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Selective C-C Bond Scission of Ketones via Visible-Light-Mediated Cerium Catalysis

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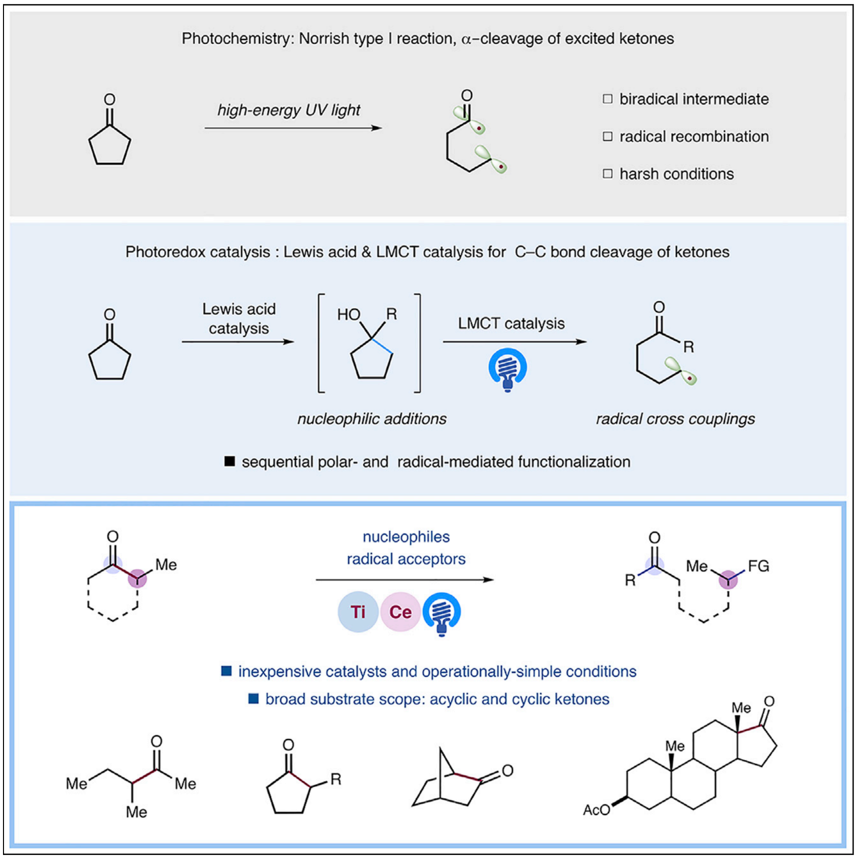
HIGHLIGHTS

Development of a photocatalyzed C–C bond scission of ketones

Ligand-to-metal charge transfer catalysis

Cooperative utilization of cerium and titanium catalysts



The Norrish type I reaction represents a powerful approach to cleave C–C bonds of ketones, yet the synthetic application has been limited because of selectivity and practicality problems. Through the catalytic utilization of the ligand-to-metal charge transfer excitation, Chen and colleagues describe a photocatalytic transformation, in which C–C bonds of ketones are exploited as unconventional handles for selective functionalizations. This protocol, with its utilization of blue LED and inexpensive cerium catalyst, has been successfully employed to cleave a broad range of ketones, regardless of cyclic or acyclic, from simple dibenzyl ketone to complex androsterone.

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Selective C-C Bond Scission of Ketones via Visible-Light-Mediated Cerium Catalysis

Yilin Chen,[1,3] Jianbo Du,[1,3] and Zhiwei Zuo[1,2,4,*]

SUMMARY

Here, we report a general catalytic manifold for the selective C–C bond scission of ketones via the exploitation of the ligand-to-metal charge transfer (LMCT) excitation mode. Through a cooperative utilization of Lewis acid catalysis and LMCT catalysis, the C–C bond of ketones could be selectively and effectively cleaved, enabling the installation of different functionalities at each carbon of the cleaved C–C bond through a sequential and orthogonal manner. This reaction manifold serves as a photocatalytic alternative to the Norrish type I reaction with the combination of visible light and inexpensive cerium salts. Under operationally simple conditions, a wide range of acyclic and cyclic ketones, from simple strained cyclobutanones to complex androsterone with less strained cyclopentanone moiety, could be successfully transformed into versatile chemical building blocks.

INTRODUCTION

The selective cleavage of C–C bonds, as counterproductive as it seems to have disassembled the critical component of organic molecule frameworks, provides intriguing opportunities to streamline complex molecule synthesis significantly.[1–3] The utilization of ubiquitous and robust C–C bonds as functional handles could enable unconventional and efficient installations of multiple functionalities concurrently[4,5] and, more importantly, offers unique opportunities to rapid complexity generation via skeletal reconstruction.[6–8] Given that ketones are commonly occurring functionalities in a wide range of easily accessible starting materials and complex natural products, the cleavage and functionalization of C–C bonds in ketones has become an emerging area for the development of novel transformations. Eminently, elegant catalytic systems employing transition metals (e.g., Rh, Ir), have enabled a variety of synthetically valuable transformations with the advancement of transition metal catalysis.[8–17] Although activation strategies including strain release, aromatization, and chelation-assistance have been successfully employed to override the thermodynamic and kinetic barriers of C–C bonds in various types of molecules, they have also imposed some limitations on the generality and scope of those catalytic transformations. Meanwhile, the ever-increasing financial and environmental demands in chemical production have spurred significant research attention in the sustainable development of low-cost and abundant metal catalysts.[18–21] To further expedite the application of C–C bond cleavage transformation in chemical synthesis, the development of general and efficient catalytic paradigms utilizing inexpensive and sustainable metal catalysts remains in high demand. Herein, we report a practical and economic catalytic system, through the cooperative utilization of abundant cerium and titanium catalysts, for the selective

The Bigger Picture

In the endeavor to search for innovative catalysis, the synthetic chemists face ever-increasing financial and environmental demands in chemical production. The development of catalytic modes employing abundant and inexpensive metal catalysts has drawn significant research attention in the chemical community with regard to addressing the current challenges in the sustainable development of chemical synthesis. The selective C–C bond cleavage and functionalizations have recently emerged as an unconventional yet advantageous synthetic strategy, nevertheless, currently predominated by transition metals such as Rh, Ir, etc. The utilization of cost-effective and abundant metal catalysts would undoubtedly expedite the synthetic application of C–C bond cleavage transformations while addressing economic and ecological concerns; more importantly, the use of metal catalysts would potentially prompt the development of new catalytic paradigms.

