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Photocatalyzed Diastereoselective Isomerization of Cinnamyl Chlorides to Cyclopropanes

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ABSTRACT: Endergonic isomerizations are thermodynamically unfavored processes that are difficult to realize under thermal conditions. We report a photocatalytic diastereoselective isomerization of acyclic cinnamyl chlorides to strained cyclopropanes. Quantum mechanical calculations (uM06-2X and DLPNO), including TD-DFT calculations, and experimental studies provide evidence for the energy transfer from an iridium photocatalyst to the allylic chloride substrate followed by C–Cl homolytic cleavage. Subsequent Cl• radical migration forms a localized triplet 1,3-diradical intermediate that, after intersystem crossing, undergoes ring-closing to form the desired product. The mild reaction conditions are compatible with a broad range of functional groups to generate chloro-cyclopropanes in high yields and diastereoselectivities. A more efficient process is developed by addition of a catalytic amount of a nickel complex, and we propose a novel role for this co-catalyst to recycle an allyl chloride byproduct generated in the course of the reaction. The reaction is also shown to be stereoconvergent, as an *E/Z* mixture of cinnamyl chlorides furnish the *anti*-chloro-cyclopropane product in high diastereoselectivity. We anticipate that the use of a visible light activated photocatalyst to transform substrates in combination with a transition metal catalyst to recycle byproducts back into the catalytic cycle will provide unique opportunities for the discovery of new reactivity.

INTRODUCTION

Molecules incorporating cyclopropanes have fascinated organic chemists for decades. The cyclopropyl group is a common motif found in many pharmaceutical products and secondary metabolites.[1] This privileged functional group is employed to increase metabolic stability, enhance potency, and decrease plasma clearance in drug-like molecules.[2] The strain associated with the cyclopropane ring system (approximately 27 kcal/mol), along with the electronic character of its bent carbon-carbon bonds, have been the subject of many seminal discoveries in chemical structure and bonding.[3] Moreover, the unique reactivity of cyclopropanes have been exploited for the synthesis of several distinct classes of products.[4]

Given the general intrigue and practical utility of cyclopropanes, synthetic chemists have developed elegant strategies for the assembly of these three-membered ring systems. To date, most approaches are based on the reaction of stable substrates with high energy reagents that provide the potential energy necessary for generating strained cyclopropanes (Figure 1). Popular strategies for cyclopropane synthesis include [2+1]-type cycloadditions between alkenes and reactive reagents, such as carbene equivalents generated from diethylzinc and dihalomethanes (Simmons-Smith reaction)[5] or metal carbenes generated from diazo compounds (Figure 1A).[6] In some cases (Figure 1B), a two-step process (Michael-type or Giese addition followed by intramolecular displacement) can be employed for the cyclopropanation of activated alkenes (e.g., sulfur ylides with enones in the Corey-Chaykovsky reaction or alkyl radicals in radical-polar crossover cyclopropanations).[7] Although these routes are well-established in the literature, they are often lacking in broad functional group tolerance and operational simplicity, and rarely employ mild conditions. More recently, photoreducible and photooxidizable C_1 reagents and olefins, in combination with a photoredox catalyst, have been developed by Suero,[8] Molander,[9] Aggarwal,[10] and others.[11]

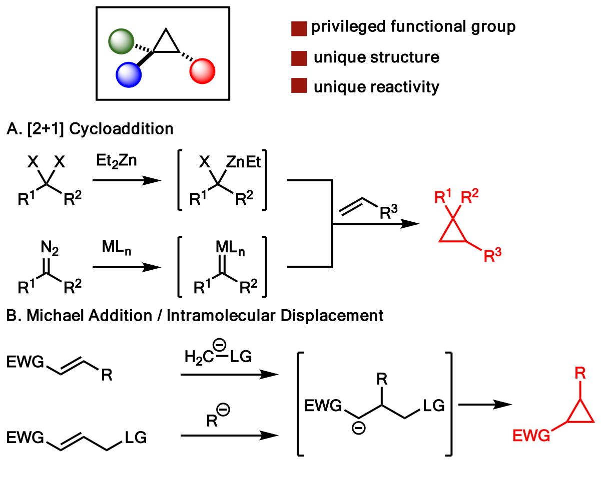


Figure 1. Classical methods to synthesize cyclopropanes.

We were interested in developing a different strategy to access strained cyclopropanes via the *unimolecular isomerization* of their low energy acyclic precursors (Figure 2A). If successful, this novel approach would be a more atomeconomic and direct synthesis of cyclopropanes. However, the thermal isomerization from a low energy substrate to a high energy strained product is an energetically endergonic process ($\Delta G_{rxn} > 0$) and hence represents an extremely challenging “*uphill*” transformation.

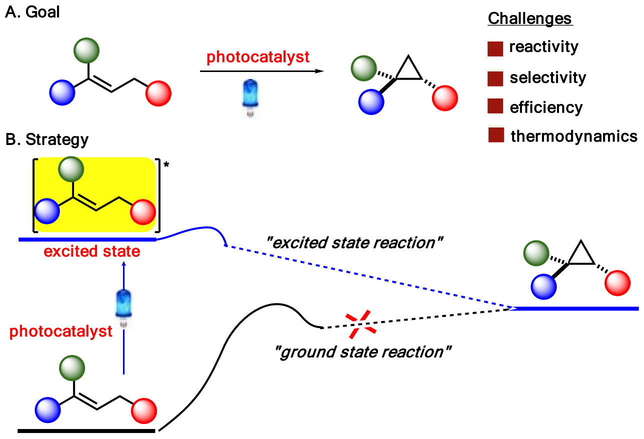


Figure 2. Energetically uphill isomerization of acyclic compounds to strained cyclopropanes.

Photochemistry has been utilized as an alternative strategy for mediating energetically endergonic isomerizations.[12] In this context, elegant photocatalytic processes have recently been reported for the isomerization of *trans*-alkenes to *cis*-alkenes[13] and of cyclic alcohols to acyclic carbonyl compounds.[14] A selective and high yielding photocatalytic isomerization of acyclic compounds to strained cyclopropanes is unprecedented, and it represents a unique challenge to the concept of controlling energetically endergonic isomerizations (Figure 2B). Herein, we present a photocatalytic system for the diastereoselective synthesis of *anti*-chloro-cyclopropanes from their acyclic cinnamyl chloride precursors. In addition to exploring the scope and synthetic utility of this general transformation, we performed experimental and computational studies to gain insight into the overall mechanism.

