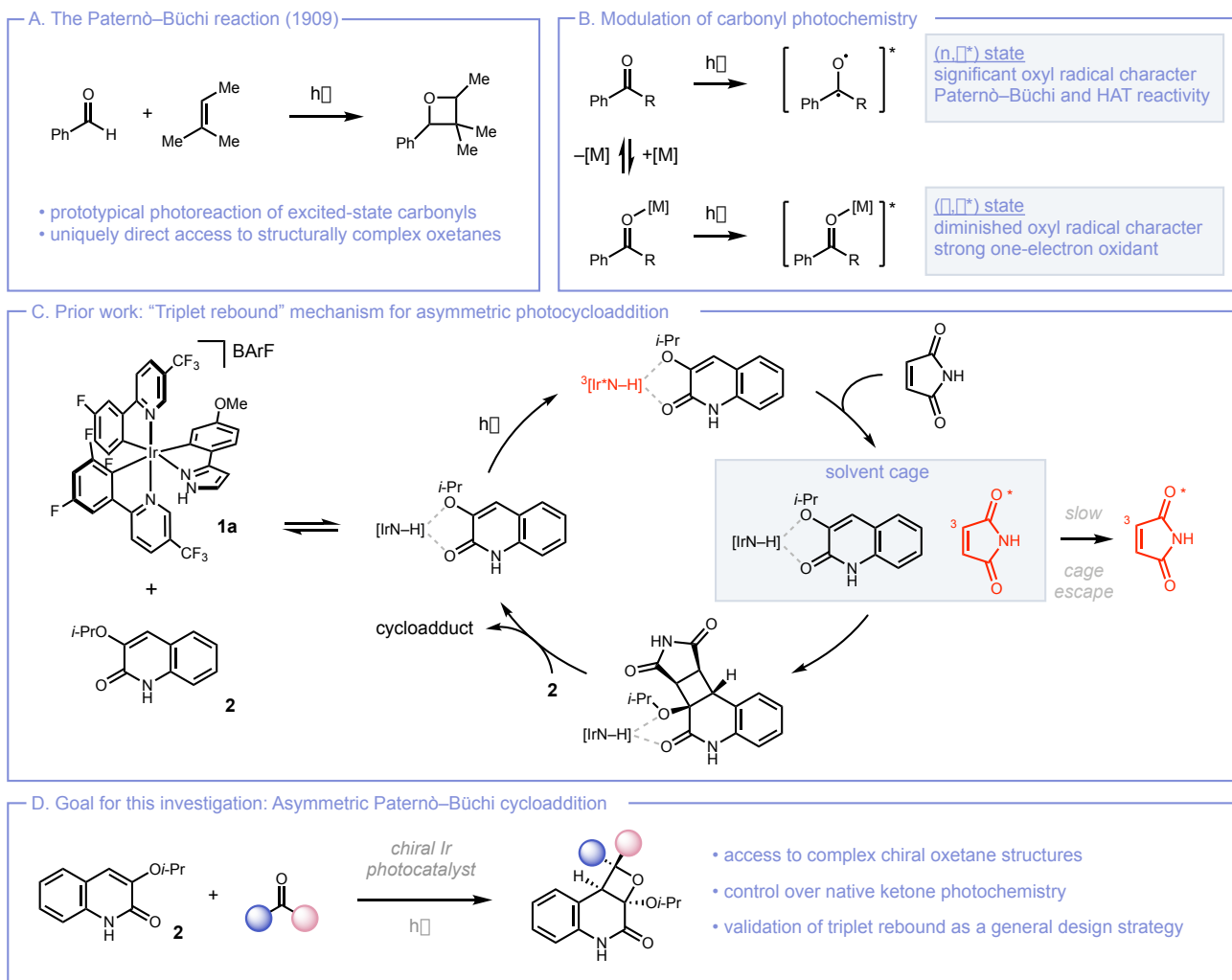


Figure 1. (A) The Paternò-Büchi reaction. (B) Coordination of the carbonyl to Lewis or Brønsted acids perturbs the electronic structure of the reactive excited state. (C) Prior work on elucidating a novel “triplet rebound” mechanism for enantioselective photocatalysis. (D) Goals of this investigation.

“rebound” because the triplet maleimide formed in this process must react within the initial encounter complex faster than cage-escape in order to account for the high enantioselectivities observed even at low catalyst loadings. Importantly, this mechanism is a unique example of an asymmetric catalytic photoreaction that controls the stereochemical behavior of an excited-state organic intermediate in its native, catalyst-unbound electronic configuration.

We wondered if this phenomenon might be generalizable to the discovery of other highly enantioselective bimolecular photoreactions. In particular, if a chiral Ir photosensitizer could control the reaction of an unbound excited state ketone in its *unperturbed* (n, π^*) configuration, this approach might enable asymmetric catalysis of the Paternò-Büchi cycloaddition for the first time. Herein, we describe the application of this triplet rebound strategy to the development of the first highly enantioselective catalytic Paternò-Büchi reaction.