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C–C bond cleavage and functionalization of a wide range of ketones under visible-light conditions.

Norrish type I reaction, the C–C bond homolysis process of excited ketones, represents one of the fundamental and powerful approaches for the direct cleavage of inert C–C bonds.[22,23] The prerequisite of high-energy UV light irradiation for n-π^* excitation and the overwhelming propensity of the excited carbonyls toward intramolecular hydrogen atom transfer (Norrish-Yang reaction) or additions (Paternò-Büchi reaction) have posed significant challenges for the development of selective transformation. Moreover, discrete biradical intermediates generated through the C–C bond scission exhibit strong preferences for decarbonylation and radical recombination, resulting in extreme difficulties to achieve high selectivity.[24,25] Therefore, despite extensive mechanistic investigations, Norrish type I reaction has not been well embraced by synthetic chemists.[23,26,27] Over the last few decades, one of the most prominent advancements in photochemistry is the introduction of photocatalysts that have the ability to transfer visible-light energy into chemical energy to enable facile single-electron activation of organic molecules into radical intermediates under user-friendly conditions, rendering photoredox catalysis a versatile platform for the development of a variety of selective transformations previously unattainable.[28–30] Several elegant photocatalytic C–C bond cleavage transformations of amine and alcohol feedstocks that utilize radical-mediated C–C bond scission strategy have been reported recently.[31–41] Although presenting intriguing opportunities, the utilization of visible-light energy for the direct cleavage of C–C bond of ketones remains largely elusive.

Under irradiation, certain metal complexes readily undergo ligand-to-metal charge transfer (LMCT) excitation, subsequently promoting homolysis of a metal-ligand bond to generate ligand-based radical intermediates in a formal reduction of the metal center, which can be employed as a rather effective way to utilize light energy for chemical activation. In contrast to commonly utilized photoinduced electron transfer (PET) activations, LMCT promotes the substrate oxidation by directly exciting the LMCT band of the coordination complex, thus challenging oxidations can be achieved in a selective fashion without interfering with other easier-to-oxidize functionalities. Nevertheless, this straightforward and selective excitation mode has been comparatively underexploited in synthetic organic chemistry, possibly because of the overwhelming popularity of iridium and ruthenium photocatalysts. Elegant applications from the Doyle, Reiser, Rovis, and König groups have demonstrated the unique synthetic potential of this mode.[42–48] Recently, we exploited LMCT excitation in a coordination-excitation-homolysis sequence for the facile activation of alcohol feedstocks under visible-light conditions.[49–52] This mode has enabled us to utilize cost-effective and sustainable cerium catalysts[53–57] to achieve selective C–C bond cleavage transformations. A series of cyclic alcohols of varied ring sizes,[49,50] as well as diversified primary alcohols with different electronic substituents,[52] can be accommodated in operationally simple protocol under mild reaction conditions. High regioselectivities of scissions, governed by the stability of the generated radical, were observed in all cases. The generality and feasibility of this catalytic platform motivated us to explore further applications of this manifold of photocatalytic cleavage of C–C bonds in the context of ketones. We specifically envisioned that in a cooperative fashion, ketones would be transferred into tertiary alcohol intermediates *in situ* via Lewis-acid-catalyzed nucleophilic additions and subsequently activated by LMCT catalysis under blue LED irradiation to initiate the radical-mediated C–C bond scission and functionalization process. Importantly, this strategy employs sequential and orthogonal approaches to install different

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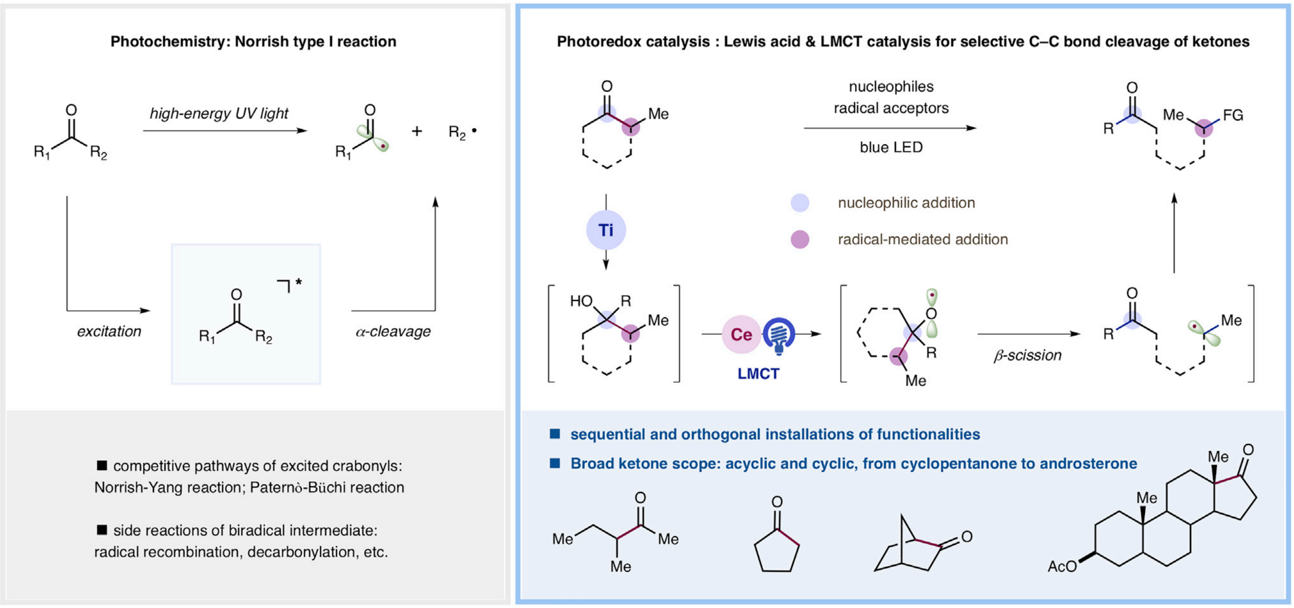

Figure 1. Selective C–C Bond Cleavage and Functionalizations via Photoredox Catalysis

functionalities at each carbon of the cleaved C–C bond, providing intriguing opportunities to develop highly selective and diversified transformations (Figure 1).