RESULTS AND DISCUSSION

Allylic chlorides were selected as an initial starting point to develop an energetically endergonic isomerization of acyclic compounds to strained cyclopropanes. Early studies with this class of substrates suggested that the photochemical isomerization of allylic chlorides could furnish cyclopropane products. UV irradiation of allyl chlorides such as **1a** with organic photosensitizers led to a mixture of rearranged products, including chloro-cyclopropanes **2a** and **4a** as well as acyclic allyl chloride **3a**, albeit in low yields and poor product selectivities (Figure 3).[15] Despite the potential utility of these transformations, their synthetic applicability remains severely limited and their mechanism is poorly defined. Based on these results and recent efforts on endergonic photocatalytic reactions, we hypothesized that the use of a photoredox catalyst and visible light, along with a deeper mechanistic understanding of this photochemical isomerization, could lead to a more efficient and functional group tolerant strategy for generating a broad range of strained chloro-cyclopropanes.[16]

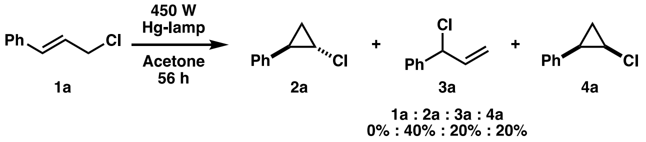
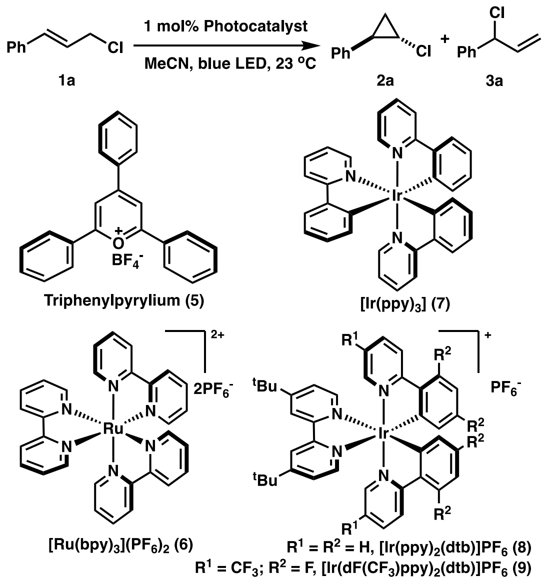


Figure 3. Early studies of photochemical isomerization of allylic chlorides.

To commence our studies, we subjected cinnamyl chloride **1a** to different photocatalysts under blue LED light irradiation (Table 1). 2,4,6-Triphenylpyrylium tetrafluoroborate (**5**), a typical metal-free organophotocatalyst, did not catalyze any conversion of cinnamyl chloride **1a** (Entry 1). We turned our attention to metal polypyridyl-based photocatalysts. The ruthenium-centered photocatalyst, $[Ru(bpy)_3](PF_6)_2$ (**6**), did not activate the cinnamyl chloride **1a** either (Entry 2). To our delight, iridium-centered photocatalyst $Ir(ppy)_3$ (**7**) partially converted linear substrate **1a** to the desired cyclopropane product **2a**, with a significant amount of undesired branched allylic chloride **3a** as byproduct (Entry 3). Interestingly, while early examples of photochemical isomerization of allylic chlorides in the presence of UV light yielded diastereomers **2a** and **4a** in a 2:1 ratio (Figure 3),[14] under our mild visible-light mediated photocatalyzed conditions, chloro-cyclopropane **2a** was formed as the only diastereomer. Additional iridium-centered photocatalysts were then examined, including $[Ir(ppy)_2(dtb)]PF_6$ (**8**) and $[Ir(dF(CF_3)ppy)_2(dtb)]PF_6$ (**9**) (Entries 4 and 5). Both of these metal polypyridyl complexes furnished full conversion of **1a** and provided a moderate yield of desired product **2a**. A significant amount of byproduct **3a** was also obtained, even if the reaction time was extended to 72 hours (Entry 6). Certain classes of allylic chlorides and other allylic substrates, including allylic bromides, iodides, fluorides, alcohols, and acetates, did not furnish the desired cyclopropane product under the reaction conditions (Table S4).

Table 1. Initial Results by Testing Various Photocatalysts.



Triphenylpyrylium (5)

[Ir(ppy)$_3$] (7)

[Ru(bpy)$_3$](PF$_6$)$_2$ (6)

R^1 = R^2 = H, [Ir(ppy)$_2$(dtb)]PF$_6$ (8)

R^1 = CF$_3$; R^2 = F, [Ir(dF(CF$_3$)ppy)$_2$(dtb)]PF$_6$ (9)

Entry[a]	Photocatalyst	Time	Ratio of 1a / 2a / 3 / 4[b]
1	5	24 hours	100%, 0%, 0%, 0%
2	6	24 hours	100%, 0%, 0%, 0%
3	7	24 hours	60%, 20%, 10%, 0%
4	8	16 hours	0%, 44%, 46%, 0%
5	9	16 hours	0%, 48%, 42%, 0%
6	9	72 hours	0%, 52%, 36%, 0%

[a] Reaction conditions: Photocatalyst (1 mol%), **1a** (0.2 mmol), MeCN (1 mL), 4 W blue LED. [b] ^{1}H NMR yields based on 1,3,5-tribromobenzene as an internal standard.

Previous mechanistic studies on similar systems supported triplet-triplet energy transfer leading to an excited triplet state as the first intermediate in these photosensitized isomerizations.[14] However, the nature of subsequent steps remain poorly understood (i.e., homolytic or heterolytic C–Cl bond breaking, zwitterionic or singlet/triplet diradical intermediates, radical-cage recombination/cyclization, etc.). In an effort to optimize the conversion of acyclic allylic chloride **1a** to cyclopropane **2a** and gain insights into the mechanism of formation of byproduct **3a**, we turned to quantum mechanical calculations. All structures were optimized using unrestricted DFT with M06-2X functional and a DGDZVP basis set in acetonitrile (SMD solvation model) as implemented in Gausian09.[17] To refine energetics, we performed subsequent single point calculations with a def2-TZVPP basis set (uM06-2X/def2-TZVPP-SMD(acetonitrile)//uM06-2X/DGDZVP-SMD(acetonitrile)). For comparison, we also performed single point energy calculations using DLPNO-CCSD(T) (with solvent corrections from (uM06-2X/def2-TZVPP-SMD(acetonitrile) single point calculations) and the def2-TZVPP basis set using ORCA software version 4.1.2.[9a,18] For simplicity, only uM06-2X singlet point calculations will be discussed in the manuscript. Minimum energy crossing points were found using the MECPro version 1.0.5.[19] Structures were visualized using CYLview version 1.0.565B .[20] See the Supporting Information for further details.