RESULTS AND DISCUSSION

The conditions we previously reported for the asymmetric quinolone-maleimide photocycloaddition seemed a logical starting point to begin our investigations. We surmised that

methyl benzoylformate (**3a**)^{9,10} in place of maleimide might participate in a mechanistically similar triplet rebound process and undergo asymmetric Paternò-Büchi cycloaddition with quinolone **2**. Indeed, oxetane **4a** is produced under these conditions in good yield but low diastereoselectivity, with both diastereomers exhibiting appreciable ee (Figure 2, entry 1). There is a dependence of the ee on the wavelength of irradiation (entries 1–3). The absorbance of **3a** tails into the visible range, and thus these results suggest that the contribution of racemic background cycloaddition can be attenuated by minimizing direct photoexcitation of the α -ketoester. We also examined the effect of various modifications to the cyclometallating phenylpyridine and hydrogen-bonding pyrazole ligands on ee, but no systematic trends were obvious from routine variation of the ligand substituents (entries 3–7). The highest ee’s in this screen were obtained using a C2-symmetric catalyst featuring a novel methylene bispyrazole ligand (entry 8, **1f**). Unfortunately, the diastereoselectivity remained poor, and the ee for both diastereomers were modest.

To test whether the d.r. could be tuned by reagent modification, we examined the reactivity of a series of α -ketoesters with varying steric bulk. To our delight, the adamantyl ester **3e** reversed the sense of diastereoselectivity and provided the

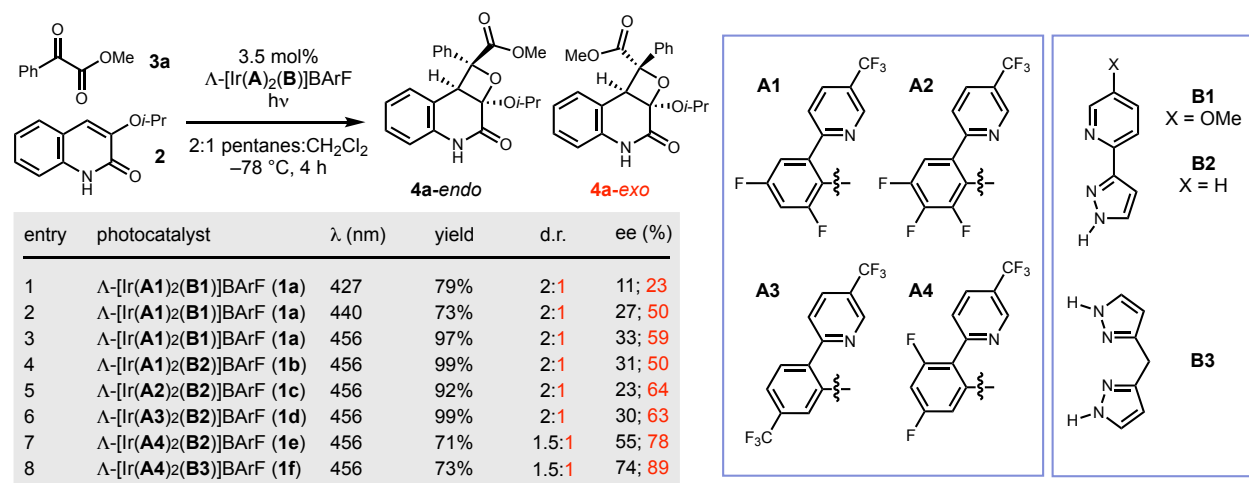


Figure 2. Optimization studies probing photocatalyst structure.

	3a	3b	3c	3d	3e
yield	99%	89%	73%	73%	74%
d.r. (endo/exo)	1.5:1	1:1	1:4	1:5	1:5
ee (%)	74; 89	65; 81	55	56	27; 56
ee (%) under air	77; 91	67; 82	77	77	62; 78
τ	0.52 μ s	0.40 μ s	2.8 μ s	3.1 μ s	3.2 μ s

Figure 3. Optimization studies probing ketoester structure and oxygen sensitivity.

oxetane product in a serviceable 5:1 d.r.; however, a concurrent erosion of ee was observed. A surprising serendipitous observation made during the course of these experiments was that the ee of the cycloaddition is consistently higher when conducted under air rather than an inert nitrogen atmosphere, with a more profound effect using bulkier esters. This improved the stereochemical purity of the major diastereomer of **4e** to 78% ee.