RESULTS AND DISCUSSION

Selective C–C Bond Cleavage of Small-Sized Cyclic Ketone and Formal [n+2] Ring Expansion

Cyclobutanone was first chosen as the template substrate to test our hypothesis, considering both the nucleophilic carbonyl addition and radical-mediated C–C bond scission can be facilitated by strain release effect. With this design in mind, commercially available and environmentally benign trimethylsilyl cyanide (TMSCN) was first chosen as the nucleophile to convert cyclic ketones into the corresponding cyanohydrin intermediates, enabling the desired C–C bond scission and concurrently presenting opportunities to construct synthetically valuable C(sp^3)–CN bonds via a radical-mediated cyano group migration strategy. Notably, the radical-mediated migration strategy has recently been elegantly employed in various synthetically valuable transformations by the Zhu group.[58–66] Importantly, we posited that the resulting cyanation product would be easily converted to lactams through a simple reductive cyclization. Lactams are biologically significant scaffolds in a variety of complex natural products and pharmaceutical agents.[67–69] Traditionally, the conversion of ketones into lactams has been accomplished by nitrogen atom insertion reactions such as Beckmann rearrangement and Schmidt reaction, which have been heavily exploited in organic synthesis to construct complex molecules.[70,71] We envisioned that this cooperative and sequential protocol would enhance the efficiency of lactam synthesis through a formal ring expansion of ketones, serving as a homologous version of Beckmann rearrangement and Schmidt reaction.

After extensive studies, we found that optimal efficiency could be achieved with cerium(IV) triflate as the LMCT catalyst under blue light irradiation (100 W commercial blue LEDs, light intensity 0.16 W/cm^2), in the presence of catalytic amount of titanium tetrachloride and 9,10-diphenylanthracene (DPA). Although cerium(IV) triflate has been used as potent Lewis acid catalyst, we failed to obtain any desired

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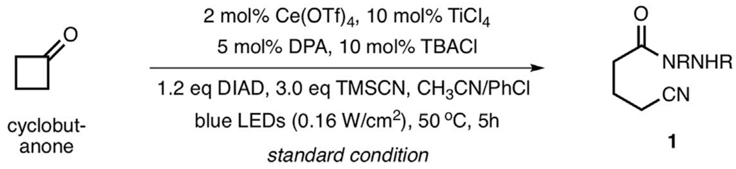

Entry	variations from standard condition	Yield (%)[a]
1	none	92
2	without $TiCl_4$	0
3	$AlEtCl_2$ instead of $TiCl_4$	9
4	$BF_3 \cdot OEt_2$ instead of $TiCl_4$	0
5	$AlCl_3$ instead of $TiCl_4$	5
6	$ZnCl_2$ instead of $TiCl_4$	10
7	without DPA	48
8	PDI instead of DPA	82
9	$Ir(ppy)_3$ instead of DPA	88
10	without $Ce(OTf)_4$	0
11	without 100 Wblue LED	0

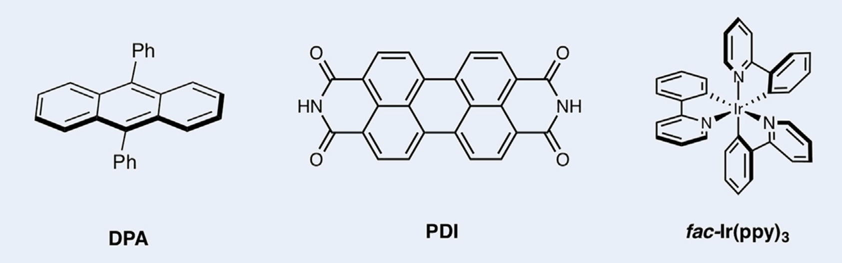

Figure 2. Optimization of C–C bond Cleavage of Cyclobutanone

All yields are determined by gas chromatography flame ionization detector (GC-FID).

product in the absence of exogenous titanium tetrachloride catalyst (entry 2, Figure 2). A careful examination of the reaction mixture indicated no sign of the corresponding cyanohydrin; however, it indicated a complete conversion of cyclobutanone to the cyanohydrin silyl ether, a protected form that cannot coordinate to cerium center to engage in LMCT catalysis (*vide infra*). Apparently, a Lewis acid that could deliver cyanohydrin *in situ* is essential, and several commonly utilized Lewis acids such as $AlEtCl_2$ and $ZnCl_2$ were found capable of facilitating the desired C–C bond scission, but relatively less effective than titanium tetrachloride. Building on the previous success of employing an additional photocatalyst to promote the turnover of the cerium catalytic cycle via PET, DPA was identified as the optimal PET catalyst among several photocatalysts. Although perylene diimide and $Ir(ppy)_3$ photocatalysts demonstrated comparable efficiency, DPA was chosen as a more affordable co-catalyst. Furthermore, control studies revealed that cerium catalyst (entry 10) and light (entry 11) are all essential to the desired reactivity. Notably, the cleaved product **1** could be easily converted to the desired

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δ-valerolactam in high efficiency via a simple hydrogenation (see Supplemental Information).