Akin to our recent calculations on photoredox cyclopropanation studies,[9a] we initially hypothesized that a photochemically generated chlorine atom could undergo regioselective Giese addition to cinnamyl chloride **1a** leading to the formation of 1,2-dichloro radical intermediate **11** (Figure 4A). In turn, this dichloro intermediate will then undergo diastereoselective ring-closing to form the desired product **2a** (Figure 4A, inset). To assess the feasibility of radical cyclization from the presumed 1,2-dichloro radical intermediate **11**, we performed quantum mechanical calculations (Figure 4B). Although calculations predict facile isomerization between 1,3- and 1,2-dichloro radical species **11**, **12**, and **13**, the barriers to undergo the desired radical cyclization from **11** leading to cyclopropane products **2a** and **4a** are > 30 kcal/mol (i.e., $\mathbf{TS}_{\mathbf{11\text{-}2a}}$ and $\mathbf{TS}_{\mathbf{11\text{-}4a}}$), and the reactions are highly endergonic. Based on these results we ruled out the formation of cyclopropane products from dichloro intermediates (**11**, **12**, and **13**). Our previously reported quantum mechanical calculations[9a] demonstrated that, under appropriate photoredox catalysis, halogen radical intermediates can undergo facile single electron transfer (SET) with the photocatalyst to form an anionic species (via a radical-polar crossover mechanism). In turn, the anionic species could then undergo facile ring-closure with concomitant release of a halide anion. However, all attempts to locate the corresponding dichloro anionic species from **11**, **12**, and **13** failed and led to direct formation of elimination products **1a** and **3a** as shown in Figure 4 (see also Figure S1A in the Supporting Information). Thus, quantum mechanical calculations ruled against formation of dichloro radical or anionic species as key intermediates in the photochemical isomerization (See Supporting Information for further details).

Next, we focused on examining cyclopropanation via a *triplet* spin state surface. TD-DFT calculations on cinnamyl chloride **1a** revealed that the lowest lying *singlet* excitation, 4.86 eV, is inaccessible directly by blue LED irradiation, which is consistent with the experimentally determined UV/Vis absorption spectrum of substrate **1a** (Figure S5).[21] We then suspected that triplet-triplet energy transfer may allow for excitation of the cinnamyl chloride to its *triplet* state.15 As shown in Figure 5, the *triplet* excited state of cinnamyl chloride **1a** is inaccessible via ruthenium (**6**) and triphenylpyrylium (**5**) *triplet* excited states. Notably, Ir-based photocatalyst **7** has the energy requirements to promote triplet-triplet energy transfer and is thus able to activate the allylic chloride substrate. Additional TD-DFT calculations affirm that excitation of the product **2a** and byproduct **3a** is not possible under these conditions (Figure 5), making this transformation photochemically irreversible and allowing for a productive endergonic isomerization.

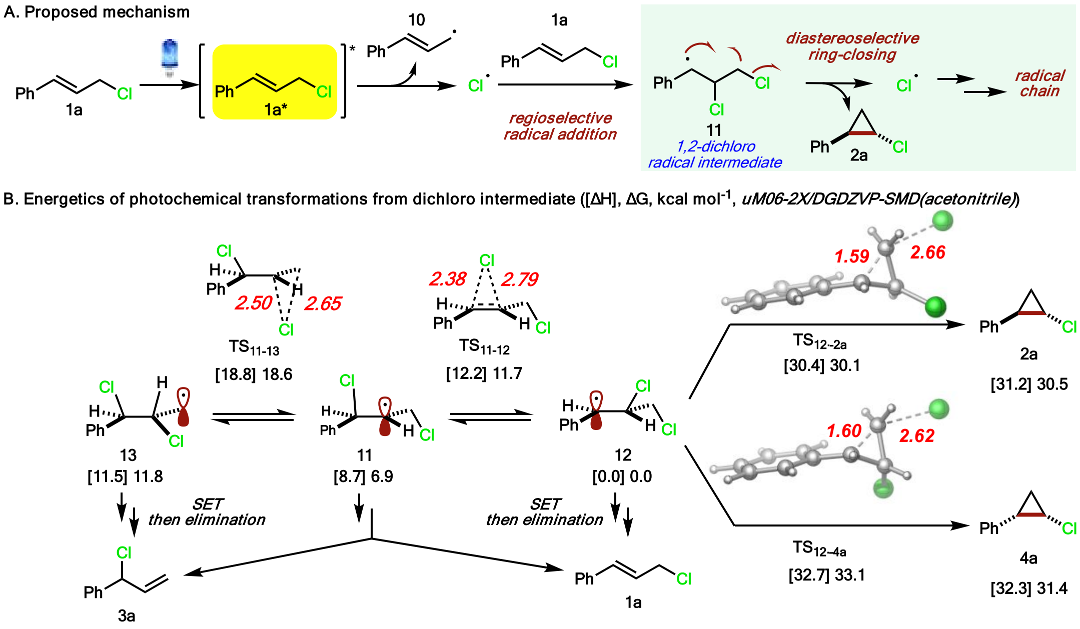


Figure 4. DFT-calculations of mechanism that proceeds through dichloro radical intermediates.