To provide a rational basis for further optimization of the asymmetric Paternò-Büchi reaction, we next elected to investigate the mechanism of the reaction in greater detail. First, we conducted NMR titration experiments to investigate the ground-state interaction of the optimal photocatalyst with each of the reactants. Upon adding varying amounts of quinolone **2** to a fixed concentration of catalyst **1f**, large downfield shifts for the N–H resonances of both the quinolone substrate and the pyrazole ligand were observed. The binding isotherm fits well to a non-cooperative 2:1 binding model for association of quinolone **2** to the catalyst, with calculated equilibrium constants of $K_{a1} = 280$ and $K_{a2} = 180$ (Figure 4A). An analogous NMR titration study was conducted using adamantyl ketoester **3e**. However, in this case, the N–H chemical shift of the catalyst remained relatively unchanged upon addition of up to 20-fold excess of the ester. Similarly, there is no evidence of direct binding between the quinolone and ketoester at any concentration. These results are consistent with a model in which the

photocatalyst engages in a reasonably strong hydrogen bonding interaction with the quinolone but with no other reaction component.

We next examined the excited-state behavior of the reaction components, beginning with steady-state luminescence quenching experiments (Figure 4B). Unexpectedly, both quinolone **2** and ketoester **3e** quench the excited state of catalyst **1f** with similar Stern–Volmer constants ($K_{SV,2} = 9400 \text{ M}^{-1}$ and $K_{SV,3e} = 4000 \text{ M}^{-1}$). Electrochemical studies in CH_2Cl_2 reveal an irreversible anodic peak potential of +1.75 V and reduction potential < -1.7 V vs SCE for quinolone **2**. Likewise, the oxidation and reduction potentials of ketoester **3e** were measured at $> +1.75$ V and -1.41 V vs SCE, respectively. These potentials are well outside of the range accessible by the excited-state photocatalyst (+1.23 V and -1.13 V), suggesting that electron transfer is highly unlikely. On the other hand, the emission of **1f** suggests a triplet energy (E_T) of 63 kcal/mol, sufficiently high for Dexter energy transfer to both **2** (55 kcal/mol) and **1f** (61 kcal/mol).¹³ Thus, in contrast to the expectation from our design strategy, triplet sensitization of both quinolone and ketoester appears to be feasible under the conditions of this reaction.

Further mechanistic detail could be obtained from time-resolved luminescence quenching experiments using excitation from a pulsed laser. In the absence of either substrate, the emission of photocatalyst **1f** was found to undergo first-order decay with a lifetime of 2.4 μ s. The addition of increasing