With the optimal conditions in hand, we next turned our attention to explore the scope of cyclic ketones in this cooperative catalytic system. As shown in Figure 3, this formal ring expansion protocol was applied to a range of cyclic ketones under mild conditions. Lewis basic functionalities, such as esters, Weinreb amide, sulfamide, and sulfone were well tolerated in this photocatalytic protocol. A series of strained cyclobutanones could be effectively cleaved and subsequently cyclized to produce the corresponding δ-lactams with moderate to excellent efficiency. Notably, the radical-mediated C–C bond scission process proved to be highly selective; through the intermediacy of the more substituted and stabilized alkyl radical intermediate, cleaved product **2a** was obtained exclusively from the unsymmetrical substituted cyclobutanone. We also found that this C-C bond cleavage and cyanation process could be more efficient when the radical produced is alpha to a quaternary carbon **5a** and **6a**. We attribute this to either the rate of cyano group transfer increasing because of the Thorpe-Ingold effect or to steric protection of the radical center.[70] This strategy has enabled the rapid construction of a rigid lactam with diazaspirononane scaffold (**6b**), a class of potent pharmacophores,[71,72,73–75] from a commercially available spiro cyclobutanone. Moreover, cyclobutanone embedded in the complex steroid framework could be reconstructed to afford a δ-lactam scaffold with synthetically useful yields.

We were delighted to find that this inexpensive catalytic system could be well adapted to a series of cyclopentanones. Under a slightly modified reaction condition, with benzotrifluoride as the co-solvent, good efficiencies were obtained for the formal insertion to generate seven-membered ring lactams. For cyclopentanones bearing α-substituents, excellent regioselectivity was obtained; the cyano group was selectively installed at the more substituted carbon. However, we did notice that this photocatalytic C–C bond cleavage is somewhat sensitive to steric hindrance, as bulkier substituents, such as cyclopentyl, adjacent to the carbonyl resulted in a slightly diminished yield (**10a**), and cyclopentanones with α-quaternary carbon centers were found to be inactive. Nevertheless, bulky substituents at C3 or C4 positions did not affect the efficiency, and good levels of stereoselectivities were induced at the newly formed tertiary carbon centers (**11a** and **12a**); however, the erosion of diastereoselectivities was observed in the unoptimized hydrogenation step. Importantly, for cycloketones possessing γ-hydrogen atoms, we did not observe any side products derived from the γ-hydrogen atom abstraction (HAT) via Norrish type II mechanism or O-radical-mediated 1,5-HAT process. The synthetic potential of this protocol could be further demonstrated in the skeleton reconstruction of androsterone. Intriguingly, the D-ring of androsterone acetate could be directly cleaved and a cyano group was installed at the C13 position with excellent regioselectivity and stereoselectivity, after subsequent hydrogenation operation generating the construction of a complex lactam with trans-fused seven-membered ring scaffold.

Selective C–C Bond Cleavage of Medium-Sized Cyclic Ketones

Because of unfavorable energetics, less strained cyclohexanones are relatively underinvestigated for C–C bond cleavage and functionalizations. Indeed, in radical-mediated ring opening transformations, strained cyclic substrates are outstanding substrates owing to their low activation energy and favorable enthalpy effect, whereas the reactions with six-membered ring substrates are generally more challenging. We then turned our attention to cyclohexanones to examine the generality of our catalytic system (Figure 4). Compared with cyclobutanones and cyclopentanones, the cyano

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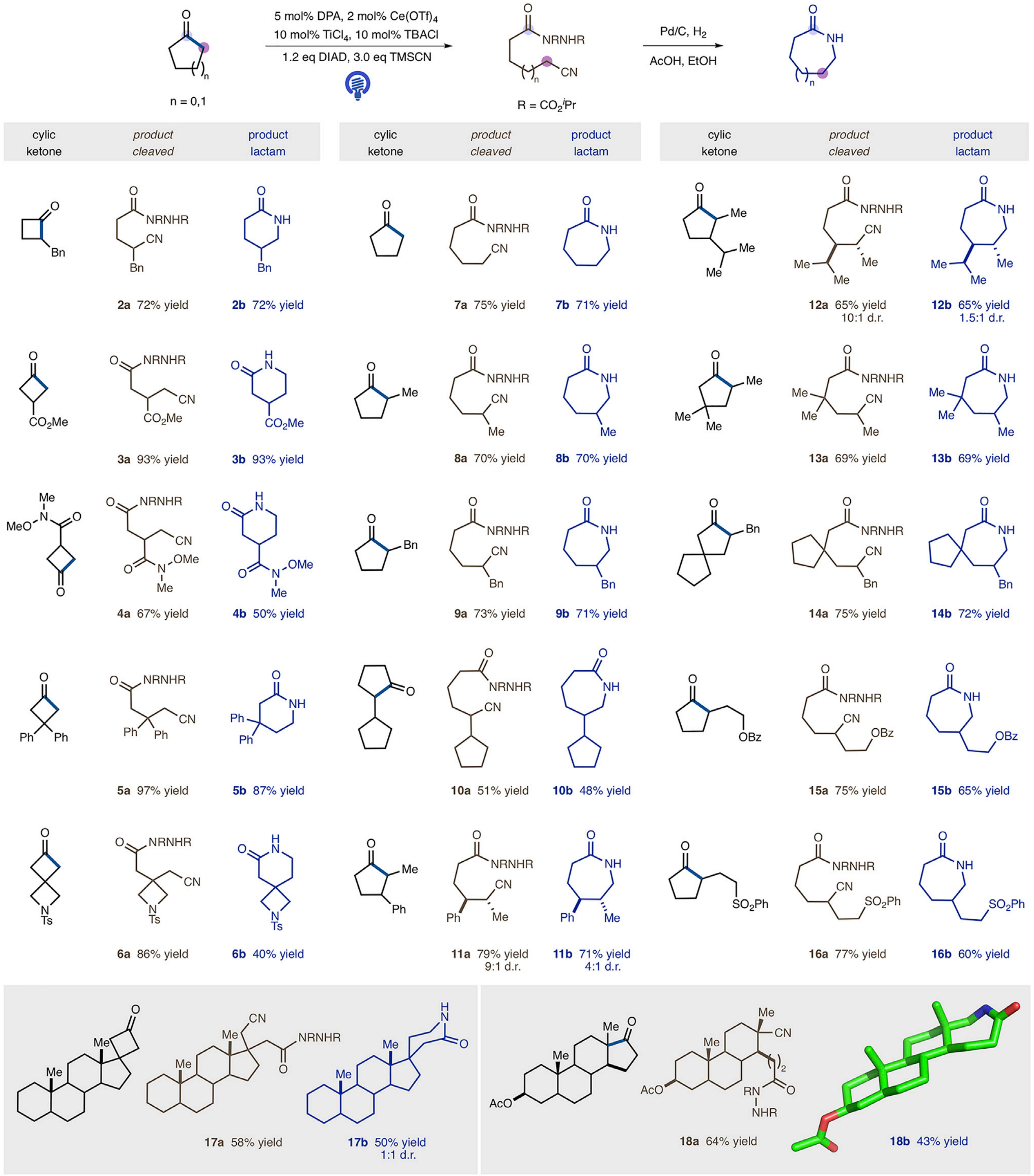