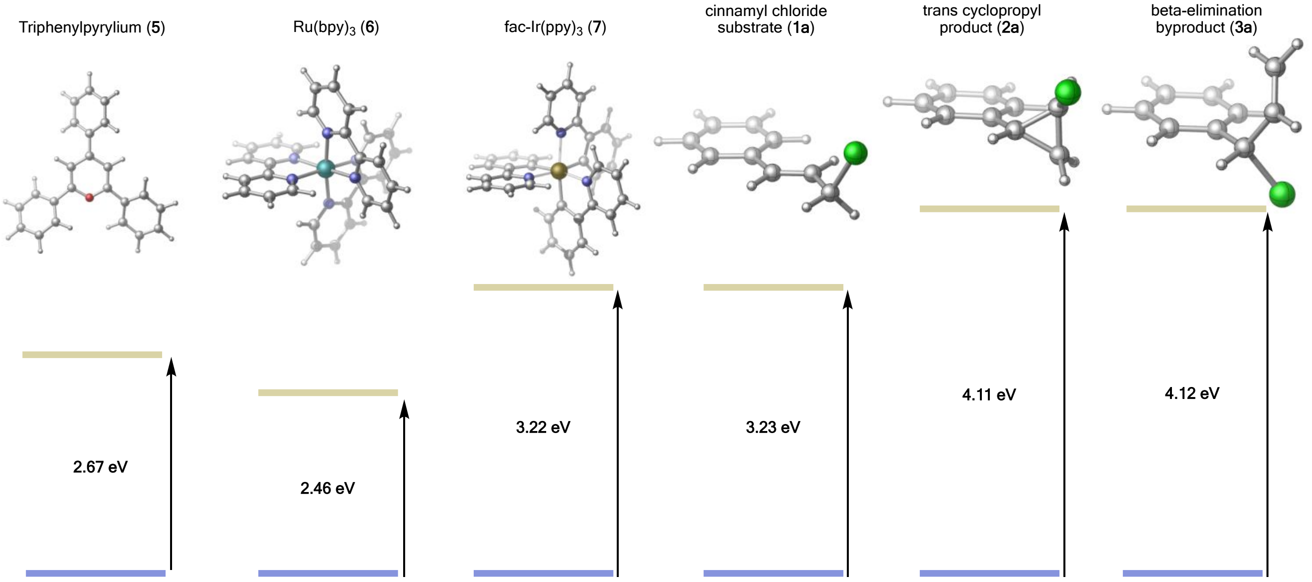


Figure 5. Lowest energy excitations to triplet states of photocatalysts and substrate (out of 10 excitations) using TD-DFT [uM062X/DGDZVP-SMD(acetonitrile)].

Assuming facile triplet-triplet energy transfer from the excited state of the photocatalyst **7** to the cinnamyl chloride **1a**$^{1''}$, the triplet intermediate **1a**$^{3'}$ can then undergo *homolytic* carbon-chlorine bond dissociation (via **TS-1a**$^{3'}$**-14**$^{3'}$) to form isoenergetic triplet radical pair **14**$^{3'}$ with an overall barrier of only ~6 kcal/mol from **1a**$^{3'}$ (Figure 6). This intermediate, albeit lower in energy, could undergo C–Cl bond formation to form 1,3-diradical triplet intermediate **15**$^{3'}$ via an almost barrierless (~4.0 kcal/mol via ultrafine IRC) Cl radical recombination (Figure S3B). We located a *triplet* transition state ring-closing from **15**$^{3'}$ to form the desired cyclopropane in the *triplet spin state* (not shown), but this process was ruled out because it has an insurmountable kinetic barrier (>40 kcal/mol) and it is endergonic by more than 35 kcal/mol from **15**$^{3'}$ (Figure S3). Importantly, from the two *triplet* diradical intermediates **14**$^{3'}$ and **15**$^{3'}$ we located the corresponding minimum energy crossing points (**MECP-14**$^{3'}$**-3a**$^{1'}$ and **MECP-15**$^{3'}$**-2a**$^{1'}$) that will form the experimentally observed branched allylic chloride and cyclopropane products **3a**$^{1'}$ and **2a**$^{1'}$, respectively after intersystem crossing. All singlet MECP had a single imaginary frequency which, upon visualization, are the desired motions that lead to products **3a**$^{1'}$ and **2a**$^{1'}$. Triplet MECP did not give imaginary frequencies, providing additional support that intersystem crossing to the singlet potential energy surface leads to the observed products. Notably, the barriers for these two minimum energy crossing points differ by only 1.9 kcal/mol, which is consistent with the formation of both products (Entry 5-6, Table 1). Further, consistent with our initial hypothesis, these two products *are thermally endergonic* in energy compared to the substrate by ~6-8 kcal/mol. Overall, since the rearranged products **3a**$^{1'}$ and **2a**$^{1'}$ are significantly higher in energy than the linear allylic chloride and the energy to undergo triplet-triplet energy transfer is much higher (4.11 eV and 4.12 eV; Figure 5), our DFT calculations suggest that this process is a result of a photochemical transformation rather than a photoinduced chain reaction. Finally, we also located the thermal concerted 1,2-sigmatropic shift/ring-closing transition state (**TS-1a$^{1'}$-2a$^{1'}$**) that will lead to product **2a$^{1'}$**, which has a barrier of ~46 kcal/mol. However, this pathway was ruled out based on unfavorable *ground state* thermodynamics and kinetics.

To improve the efficiency of the photocatalyzed cyclopropanation, we hypothesized that a co-catalyst could be introduced to the reaction to *recycle* branched allylic chloride *byproduct* **3a** back into the catalytic cycle. One potential strategy would be to isomerize byproduct **3a** back to substrate **1a** with a co-catalyst that can generate metal-allyl complex **16**, such as $Pd_2(dba)_3$, $[Ir(COD)Cl]_2$, or $Ni(COD)_2$ (Table 2).[22] The use of dual catalyst systems based on photocatalysts and transition metal complexes is an emerging area or research, with several proposed roles of the transition metal complexes in light mediated processes.[23,24] In our cyclopropanation system, palladium, iridium, and nickel catalysts depressed the generation of byproduct **3a** and increased the yield of desired product **2a** (Entries 1-3). Among these co-catalysts, $Ni(COD)_2$ provided the most satisfying results, including full conversion of cinnamyl chloride **1a**, total depression of branched allylic chloride **3a**, and highest yield of cyclopropane **2a** (76%, Entry 3). To further improve the yield of cyclopropanation, we screened a variety of ligands for the Ni(0) co-catalyst. The coordinating ability of phosphine ligand **17** was too strong to fully isomerize **3a** (Entry 4). Compared to bipyridine **18** (Entry 5), bisoxazole **19** (Entry 6) provided higher reactivity and yield of the desired product (86%). To ensure the full coordination and solvation of $Ni(COD)_2$/ligand complex, 12 mol% **19** was used, which resulted in 92% isolated yield of cyclopropane **2a** (Entry 7).