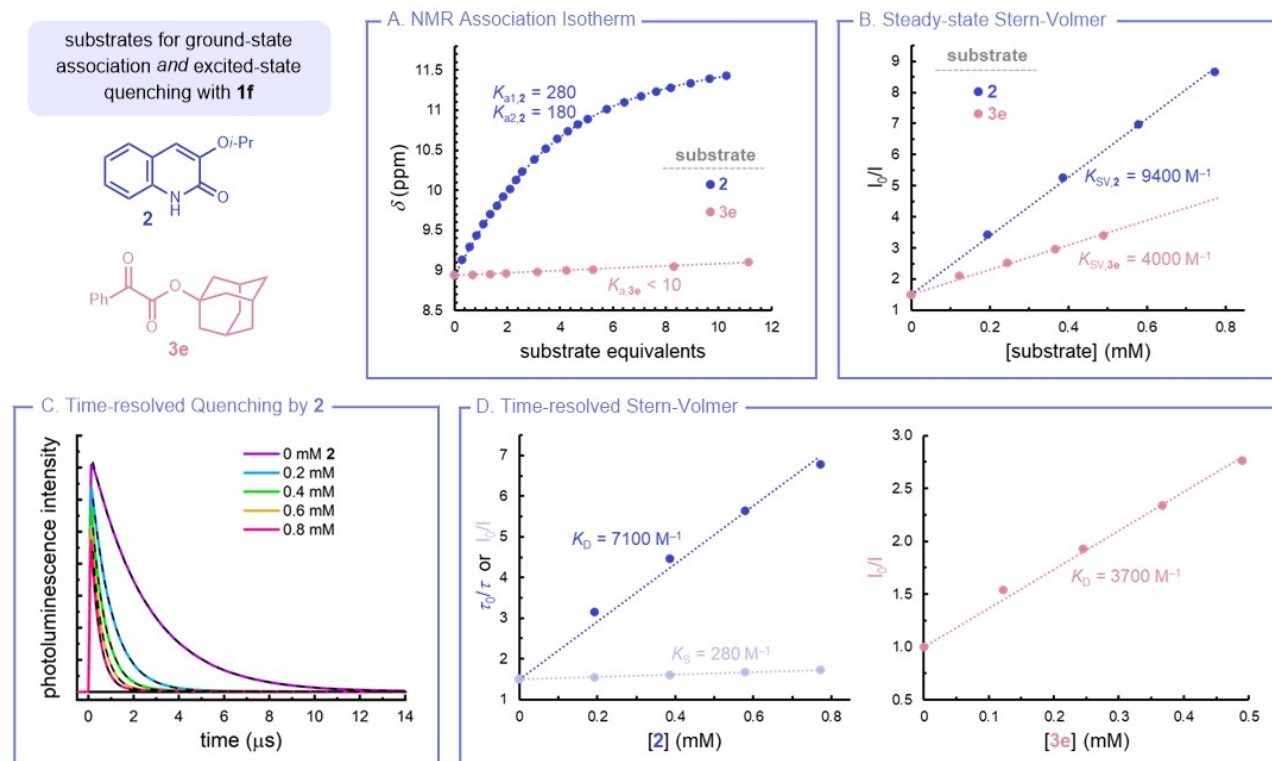


Figure 4. (A) NMR association isotherm for the ground-state interaction of photocatalyst **1f** and **2** or **3e**. Dotted line corresponds to a 1:2 binding model (**2**) or 1:1 binding model (**3e**). (B) Stern-Volmer analysis of the steady-state emission quenching of **1f** by either **2** or **3e**. Dotted lines correspond to a linear regression best fit. (C) Time-resolved emission of photocatalyst **1f** with 0 mM **2** (purple line) and at increased concentrations. The first-order decays are fit with single-exponentials (black, dashed lines). (D) Stern-Volmer analysis of time-resolved emission of **1f** in the presence of **2** (left) or **3e** (right).

concentrations of quinolone **2** resulted in both a decrease in the emission intensity immediately after laser excitation and in the lifetime of the emission. The static and dynamic quenching components were separately subjected to Stern–Volmer analysis (Figure 4C). The Stern–Volmer quenching constant for the static-quenching component ($K_S = 290 \text{ M}^{-1}$) was very similar to the calculated **1f**:**2** association constant (280 M^{-1}), supporting the assignment of this quenching as a result of the ground-state binding interaction.¹⁴ In contrast, the Stern–Volmer constant for the dynamic quenching component in this experiment was much higher ($K_D = 7100 \text{ M}^{-1}$). Thus, these data support that most of the observed steady-state luminescence quenching by **2** arises from bimolecular, collisional Dexter energy transfer rather than from an intracomplex energy-transfer event between the photocatalyst and bound quinolone.

Similar time-resolved experiments were conducted using ketoester **3e**. Upon addition of increasing concentrations of **3e**, only the lifetime of excited **1f** is affected, with no observable effect on the initial luminescence intensity. The Stern–Volmer constant from this experiment ($K_D = 3700 \text{ M}^{-1}$) also closely matches the results of the steady-state quenching studies (4000 M^{-1}). This result is consistent with the negligible binding interaction observed from NMR titration studies, supporting the interpretation that quenching by **3e** is purely a result of collisional Dexter energy transfer.

Collectively, these data indicate that the quenching of photocatalyst **1f** is dominated by two bimolecular energy transfer processes, both of which could potentially lead to formation of the Paternò–Büchi product (Figure 5). First, dynamic quenching of

the substrate–catalyst adduct by α -ketoester **3e** can occur to produce the corresponding triplet-state **3e***. If this intermediate reacts with bound substrate within the solvent cage, the Paternò–Büchi reaction can occur via a triplet rebound mechanism under the stereocontrolling influence of the chiral catalyst, resulting in formation of enantioenriched oxetane **4e**. We speculated that the lower ee of this reaction compared to the maleimide–quinoline cycloaddition we previously studied might be due to the much longer lifetime of triplet benzoylformates compared to that of maleimide. The latter is reported to be ca. 170 ns ;¹⁵ we measured the lifetimes of the benzoylformates studied in our system to be quite a bit longer (Figure 3, 0.40 – $3.20 \mu\text{s}$).¹⁶ These longer lifetimes would be expected to enable more efficient cage escape; reaction of free triplet **3e*** with unbound quinolone **2** in solution would not be expected to occur with any stereocontrol. This hypothesis is consistent with the observation that the longest-lived ketoesters in this study give lower ee's of Paternò–Büchi cycloadducts (Figure 3). It also offers a satisfying rationale for the effect of air on the ee of the reaction. The presence of dissolved oxygen would quench **3e***, decrease its lifetime, and effectively decrease the partition of oxetane formation that occurs in bulk solution. The observation that the effect of air is most pronounced with bulkier α -ketoester **3e**, which has a longer triplet lifetime than the methyl ester **3a**, is also consistent with this rationale.

Alternatively, the luminescence quenching data also suggest that excited-state **1f*** can undergo competitive energy transfer to quinolone **2** through a bimolecular, collisional Dexter mechanism (Figure 5). The resulting triplet quinolone **2*** might also