Figure 3. Substrate Scope of the Formal [n+2] Ring Expansion[a]

[a]All cited yields are isolated yields; the yields reported for the lactam products are based on the cyclic ketone-starting materials. Diastereoselectivities were determined by ^{1}H NMR analysis of the crude reaction mixture. See the Supplemental Information for experimental details.

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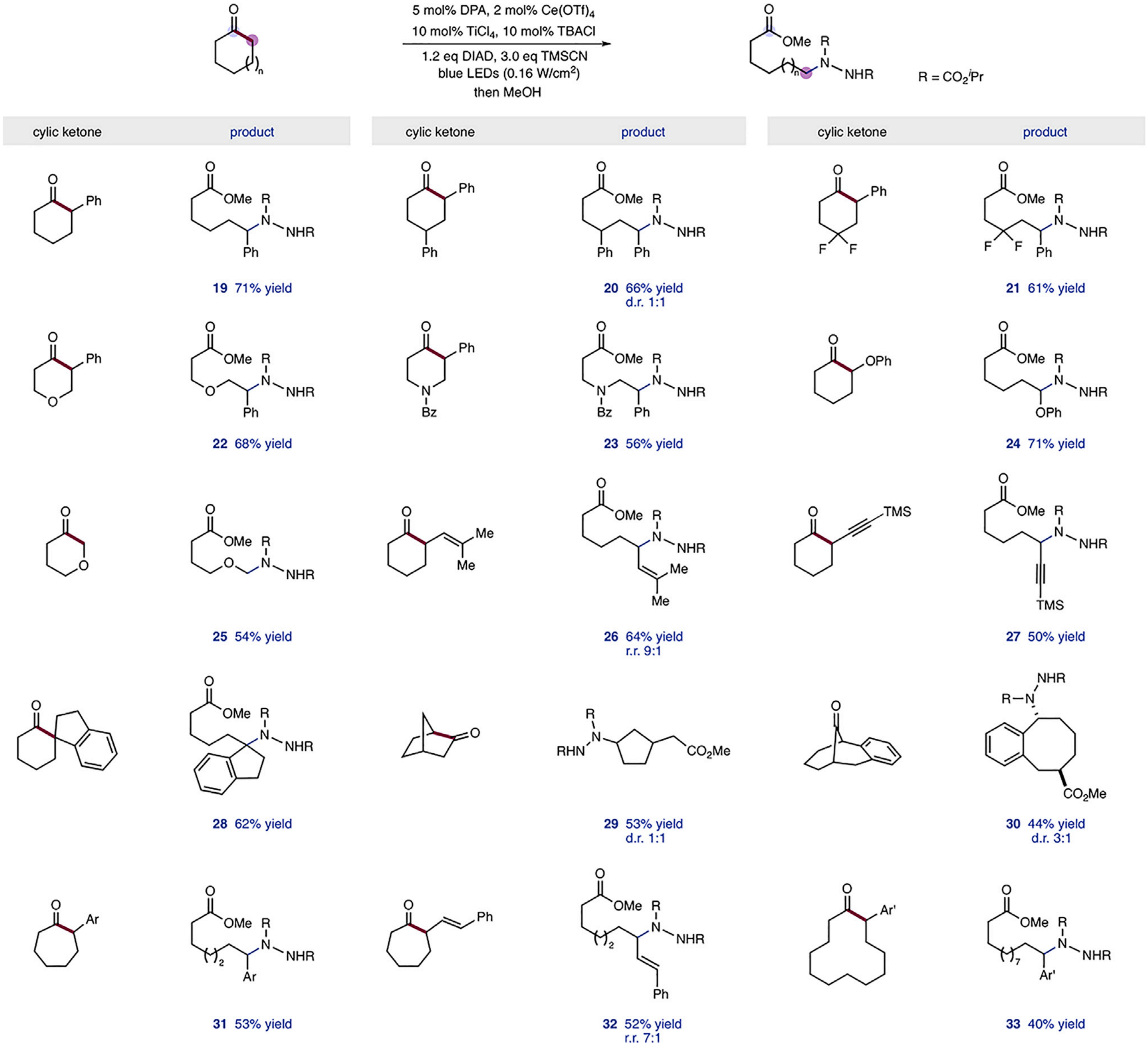

Figure 4. Substrate Scope of the C–C bond Cleavage of Cycloketones[a]

[a]All cited yields are isolated yields. Diastereoselectivities were determined by ^{1}H NMR analysis of the crude reaction mixture. See the Supplemental Information for experimental details. Ar = 2-napthenyl, Ar′ = 4-fluorobenzyl.