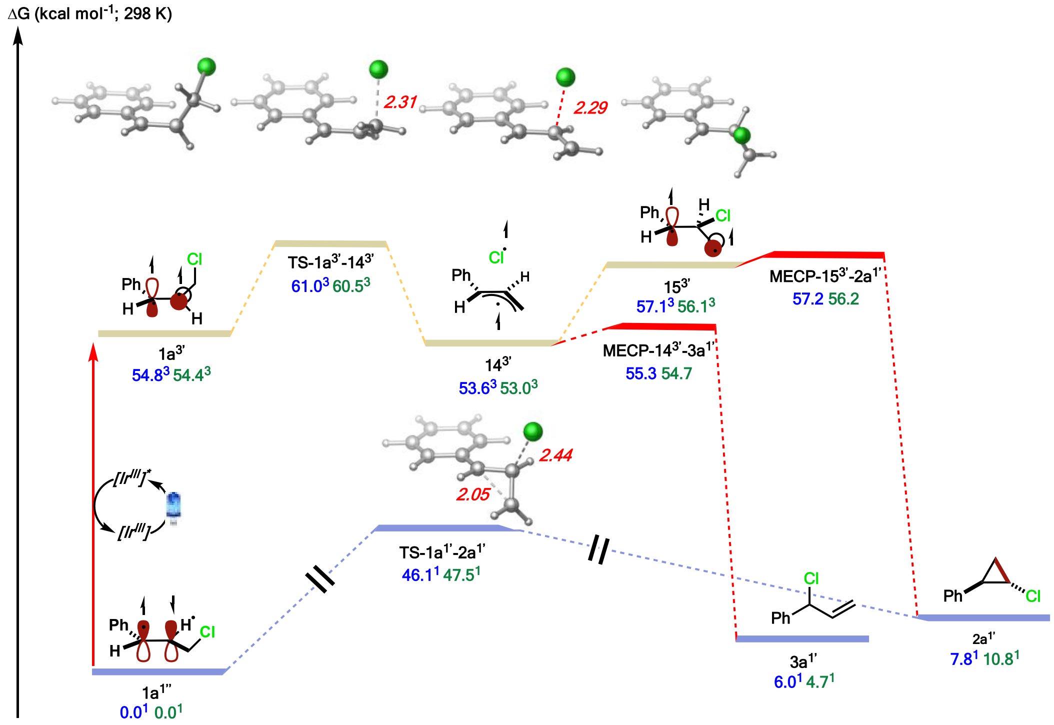
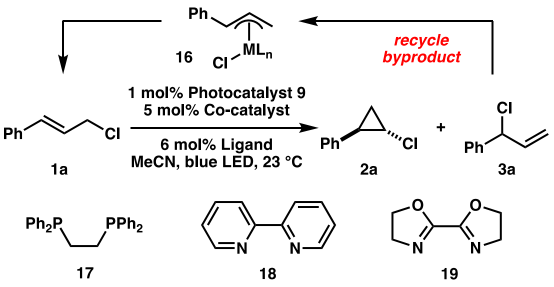


Figure 6. Energetics for photocatalytic isomerization. Free energies, in kcal/mol, are from UM06-2X/def2-TZVPP-SMD(acetonitrile) (blue) and DLPNO-CCSD(T)/def2-TZVPP-SMD(acetonitrile) (green) calculations.

Table 2. Optimization of Dual Catalyst System.



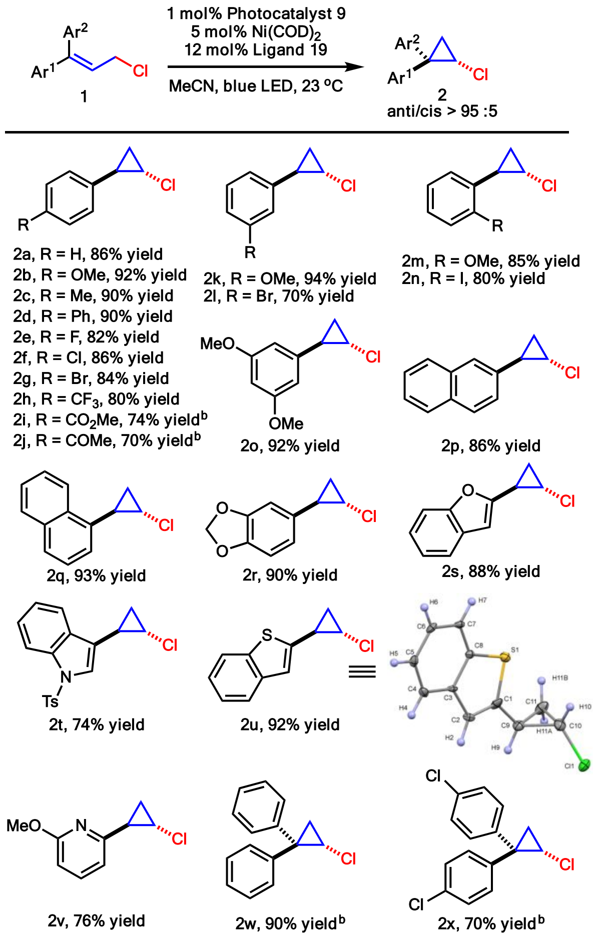
Entry[a]	Co-catalyst	Ligand	Time (hours)	Ratio of 1a / 2a / 3a[b]
1	$Pd_2(dba)_3$	None	16	16%, 64%, 0%
2	$[Ir(COD)Cl]_2$	None	16	8%, 58%, 14%
3	$Ni(COD)_2$	None	16	0%, 76%, 0%
4	$Ni(COD)_2$	17	24	0%, 70%, 12%
5	$Ni(COD)_2$	18	24	0%, 84%, 0%
6	$Ni(COD)_2$	19	12	0%, 86%, 0%
7[c]	$Ni(COD)_2$	19	4	0%, 92%, 0%

[a] Reaction conditions: Photocatalyst (1 mol%), co-catalyst (5 mol%), ligand (6 mol%), **1a** (0.2 mmol), MeCN (1 mL), 4 W blue LED. [b] NMR yields. [c] 12 mol% **19** was used.

With the optimal reaction conditions in hand, we evaluated the scope of this photocatalyzed *anti*-cyclopropanation reaction with various substituted acyclic cinnamyl chlorides **1** (Table 3). The reaction exhibited great tolerance to aromatic systems with a broad range of substituents. On the *para*-position, electron-donating groups (MeO, **2b**), alkyl substitution (Me, **2c**), aromatic rings (Ph, **2d**), halogens (F, Cl, Br; **2e-g**) and electron-withdrawing groups (CF_3, CO_2Me, C(=O)Me; **2h-j**) all provided the desired cyclopropanation products with high *anti*-selectivity (>95:5) and yields (up to 92%). Similar functional group compatibility was exhibited among the substituents on the *meta*- and *ortho*- positions (**2k-n**). Multi-substituted (**2o**) and fused aromatic rings (**2p** and **2q**) also afforded satisfying results. To our delight, this reaction showed tolerance to various heterocycles (**2r-v**), such as 1,3-benzodioxole, benzofuran, benzothiophene, indole, and pyridine. 1,1-Di-aryl-substituted allylic chlorides were also examined. The corresponding cyclopropane products were obtained with high yields (**2w** and **2x**).

