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Research Article

UV Light Is No Longer Required for the Photoactivation of 1,3,4-Oxadiazolines

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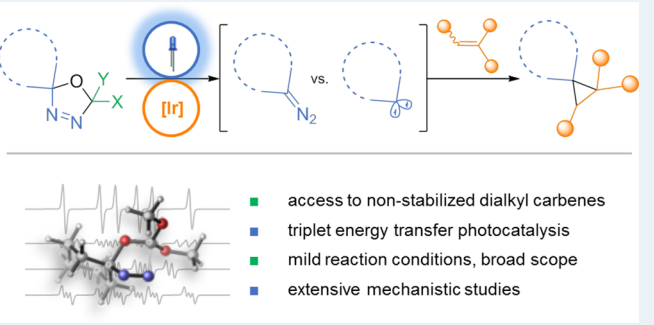
ABSTRACT: Carbenes play a key role in a plethora of organic transformations. Although stabilized diazo carbonyl compounds predominate as a source of electrophilic carbenes, the hazardous nature of nonstabilized analogues calls for their in situ generation from stable precursors. Among these, 1,3,4-oxadiazolines serve as diazoalkane surrogates under UV light irradiation. In view of their high stability, diverse reactivities, and straightforward synthesis, milder methodologies for the activation of these compounds that permit the use of UV-light-sensitive substrates are highly valued. Herein, we report the visible-light-induced activation of oxadiazolines by triplet energy transfer catalysis that, in contrast to UV-induced processes, alters their reactivity and enables the generation of carbenes. The formed reactive species react with electron-poor olefins, thereby giving valuable spirocyclopropanes. Mechanistic investigations, both theoretical and experimental, uncover plausible pathways and highlight the importance of the triplet energy transfer steps.



KEYWORDS: *triplet energy transfer photocatalysis, photosensitization, diazoalkanes and dialkyl carbenes, 1,3,4-oxadiazolines, visible-light induced transformations, spirocyclopropane synthesis*

INTRODUCTION

Carbene chemistry represents an extremely valuable branch of organic synthesis that has already proven to be a powerful tool for the construction of a wide range of C−C and C−X bonds,[1−3] including transformations of pharmaceutical interest.[4−6] Over the years, various precursors of carbene intermediates were developed, among which diazo carbonyl compounds stand at the forefront generating this reactive species under thermal[7] and photochemical[2,8−10] conditions or in metal-catalyzed reactions.[11−14] Most of their applications are, however, limited to stabilized reagents with at least one electron-withdrawing group adjacent to the diazo carbon atom.[7,15] In contrast, the safe synthetic use of nonstabilized counterparts requires in situ generation from, for example, hydrazones,[16−20] diazirines,[21,22] or 1,3,4-oxadiazolines.[23,24]

Compared with other diazo surrogates, 1,3,4-oxadiazolines exhibit high stability and the unique ability to provide distinct reactive intermediates depending on the conditions used (Scheme 1A). The well-known reactivity is based on thermolysis to ylides that spontaneously decompose into heteroatom-substituted carbenes.[24,25] Along this line, they have been widely studied by Warkentin and implemented as dimethoxycarbene surrogates in the synthesis of structurally diverse heterocycles.[26−30] Although effective in the formation of α-X (X = O, N, S) divalent carbon species, 1,3,4-oxadiazolines were only evidenced to give alkylidene carbenes trapped as pyridinium ylides under laser flash photolysis (LFP) at 308 nm.[31−33] When exposed to UV light, nonstabilized diazo compounds are, however, generated.[34−36] While the first photolysis report dates back to 1968,[34] it was only recently that the Ley group proposed their application as diazo precursors in UV-light-induced aryl−alkyl cross-coupling[37] and C−H functionalization reactions of aldehydes.[38−40]

The use of highly energetic UV light often, however, leads to undesired side reactions and precludes broader applications of these stabile and easily available precursors. To address these challenges, we propose a novel strategy for the activation of 1,3,4-oxadiazolines on the basis of the energy transfer event taking place under visible light irradiation. We illustrate the utility of the developed methodology in the photosensitized synthesis of the precious spirocyclopropane skeleton (Scheme 1B).

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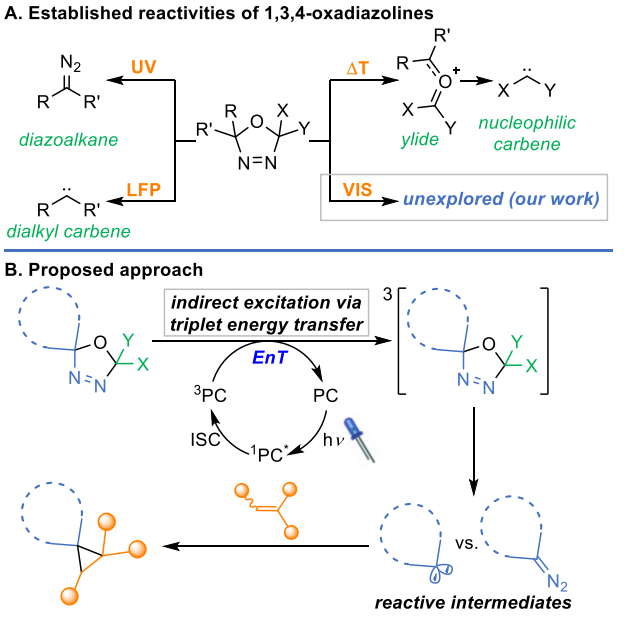
Scheme 1. Reactivity of oxadiazolines



RESULTS AND DISCUSSION

Proposed Strategy. Visible-light-mediated energy transfer (*E*nT) catalysis has already emerged as a beneficial tool to give access to highly reactive species via indirect excitation (sensitization) of a substrate by a photocatalyst in its excited state.[41,42] Such processes occur productively if a sensitizer features a sufficient triplet energy level of lifetime long enough to transfer the energy to an intended molecule rather than to follow another relaxation pathway. The feasibility of the *E*nT process can therefore be estimated on the basis of the similarities between the triplet excited state energies of a photocatalyst and a substrate. Consequently, we began our investigations with density functional B3LYP/6-31G(d,p) calculations to assess $S_0 \rightarrow T_1$ excitation maxima corresponding to triplet energy values for a set of 5,5-cyclohexylidene oxadiazolines **1**–**5** with different substitution patterns at the position C_2 (Figure 1).