group migration and subsequent reductive cyclization in these cases would be rendered entropically unfavorable; thus, the C–C bond cleavage would lead to the generation of a ω-aminated acyl cyanide product, which upon alcohol hydrolysis would generate a synthetically versatile carboxylic ester. Under previous optimized conditions through a simple methanol hydrolysis workup, the most substituted C–C bond in 2-phenylcylcohexanone was selectively cleaved to form the ω-aminated carboxylic ester **19** with high efficiency. Notably, even in the presence of an acidic α-proton, no α-amination side product was observed in this reaction. As shown in Figure 4, a variety of cyclohexanone substrates could be cleaved with good efficiency and high regioselectivity under the mild reaction condition; moreover, commonly occurring functional groups including ether (**22** and **24**), amide (**23**), alkene (**26** and **32**), and

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alkyne (**27**) could be well tolerated. In general, the outcome of the radical-mediated C–C bond scission is determined by the stability of the generated carbon-centered radical; thus, in the cases of α-substituted cyclohexanones, the C–C bond between the most substituted α-carbon and the carbonyl group was selectively cleaved. In dihydropyran-3-one, the C–C bond adjacent to the oxygen atom was selectively cleaved to form the desired product **25** via the amination of a stabilized α-oxy radical. The α-pyrenyl and trimethylsilyl acetylene functional groups were found to be compatible with the alkoxy radical-mediated scission process; no cyclization side product was observed (**26** and **27**). Ketones embedded in a bridged scaffold such as norcamphor and α γ-bridged β-tetralone could also be activated using this practical catalytic system, transferring these commonly occurring bridged cycles into aminated carbon cycles (**29** and **30**). Furthermore, this cerium catalytic system can also be applied to ketones with larger ring systems; substituted 7- and 12-memebered cyclic ketones also proved to be viable substrates.

Selective C–C Bond Cleavage of Acyclic Ketones

Different from cyclic ketones, linear ketones with γ-hydrogen atoms readily undergo intramolecular γ-HAT directly after carbonyl excitation; thus, Norrish type II pathways (for example, Norrish-Yang reaction) predominate over the C–C bond scission, rendering acyclic ketones as challenging substrates in Norrish type I reaction. Meanwhile, without the promotion of strain release effect, the radical-mediated C–C bond scission of linear molecules would be more sluggish. We were keen to examine the generality of the cerium catalytic system with respect to acyclic ketones (Figure 5). The previously optimized conditions were utilized; the α-C–C bond of dibenzyl ketone was successfully cleaved, and carboxylic ester and hydrazine functionalities were installed at different carbon fragments. Even though the electrophilic reactivity of the carbonyl group was partially obstructed by the sterically demanding isopropyl groups, good efficiency was achieved for diisopropyl ketone. Importantly, good selectivities were obtained with various unsymmetrical acyclic ketones; the α-C–C bond adjacent to substitutes with better radical stabilization capacity was preferentially cleaved. As demonstrated in various aliphatic ketones such as 1-phenyl-2-hexanone, methyl isobutyl ketone, benzyl cyclohexyl ketone, *n*-butyl cyclohexyl ketone, and acetyladamantane, only one set of cleaved products were obtained. Preeminently, this cerium catalytic system can be readily adapted to linear ketones with multiple γ-hydrogen atoms; good efficiencies of C–C bond cleavage were achieved without the interference of γ-C–H amination. (**38**, **39**, **41**, **43**, and **45**)

In contrast to aliphatic ketones, aromatic ketones can be readily excited to generate a rather long-lived triplet state and, thus, have been frequently used as photocatalysts in HAT and other types of photocatalytic transformations.[76] The innate photoactivity of these aromatic ketones did not interrupt the cerium catalytic cycle, and several substituted acetophenones could be effectively cleaved, further demonstrating the generality and compatibility of this practical catalytic system. Notably, excellent regioselectivities were also observed, and the C(sp^2)–C(sp^3) bonds got selectively cleaved in these cases, regardless of the substitutes on the sp^3–carbon being benzyl, oxymethylene, or cyclohexyl groups.

Mechanistic Investigations

Despite nucleophilic cyanide addition to ketones being well documented, the reversible nature of the transformation and the unstable property of cyanohydrins has made it rather difficult to elucidate the detailed catalytic cycles. 2-Benzyl cyclopentanone was chosen as the template to carry out control experiments as the corresponding cyanohydrin **49** and cyanohydrin silyl ether **50** could be isolated. A closer