Further experiments were carried out to explore the synthetic potential of this photocatalyzed cyclopropanation reaction (Figure 7). First, this transformation can be easily performed on gram-scale (Figure 7A). Starting from 10 mmol of commercially available cinnamyl chloride **1a**, 1.32 g of product **3a** was obtained in 87% yield with high *anti*-selectivity under mild reaction conditions. In addition, substrate **1d** furnished cyclopropane product **2d** in 94% yield. We then investigated the transformation of the C–Cl bond of chloro-cyclopropane **2d** (Figure 7B). By using an *in situ* generated lithium morpholin-4-ide, the C–Cl bond was efficiently transformed to a C–N bond without breaking the cyclopropyl ring. Interestingly, amino-cyclopropane product **20** was obtained in 86% yield with high retention of stereochemistry, which was confirmed by X-ray crystallography.

Table 3. Substrate Scope.[a]



[a] Reaction conditions: Photocatalyst (1 mol%), co-catalyst (5 mol%), ligand (12 mol%), **1a** (0.2 mmol), MeCN (1 mL), 4 W blue LED, 4 hours, isolated yields. [b] 48 hours.

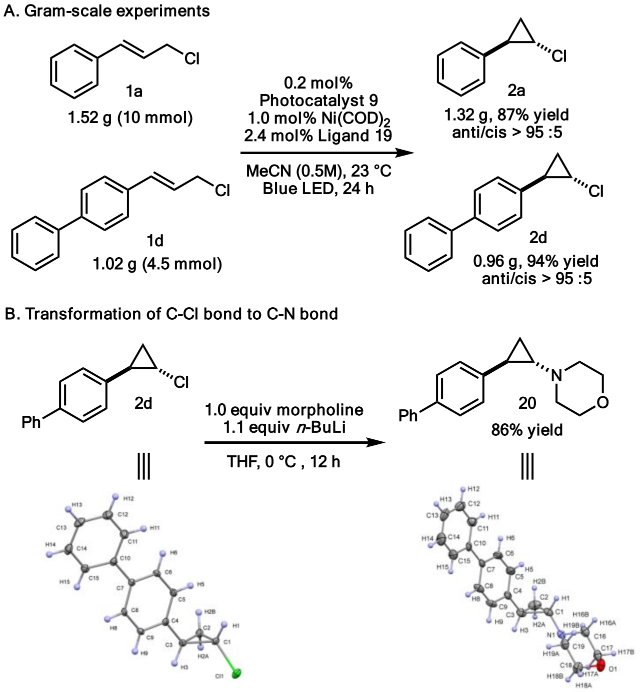


Figure 7. Synthetic utility of cyclopropanation.

We carried out a series of control experiments to gain insight into the mechanism of dual nickel/photocatalyzed cyclopropanation (Figure 8). First, a mixture of allylic chlorides (*Z*)-**1a**, (*E*)-**1a**, and **3a** cleanly furnished *anti*-cyclopropane **2a** with similarly high diastereoselectivity (equation 1), which suggests that the mechanism involves a common intermediate that can be accessed by either linear *Z*- or *E*-allylic chloride substrates as well as branched allylic chloride byproduct **3a**. This observation represents a practical advantage to the method, as a mixture of alkene isomers of the starting material leads to the *anti*-chloro-cyclopropane product **2a** through a stereoconvergent mechanism. In addition, under the optimal reaction conditions, cinnamyl bromide did not provide any cyclopropanation product. In a crossover experiment of cinnamyl bromide and 2-napthyl substituted cinnamyl chloride, the crossover product **2a** was observed (equation 2). In line with prior computational work, this experiment implies dissociation of the C–Cl bond and bimolecular recombination during the reaction process. Interestingly, by using compound **22** as substrate, cyclopropane **23** was obtained instead of the expected cyclopropane **24** (equation 3), which is consistent with Cl migration during the reaction. A radical clock experiment with substrate **25** (equation 4) and radical-trapping experiment with TEMPO (equation 5) both support the involvement of free radical intermediates in the cyclopropanation mechanism.

Steady-State and time-resolved absorption and photoluminescence spectroscopies were used to seek additional mechanistic information on the role of the iridium photoredox catalyst. The iridium photosensitizer **9** exhibits properties that are typical of compounds with low-lying metal-to-ligand charge transfer (^{3}MLCT) excited states (Figure S6).[25] Room temperature photoluminescence centered at 470 nm was observed with an excited-state lifetime of 2.26 ± 0.20 μs. Both the steady-state as well as the time-resolved photoluminescence were efficiently quenched by various cinnamyl chloride derivatives used in the photocatalytic reactions. The quenching data was well described by the Stern-Volmer model that provided quenching rate constants, k_q that ranged from 0.47 x10^9 M^{-1}s^{-1} (**1p**) to 3.06 x10^9 M^{-1}s^{-1} (**1i**) (Figure 9 and Figures S7-S15). Stern-Volmer plots using ratios of the steady-state (PLI$_0$/PLI) or time-resolved (τ_0/τ) photoluminescence were linear and coincident under the conditions used.[26] This observation ruled out *static quenching* through the formation of a ground-state adduct but rather indicated that the excited-state quenching mechanism was solely *dynamic*, *i.e.* that the excited-state iridium photosensitizer and the cinnamyl chloride derivative must diffuse to form an encounter complex leading to excited-state reactivity. Control Stern-Volmer experiments with **(*Z*)-1a** and **2a** were nonlinear with concentration, an observation most consistent with the formation of a less emissive adduct (Figures S16-S17). At low concentration, the Stern-Volmer slope for excited-state quenching by **(*Z*)-1a** was slightly steeper than with the corresponding **(*E*)-1a** isomer.