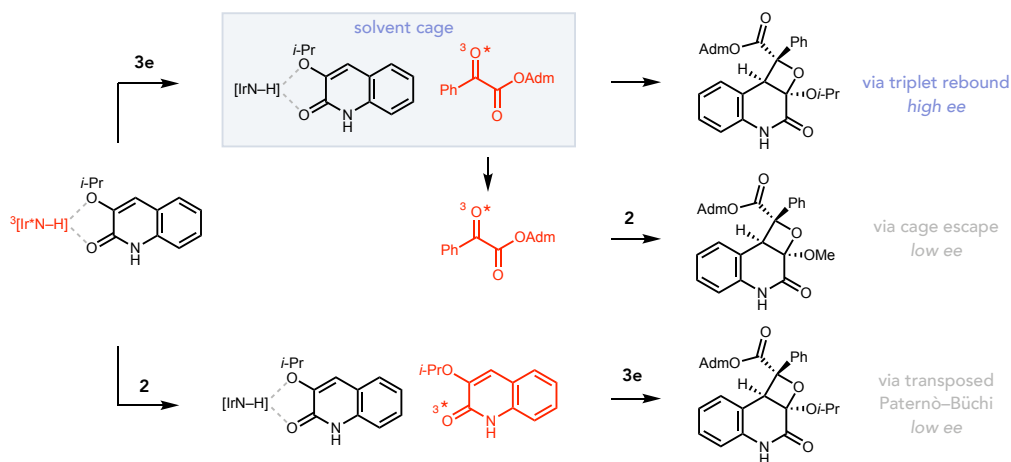
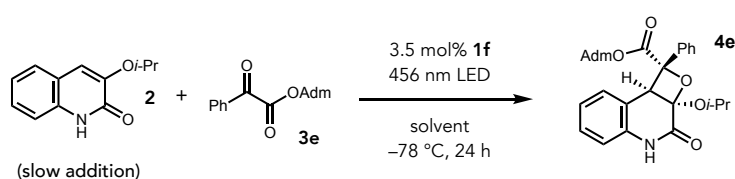
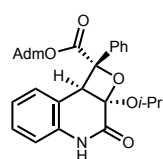


Figure 5. Competing product-forming pathways.

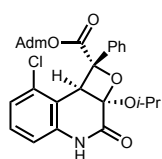


entry	solvent	yield	e.e.
1	pentanes/CH ₂ Cl ₂ (2:1)	87%	86%
2	PhCH ₃	71%	96%
3	PhCH ₃ + 2% CH ₂ Cl ₂	65%	96%
4 ^a	PhCH ₃ + 2% CH ₂ Cl ₂	84%	97%

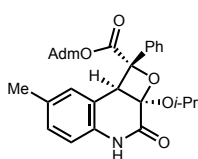
^a Reaction conducted at 20 mM [**2**] instead of 5 mM



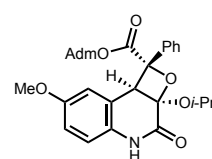
4e, 77% (84%)
>20:1 d.r.
97% ee



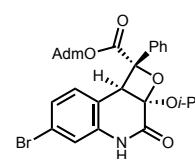
5, 44% (73%)
>20:1 d.r.
91% ee



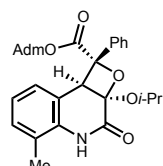
6, 71% (65%)
>20:1 d.r.
97% ee



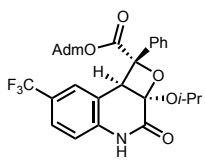
7, 42% (48%)
13:1 d.r.
88% ee



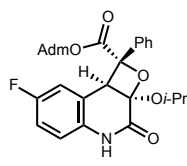
8, 69% (80%)
>20:1 d.r.
89% ee



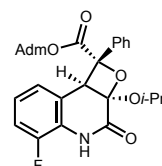
9, 22% (33%)
5:1 d.r.
82% ee



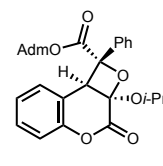
10, 51% (46%)
9:1 d.r.
71% ee



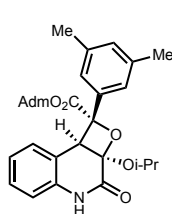
11, 31% (50%)
4:1 d.r.
51% ee



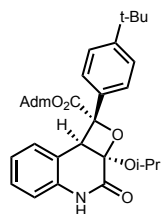
12, 65% (86%)
13:1 d.r.
54% ee



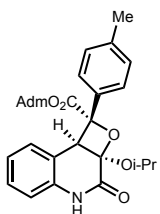
13, 0%



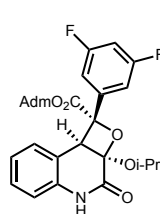
14, 76% (79%)
8:1 d.r.
90% ee



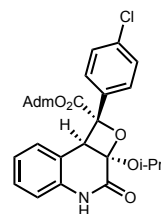
15, 53% (64%)
10:1 d.r.
90% ee



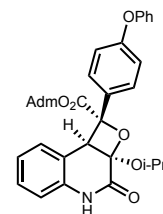
16, 72% (61%)
>20:1 d.r.
76% ee



17, 37% (39%)
2:1 d.r.
85% ee



18, 65% (78%)
6:1 d.r.
83% ee



19, 47% (58%)
16:1 d.r.
76% ee

Figure 6. Final optimization and scope studies. Yields in parentheses determined by ¹H NMR analysis.

generate the oxetane product upon reaction with ground-state ketoester **3e**. The reaction of an excited-state alkene with a ground-state carbonyl compound has been referred to as a

transposed Paternò-Büchi reaction.¹⁷ In this case, however, the reaction of unbound **2*** would not be expected to proceed with high stereinduction absent a strong binding interaction with

the chiral photocatalyst, providing another pathway to decrease the ee of the oxetane product in this process. This hypothesis would suggest that the ee of the oxetane might be increased if the rate of dynamic quenching by quinolone **2** could be decreased.