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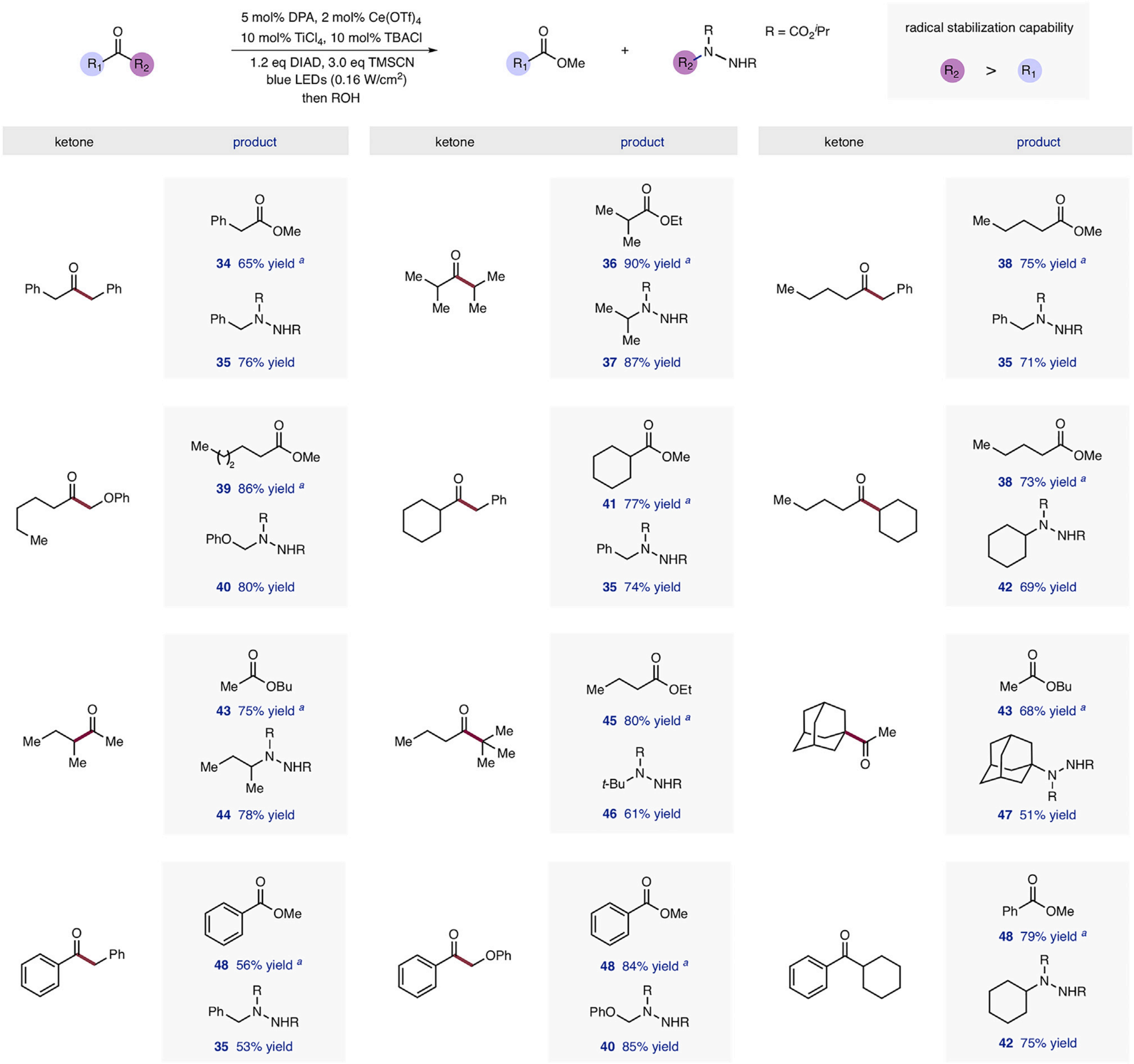

Figure 5. Substrate Scope of the C–C Bond Cleavage of Acyclic Ketones[a]

[a]Yields are determined by GC-FID. See the Supplemental Information for experimental details.

look into the Lewis-acid-catalyzed nucleophilic addition step revealed that cerium triflate only promoted the generation of cyanohydrin silyl ether **49**, which is non-coordinative and, thus, inactive in the LMCT cycle, whereas the desired cyanohydrin can be generated in the presence of titanium tetrachloride. Furthermore, titanium tetrachloride could also promote the conversion of cyanohydrin silyl ether **49** into cyanohydrin **50**. Now with the purified cyanohydrin **50** at hand, control experiments under the photocatalytic conditions were performed. We found that cerium catalyst alone could promote the C–C bond cleavage to generate the desired product **9a** with high yield, whereas titanium tetrachloride only led to the formation of 2-benzyl cyclopentone through the reverse addition. Considering that the LMCT excitations of titanium(IV) and cerium (IV) compounds have been reported before and cyanohydrin complexes of both metal species could form during the reaction,[77,78] ultraviolet-visible (UV-vis) experiments were carried out to illuminate the observed photoactivity. As shown in Figure S2, the corresponding cerium(IV) complex exhibits a more red-shift and broad LMCT absorption band compared with the titanium complex and, thus, can be effectively photoexcited by the blue LED light, whereas the *in-situ*-formed titanium complexes barely absorb photons in the 400–450 nm region, rendering titanium tetrachloride photoinactive under the current blue light conditions. We did observe trace amount of product formation when the reaction was irradiated with a 365-nm LED in the sole presence of titanium tetrachloride. Furthermore, a full set of control studies with three different types of ketones, including strained and less strained cyclic ketones, as well as linear ketone, clearly confirmed that the desired C–C bond cleavage reaction could proceed without DPA, suggesting DPA is not responsible for the LMCT and β-scission. The Stern-Volmer quenching study further suggests that excited DPA could functionalize as the PET catalyst to facilitate the reductive quenching of the nitrogen-centered radical intermediate and the turnover of cerium cycle.

The proposed mechanism is based on these experiments and is shown in Figure 6. Under catalytic amount of titanium tetrachloride, cyanohydrins are generated *in situ* from the nucleophilic additions of TMSCN with cyclic ketones. Under blue light irradiation, the coordination complex of cerium(IV) and cyanohydrin would be excited to promote the homolysis of the Ce–O bond to generate an O-centered radical species. The subsequent β-scission event leads to the cleavage of the α-C–C bond and generation of a distal carbon-centered radical. In the cases of cyclobutanones and cyclopentanones, the alkyl radical undergoes an intramolecular addition to the acyl cyanide and triggers the migration of the cyanide group to generate a nucleophilic carbonyl radical (through 5-membered ring intermediates for cyclobutanones, or 6-membered ring intermediates for cyclopentanones), whereas in 6-membered and lager cyclic ketones, as well as acyclic ketones, the intermolecular addition and cyanide group migration would be rendered entropically challenging. Trapping of the resultant carbon-centered radical by azodicarboxylate followed by a photoinduced single-electron reduction with DPA would yield the desired cleaved product and generate a radical cation of DPA, which would engage single-electron transfer with cerium(III) to complete the cerium cycle.

In summary, we have developed a general and practical strategy for the selective C–C bond cleavage and functionalization of ketones. Through the catalytic utilization of the LMCT excitation mode, the C–C bond of ketones could be selectively cleaved, concurrently enabling the installation of different functionalities at the cleaved carbonyl and aliphatic carbons. Under operationally simple conditions with simple blue LED light and an inexpensive cerium catalyst, a broad range of ketones, whether cyclic or acyclic, from simple dibenzyl ketone to complex androsterone, could be transferred into versatile chemical building blocks. Of note, high levels of regioselectivity governed by the radical-mediated C–C bond scission process could be achieved in all cases. This photocatalytic manifold serves as a more compatible and selective alternative to the Norrish type I reaction, offers intriguing opportunities for further C–C bond scission transformations.