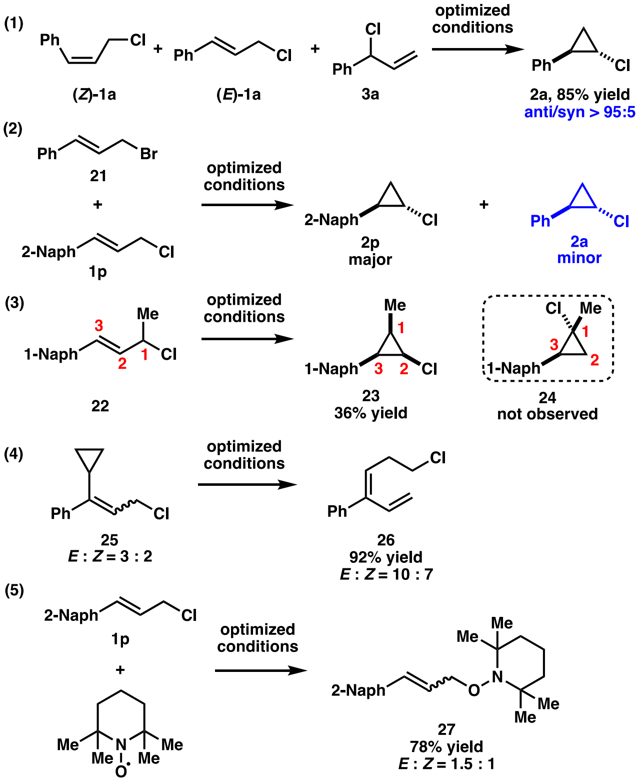


Figure 8. Mechanistic Control Experiments.

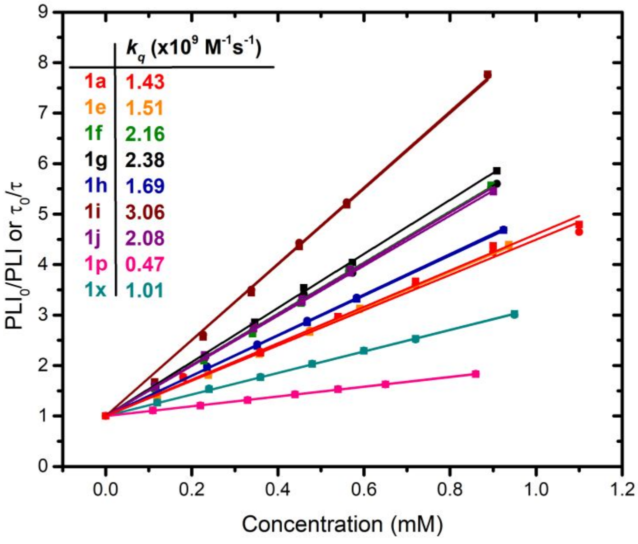


Figure 9. Stern-Volmer plots determined by steady-state (solid squares) and time-resolved (solid circles) photoluminescence for the indicated cinnamyl chloride derivatives. The quenching rate constants (k_q (x10^9 M^{-1}s^{-1})) are indicated for each cinnamyl chloride derivative.

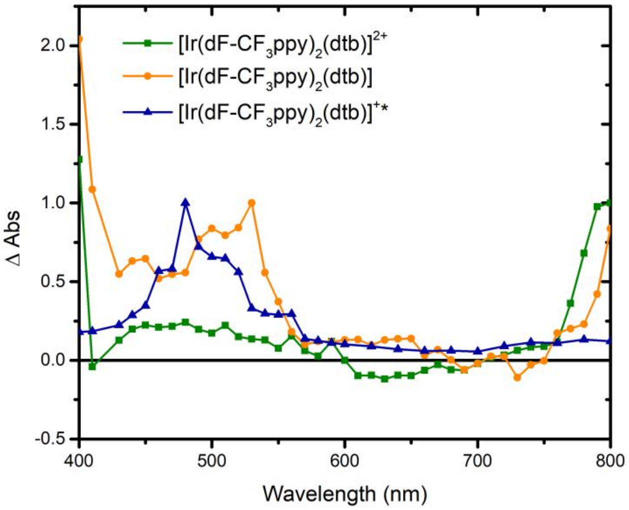


Figure 10. Absorption spectra of the oxidized [Ir(dF-CF$_3$ppy)$_2$(dtb)]$^{2+}$ (green), reduced [Ir(dF-CF$_3$ppy)$_2$(dtb)] (orange) and excited-state [Ir(dF-CF$_3$ppy)$_2$(dtb)]$^{+*}$ (blue) obtained by transient absorption spectroscopy in argon purged acetonitrile at room temperature (See supporting information for additional experimental details).

Excited-state mechanistic investigations were performed using nanosecond transient absorption spectroscopy with pulsed 420 nm light excitation. First, key spectra such as the excited-state absorption spectra as well as the one-electron reduced and one-electron oxidized absorption spectra of **9** were determined (Figure 10 and Figures S18-S19).[27] These spectra are of paramount importance as they inform on the oxidation state of the iridium photosensitizer during photoredox catalysis. The excited-state absorption spectrum (blue) was characterized by an increased ΔAbs between 440 and 550 nm with a maximum centered at 480 nm. The mono-reduced species exhibited a maximum at 530 nm (orange), whereas the singly oxidized species exhibited weak absorption features between 440 nm and 550nm as well as above 750 nm (green). Interestingly, nanosecond transient absorption spectroscopy performed in the presence of cinnamyl chlorides **1a** or **1i** led to a drastic excited-state quenching, with an excited-state lifetime that decreased from 2.32 µs to ~10 ns (Figure 11A and Figure S20). This confirmed the excited-state quenching data quantified by Stern-Volmer experiments but did not provide evidence for the products of the quenching reactions. Had oxidative or reductive quenching of the excited state occurred in the presence of cinnamyl chlorides with cage escape yields greater than 5%, the Ir complex would have reported on the redox chemistry, contrary to what was observed. The inability to observe redox products implies either electron transfer with rapid recombination or energy transfer. Note that the photo-induced *trans-cis* isomerization of cinnamic acid derivatives with an iridium photosensitizer was recently reported to occur via triplet-triplet energy transfer.[28]

The excited-state reactivity of photocatalyst **9** with a cinnamyl amine **28** was investigated to distinguish between electron transfer and energy transfer (Figure 11B). This cinnamyl amine derivative was suspected to undergo facile electron transfer with photoredox catalysts. A quenching rate constant (k_q = 7.23 x10^9 M^{-1}s^{-1}) was determined by Stern-Volmer analysis. Furthermore, nanosecond transient absorption spectroscopy provided undisputable evidence for electron transfer between photocatalyst **9** and cinnamyl amine **28**, with a spectral signature corresponding to both the oxidized amine and the mono-reduced iridium sensitizer. Hence, the lack of spectroscopic signature observed for cinnamyl chloride **1a** or **1i** in the presence of photoexcited catalyst **9** is more consistent with an excited-state quenching mechanism that involves *energy transfer* from the excited-state Ir* to cinnamyl chloride derivatives.