We wondered, therefore, if the stereoselectivity of the reaction might be improved by minimizing the concentration of **2** through slow addition (Figure 6). Indeed, addition of **2** via syringe pump over 10 h afforded oxetane **4e** in excellent yield, >20:1 d.r., and 86% ee. Conducting the reaction in toluene improved the selectivity to 96%, although the reproducibility of this result proved to be poor, potentially due to the observed poor solubility of the photocatalyst in pure toluene. Pre-mixing **1f** in a minimal amount of CH₂Cl₂ improves its solubility, restores the reproducibility of the reaction, and improves the enantioselectivity of the cycloadduct to 96% ee. Finally, increasing the concentration of the reaction from 5 mM in **2** to 20 mM resulted in a modest improvement of the yield and ee to 76% and 98%, respectively.¹⁸

We next conducted an examination of the scope of this reaction under these optimized conditions. The quinolone reaction component proved reasonably tolerant of substitution. Both electron-donating and modestly electron-withdrawing substituents could be introduced to all positions on the aromatic ring without substantial loss of enantioselectivity; strongly electron-withdrawing substituents, however, had a significant deleterious effect on enantioselectivity, and a coumarin lacking a hydrogen-bonding N–H moiety failed to produce any Paternò–Büchi product. The ketoester reaction component proved to be much more sensitive towards structural variation, often in unpredictable ways. For instance, while alkyl substituents were generally well-tolerated on the arene ring of the benzoylformate ester, a *p*-methyl-substituted ketoester gave significantly lower ee. More strongly electron-donating and -withdrawing substituents similarly had unpredictable effects on the ee of the reaction. This seems consistent with the hypothesis that this reaction proceeds through an excited-state ketoester, and that modest structural changes might alter its triplet lifetime and degree of cage escape, thus leading to a sensitive relationship between structure and enantioselectivity.

CONCLUSIONS

A mechanistically informed optimization process has resulted in the development of the first highly-enantioselective Paternò–Büchi reaction sensitized by a novel chiral hydrogen-bonding Ir photosensitizer. The combined mechanistic data are consistent with a triplet rebound mechanism. Steady-state and time-resolved spectroscopic measurements indicate that the photocatalyst selectively binds the quinolone component of this photoreaction with minimal static quenching, and careful

control over the experimental reaction parameters enables selective dynamic quenching by the ketoester component, which can react within the initial encounter complex to provide the oxetane product with excellent enantioselectivity. Thus this reaction design enables control over the stereochemical behavior of an excited-state carbonyl compound without coordination to a Lewis or Brønsted acidic catalyst that would perturb its electronic structure and its reactivity. Thus, this investigation suggests that rational application of the triplet rebound mechanism might provide a strategy for asymmetric catalysis of a range of carbonyl photoreactions that have remained elusive to date. However, scope studies indicate a surprising and unpredictable sensitivity of the reaction stereoselectivity to the structure of the ketoester reaction component. Thus, controlling the stereochemical behavior of excited-state organic compounds in their native unbound state remains a substantial challenge that merits further investigation.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental details, characterization data for all new compounds, binding titration studies, photophysical measurements, NMR spectra, HPLC chromatograms, X-ray crystallographic data, and binding titration studies (PDF)

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REFERENCES

¹ D'Auria, M. The Paternò–Büchi Reaction—a Comprehensive Review. *Photochem. Photobiol. Sci.* **2019**, *18*, 2297–2362.

² Paterno, E.; Chieffi, G. Sintesi in chimica organica per mezzo della luce. Nota II. Composti degli idrocarburi non saturi con aldeidi e chetoni. *Gazz. Chim. Ital.* **1909**, *39*, 341–361.

³ (a) Fréneau, M.; Hoffmann, N. The Paternò–Büchi Reaction—Mechanisms and Application to Organic Synthesis. *J. Photochem.*

Photobiol. C Photochem. Rev. **2017**, *33*, 83–108. (b) Franceschi, P.; Cuadros, S.; Goti, G.; Dell'Amico, L. Mechanisms and Synthetic Strategies in Visible Light-Driven [2+2]-Heterocycloadditions. *Angew. Chem. Int. Ed.* **2023**, *62*, e202217210.

⁴ (a) Bull, J. A.; Croft, R. A.; Davis, O. A.; Doran, R.; Morgan, K. F. Oxetanes: Recent Advances in Synthesis, Reactivity, and Medicinal Chemistry. *Chem. Rev.* **2016**, *116*, 12150–12233. (b) Bauer, M. R.; Di

Fruscia, P.; Lucas, S. C. C.; Michaelides, I. N.; Nelson, J. E.; Storer, R. I.; Whitehurst, B. C. Put a Ring on It: Application of Small Aliphatic Rings in Medicinal Chemistry. *RSC Med. Chem.* **2021**, *12*, 448–471.