EXPERIMENTAL PROCEDURES

General Procedure of the Photocatalytic C–C Bond Scission of Ketones

A 8-mL vial was charged with 2-phenylcyclohexanone (35 mg, 0.2 mmol, 1.0 equiv), DIAD (48 μL, 0.24 mmol, 1.2 equiv), DPA (3.3 mg, 10 μmol, 0.05 equiv), $Ce(OTf)_4$

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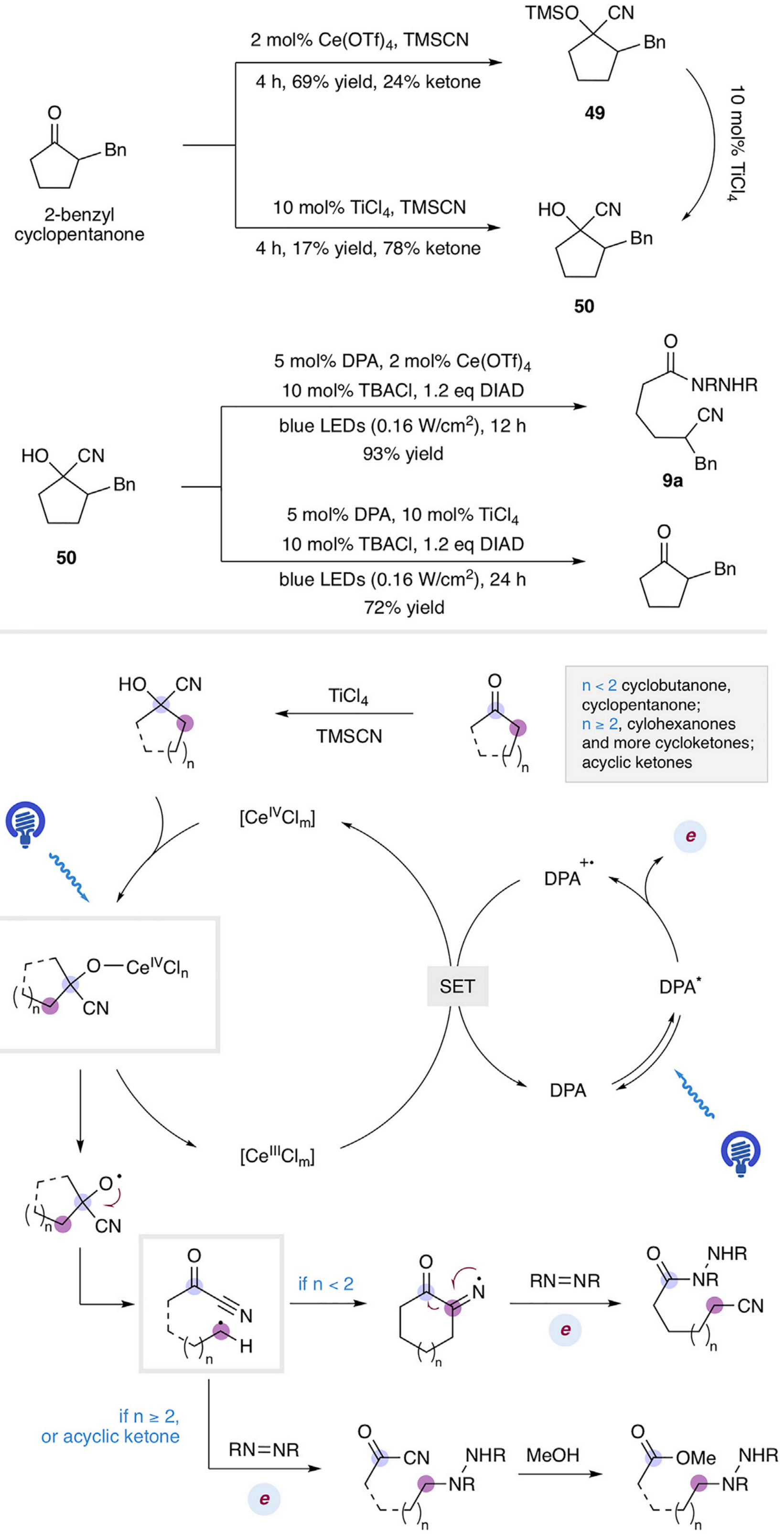

Figure 6. Mechanistic Investigations and Proposed Mechanism

(2.9 mg, 4 μmol, 0.02 equiv), and *n*-Bu_4NCl (5.5 mg, 20 μmol, 0.1 equiv) in glovebox; then, the vial was sealed with a poly-tetrafluoroethylene-lined cap before CH_3CN (1 mL) and $PhCF_3$ (1 mL) were added. $TiCl_4$ (0.1 mL, 0.2 M in CH_3CN, 0.1 equiv) and TMSCN (76 μL, 0.6 mmol, 3 equiv) were then added to the reaction solution at 0°C. The reaction mixture was degassed by Argon sparging for 2 min at 0°C, then irradiated with a 100 W blue LED lamp (at approximately 4 cm away from the light source, 0.16 $W \cdot cm^{-2}$). After the ketone was consumed, anhydrous methanol (4 mL) and triethylamine (42 μL, 0.3 mmol, 1.5 equiv) were added, and the solution was stirred for 2 h before being concentrated *in vacuo*. Purification by flash chromatography on silica gel (20% acetone in hexanes) provided the desired product.

DATA AND CODE AVAILABILITY

Crystal structure data of compound 18b (CCDC: 1960040) has been deposited in the Cambridge Structural Database.

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at https://doi.org/10.1016/j.chempr.2019.11.009.

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AUTHOR CONTRIBUTIONS

Z.Z., Y.C., and J.D. conceived the research. Y.C. and J.D. carried out experiments and analyzed results. Z.Z. and Y.C. wrote the manuscript with input from all the authors.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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