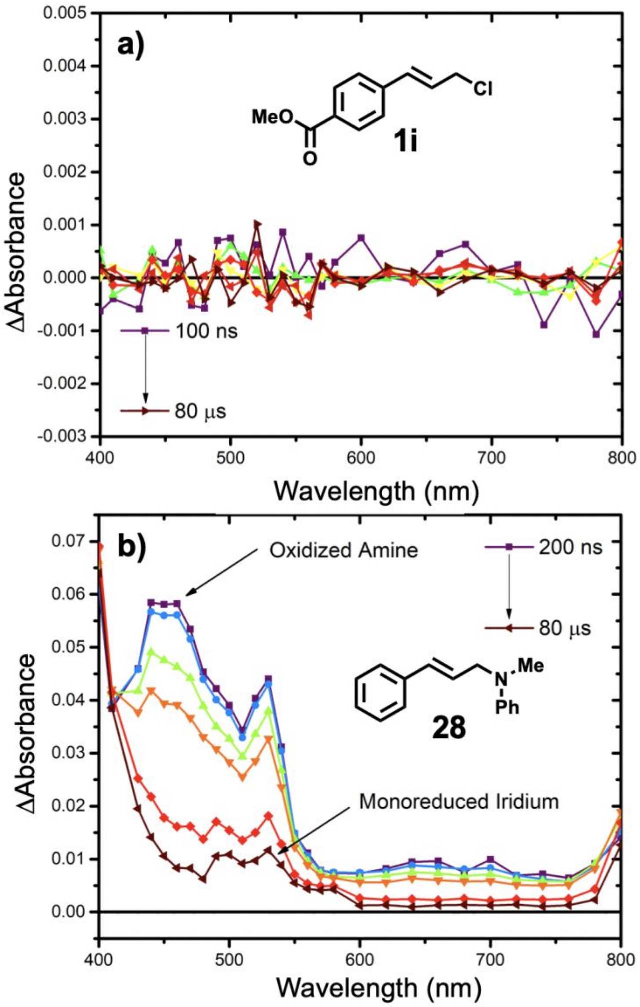


Figure 11. Pulsed 420 nm (2mJ/Pulse) transient absorption spectroscopy of an argon purged acetonitrile solution containing [Ir(dF-CF$_3$ppy)$_2$(dtb)]$^+$ and the cinnamyl derivatives **1i** and **28**. (See supporting information for additional experimental details).

On the basis of these experimental investigations and DFT calculations, we propose the mechanism depicted in Figure 12. Cinnamyl chloride **1a** is activated to the excited state **1a*** after energy transfer from irradiated Ir(III) photocatalyst **9***. Subsequently, a triplet-allyl-pair (**14**) containing chlorine radical is formed from the excited complex **1a***. There are two pathways for intermediate **14**. One path involves a direct intersystem crossing, which provides the undesired branched byproduct **3a**. The other path proceeds through triplet-β-Cl intermediate **15**, which then provides the desired cyclopropanation product **2a** after an intersystem crossing. We propose that byproduct **3a** can be recycled into the catalytic cycle via oxidative addition with Ni(0) complex **29** to form nickel allyl complex **30**, which improves the overall efficiency of the photocatalytic process. At this time, we cannot rule out the possibility that cinnamyl chloride **1a** undergoes an oxidative addition with nickel catalyst **29** to form allyl-Ni(II) complex **30**, which is then activated to the excited state **30*** via energy transfer from irritated Ir(III) photocatalyst **9***.[29] We are currently conducting mechanistic studies to examine the role of photoexcited nickel-allyl complexes.

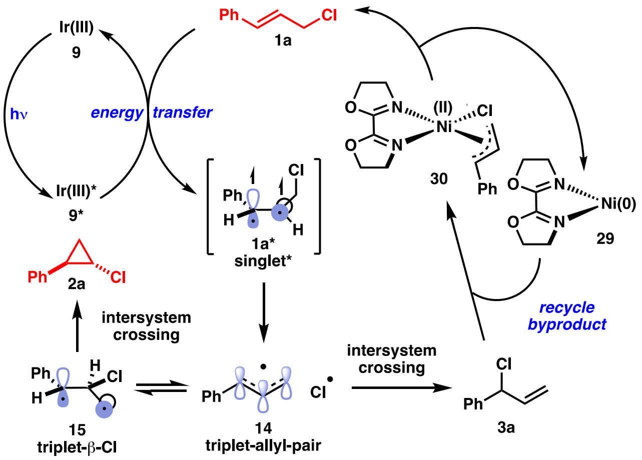


Figure 12. Proposed mechanism.

CONCLUSION

In summary, we have developed dual catalyst system for the efficient photocatalytic isomerization of acyclic cinnamyl chlorides that is highly diastereoselective for the formation of *anti*-chloro-cyclopropanes. We provide experimental and computational evidence for the energy transfer from an iridium photocatalyst to the allylic chloride substrates, followed by a cycloisomerization to the strained cyclopropane products. The reaction demonstrates broad functional group compatibility, which can be attributed to the mildness of activation with visible light. Computational studies provided insight into the mechanism of the reaction and guided the development of a more efficient process by addition of a nickel co-catalyst. We propose a novel role for the nickel catalyst to recycle a byproduct generated in the course of the reaction. We anticipate that the use of a visible light activated photocatalyst to transform substrates in combination with a transition metal catalyst to recycle byproducts back into the catalytic cycle will provide unique opportunities for the discovery of new reactivity.

ASSOCIATED CONTENT

Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org. Experimental details, characterization data, spectral data, and computational results.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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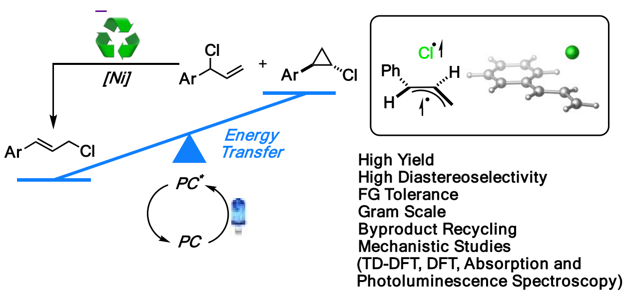

High Yield
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Mechanistic Studies
(TD-DFT, DFT, Absorption and
Photoluminescence Spectroscopy)