⁵ (a) Gotthardt, H.; Lenz, W. Unusually High Asymmetric Induction in the Photochemical Formation of Oxetanes. *Angew. Chem. Int. Ed. Eng.* **1979**, *18*, 868–868. (b) Koch, H.; Runsink, J.; Scharf, H.-D. Investigation of Chiral Induction in Photochemical Oxetane Formation. *Tetrahedron Lett.* **1983**, *24*, 3217–3220. (c) Bach, T.; Schröder, J.; Brandl, T.; Hecht, J.; Harms, K. Facial diastereoselectivity in the photocycloaddition of chiral *N*-acyl enamines to benzaldehyde. *Tetrahedron* **1998**, *54*, 4507–4520. (d) Bach, T.; Bergmann, H.; Harms, K. High Facial Diastereoselectivity in the Photocycloaddition of a Chiral Aromatic Aldehyde and an Enamide Induced by Intermolecular Hydrogen Bonding. *J. Am. Chem. Soc.* **1999**, *121*, 10650–10651.

⁶ (a) Yoon, T. P. Photochemical Stereocontrol Using Tandem Photoredox-Chiral Lewis Acid Catalysis. *Acc. Chem. Res.* **2016**, *49*, 2307–2315. (b) Huang, X.; Meggers, E. Asymmetric Photocatalysis with Bis-Cyclometalated Rhodium Complexes. *Acc. Chem. Res.* **2019**, *52*, 833–847. (c) Burg, F.; Bach, T. Lactam Hydrogen Bonds as Control Elements in Enantioselective Transition-Metal-Catalyzed and Photochemical Reactions. *J. Org. Chem.* **2019**, *84*, 8815–8836. (d) Großkopf, J.; Kratz, T.; Rigotti, T.; Bach, T. Enantioselective Photochemical Reactions Enabled by Triplet Energy Transfer. *Chem. Rev.* **2022**, *122*, 1626–1653. (e) Genzink, M. J.; Kidd, J. B.; Swords, W. B.; Yoon, T. P. Chiral Photocatalyst Structures in Asymmetric Photochemical Synthesis. *Chem. Rev.* **2022**, *122*, 1654–1716.

⁷ (a) Leermakers, P. A.; Rusakowicz, R.; Byers, G. W. Electronically Excited Aromatic Carbonyl Compounds in Hydrogen Bonding and Acidic Media. *J. Am. Chem. Soc.* **1971**, *93*, 3263–3266. (b) Lewis, F. D.; Howard, D. K.; Oxman, J. D. Lewis Acid Catalysis of Coumarin Photodimerization. *J. Am. Chem. Soc.* **1983**, *105*, 3344–3345. (c) Fukuzumi, S.; Satoh, N.; Okamoto, T.; Yasui, K.; Suenobu, T.; Seko, Y.; Fujitsuka, M.; Ito, O. Change in Spin State and Enhancement of Redox Reactivity of Photoexcited States of Aromatic Carbonyl Compounds by Complexation with Metal Ion Salts Acting as Lewis Acids. Lewis Acid-Catalyzed Photoaddition of Benzyltrimethylsilane and Tetramethyltin via Photoinduced Electron Transfer. *J. Am. Chem. Soc.* **2001**, *123*, 7756–7766.

⁸ (a) Stegbauer, S.; Jeremias, N.; Jandl, C.; Bach, T. Reversal of Reaction Type Selectivity by Lewis Acid Coordination: The Ortho Photocycloaddition of 1- and 2-Naphthaldehyde. *Chem. Sci.* **2019**, *10*, 8566–8570. (b) Stegbauer, S.; Jandl, C.; Bach, T. Chiral Lewis Acid Catalysis in a Visible Light-Triggered Cycloaddition/Rearrangement Cascade. *Chem. Sci.* **2022**, *13*, 11856–11862.

⁹ Zheng, J.; Dong, X.; Yoon, T. P. Divergent Photocatalytic Reactions of α -Ketoesters under Triplet Sensitization and Photoredox Conditions. *Org. Lett.* **2020**, *22*, 6520–6525.

¹⁰ For a contemporaneous report of a photocatalytic Paternò–Büchi cycloaddition of α -ketoesters, see: Rykaczewski, K. A.; Schindler, C. S. Visible-Light-Enabled Paternò–Büchi Reaction via Triplet Energy Transfer for the Synthesis of Oxetanes. *Org. Lett.* **2020**, *22*, 6516–6519.

¹¹ (a) Skubi, K. L.; Kidd, J. B.; Jung, H.; Guzei, I. A.; Baik, M. H.; Yoon, T. P. Enantioselective Excited-State Photoreactions Controlled by a Chiral Hydrogen-Bonding Iridium Sensitizer. *J. Am. Chem. Soc.* **2017**, *139*, 17186–17192. (b) Zheng, J.; Swords, W. B.; Jung, H.; Skubi, K. L.; Kidd, J. B.; Meyer, G. J.; Baik, M.-H.; Yoon, T. P.

Enantioselective Intermolecular Excited-State Photoreactions Using a Chiral Ir Triplet Sensitizer: Separating Association from Energy Transfer in Asymmetric Photocatalysis. *J. Am. Chem. Soc.* **2019**, *141*, 13625–13634. (c) Swords, W. B.; Chapman, S. J.; Hofstetter, H.; Dunn, A. L.; Yoon, T. P. Variable Temperature LED–NMR: Rapid Insights into a Photocatalytic Mechanism from Reaction Progress Kinetic Analysis. *J. Org. Chem.* **2022**, *87*, 11776–11782. (d) Swords, W. B.; Lee, H.; Park, Y.; Llamas, F.; Skubi, K. L.; Park, J.; Guzei, I. A.; Baik, M.-H.; Yoon, T. P. Highly Enantioselective 6π Photoelectrocyclizations Engineered by Hydrogen Bonding. *J. Am. Chem. Soc.* **2023**, *145*, 27045–27053.

¹² (a) Chen, L.-A.; Xu, W.; Huang, B.; Ma, J.; Wang, L.; Xi, J.; Harms, K.; Gong, L.; Meggers, E. Asymmetric Catalysis with an Inert Chiral-at-Metal Iridium Complex. *J. Am. Chem. Soc.* **2013**, *135*, 10598–10601. (b) Chen, L.-A.; Tang, X.; Xi, J.; Xu, W.; Gong, L.; Meggers, E. Chiral-at-Metal Octahedral Iridium Catalyst for the Asymmetric Construction of an All-Carbon Quaternary Stereocenter. *Angew. Chem., Int. Ed.* **2013**, *52*, 14021–14025. (c) Lewis, K. G.; Ghosh, S. K.; Bhuvanesh, N.; Gladysz, J. A. Cobalt(III) Werner Complexes with 1,2-Diphenylethylenediamine Ligands: Readily Available, Inexpensive, and Modular Chiral Hydrogen Bond Donor Catalysts for Enantioselective Organic Synthesis. *ACS Cent. Sci.* **2015**, *1*, 50–56. (d) Xu, W.; Arieno, M.; Löw, H.; Huang, K.; Xie, X.; Cruchter, T.; Ma, Q.; Xi, J.; Huang, B.; Wiest, O.; Gong, L.; Meggers, E. Metal-Templated Design: Enantioselective Hydrogen-Bond-Driven Catalysis Requiring Only Parts-per-Million Catalyst Loading. *J. Am. Chem. Soc.* **2016**, *138*, 8774–8780. (e) Ghosh, S. K.; Ganzmann, C.; Bhuvanesh, N.; Gladysz, J. A. Werner Complexes with ω -Dimethylaminoalkyl Substituted Ethylenediamine Ligands: Bifunctional Hydrogen-Bond-Donor Catalysts for Highly Enantioselective Michael Additions. *Angew. Chem., Int. Ed.* **2016**, *55*, 4356–4360.

¹³ The triplet energies of photocatalyst **1f** and of ketoester **3e** were estimated from their luminescence spectra; see the Supporting Information for details. The triplet energy of quinolone **2** was estimated computationally and is reported in Reference 11b.

¹⁴ Interestingly, we observed no static quenching by the same quinolone in our previous study (Reference 11b). The photocatalyst in these two studies, however, are structurally quite different. Thus this observation is consistent with the inference from our previous studies that the structure of the catalyst–substrate interaction, and thus the efficiency of intracomplex Dexter energy transfer, is highly sensitive to structural perturbation.

¹⁵ von Sonntag, J.; Beckert, D.; Knolle, W.; Mehnert, R. Electron Transfer as the Initiation Mechanism of Photocurable Maleimide-Vinyl Ether Based Resins. *Radiat. Phys. Chem.* **1999**, *55*, 609–613.

¹⁶ The lifetimes of excited-state benzoylformate esters in benzene have also been reported to be on the microsecond timescale: Fedorov, A. V.; Danilov, E. O.; Rodgers, M. A. J.; Neckers, D. C. Time-Resolved Step-Scan Fourier Transform Infrared Spectroscopy of Alkyl Phenylglyoxylates. *J. Am. Chem. Soc.* **2001**, *123*, 5136–5137.

¹⁷ Kumarasamy, E.; Raghunathan, R.; Kandappa, S. K.; Sreenithya, A.; Jockusch, S.; Sunoj, R. B.; Sivaguru, J. Transposed Paternò–Büchi Reaction. *J. Am. Chem. Soc.* **2017**, *139*, 655–662.

¹⁸ The absolute configurations of chiral catalyst **1f** and Paternò–Büchi cycloadduct **4** were determined by X-ray crystallography. See the Supporting Information for full details.