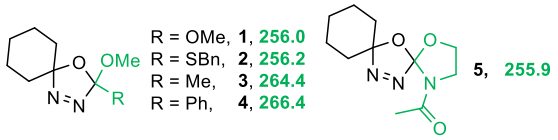


Figure 1. E_T values of oxadiazolines **1**–**5** (kJ/mol).

The calculated triplet energies are at a similar level with slightly lower values exhibited by compounds **1**, **2**, and **5**. In view of its stability and synthetic feasibility, the 5,5-cyclohexylidene-2,2-dimethoxy analogue **1** was selected for further theoretical investigations and initial experiments.

Considering the prospective rich chemistry of compound **1**, various decomposition pathways were computationally investigated at singlet (both ground and first excited) and triplet potential energy surfaces (PES) (Figure 2). Generally, concerted, one-step transformations were identified at singlet PESs, with considerably lower barrier heights for excited states. For example, cycloelimination of diazoalkane **7** from oxadiazoline **1** is associated with an activation energy of only 11.7 kJ/mol for the excited state S_1, which is significantly lower than the respective value for the ground state S_0 (121.0 kJ/mol). This is in line with the known facile UV-induced generation of diazoalkanes from 1,3,4-oxadiazolines.[23] On the contrary, a more complex reactivity pattern emerged for the system in the triplet spin state.

Typically, reaction trajectories involve consecutive bond cleavage and the presence of diradical intermediates. The most feasible pathway initiates with scission of the C_2–N_3 bond within oxadiazoline **1** leading to diazenyl intermediate **I** ($\Delta G‡$ = 14.1 kJ/mol), followed by a practically barrierless dissociation of N_2, and finally, the liberation of the triplet carbene **II** ($\Delta G‡$ = 52.3 kJ/mol). The elimination of diazoalkane **7** from intermediate **I** is also accessible ($\Delta G‡$ = 34.4 kJ/mol). Further analysis of the potential energy surface around **TS1** (Figure 2B) revealed a flat region and viability of the bifurcation of the reaction trajectory, thereby enabling direct decomposition of precursor **1** in the triplet state **T1** to compound **7**. Moreover, the subsequent carbene formation with the nitrogen extrusion from triplet diazoalkane **7** should proceed noticeably easier than for the molecule in the singlet ground state S_0 ($\Delta G‡$ = 63.8 kJ/mol from triplet **7** in comparison with $\Delta G‡$ = 125.1 kJ/mol calculated for the singlet ground state S_0). Given the relatively high barrier for this process, a prior relaxation of triplet diazoalkane **7** to a singlet ground state S_0 and further participation of the latter in reaction pathways seems also probable.

Taking into account the relatively high value of E_T = 256.0 kJ/mol [calculated with the B3LYP/6-31G(d,p)] for oxadiazoline **1**, among the typically used triplet sensitizers, iridium catalyst $\{Ir[dF(CF_3)ppy]_2(dtbpy)\}PF_6$ (**6**) with E_T = 258 kJ/mol should promote energy transfer from its exited state to compound **1**.[42] We supported our hypothesis by illuminating reagent **1** with blue light in the presence of catalyst **6**. Almost complete conversion of substrate **1** was observed, in contrast to the catalyst-free experiment (Scheme 2). Dimethyl carbonate (**8**), cyclohexanone (**9**), and cyclohexene (**10**) were identified as main products, with the latter one resulting from the 1,2-H migration, a transformation typical for alkylidene carbenes,[33] which suggests its formation in a triplet energy transfer process.

Cyclopropanation Optimization Studies. The known activation modes of oxadiazolines give access to ylides, diazo compounds, and carbenes — either dialkyl or heteroatom-substituted, both of nucleophilic type but differing in stability and reactivity.[43,44] Therefore, for the further studies, electron-poor olefins were selected as electrophilic reaction partners. The blue-light-induced model reaction of oxadiazoline **1** with phenyl–vinyl sulfone (**11**) in the presence of catalyst **6** furnished cyclopropane **12** in 41% yield (Table 1, entry 1) along with traces of (*E*)-olefin **13**. Control experiments proved light and the catalyst as factors required for the formation of product **12**, which is inaccessible via a thermal approach (entries 2–4). Optimization studies revealed that a simple modification, such as lowering an excess of oxadiazoline **1**, led to an almost 2-fold increase in the yield of cyclopropane **12** with traces of (*E*)-olefin **13** also formed (entry 5). It is noteworthy that the reaction is only slightly sensitive to the presence of air and moisture and proceeds effectively under blue light irradiation of both low and high intensity; however, a significant decrease of the yield was observed in the case of highly concentrated solutions [for details see Supporting Information (SI) Section 5]. Notably, we were able to reduce both the catalyst loading to only 0.25 mol % and the reaction time to 1 h while maintaining the high reaction efficacy (entry

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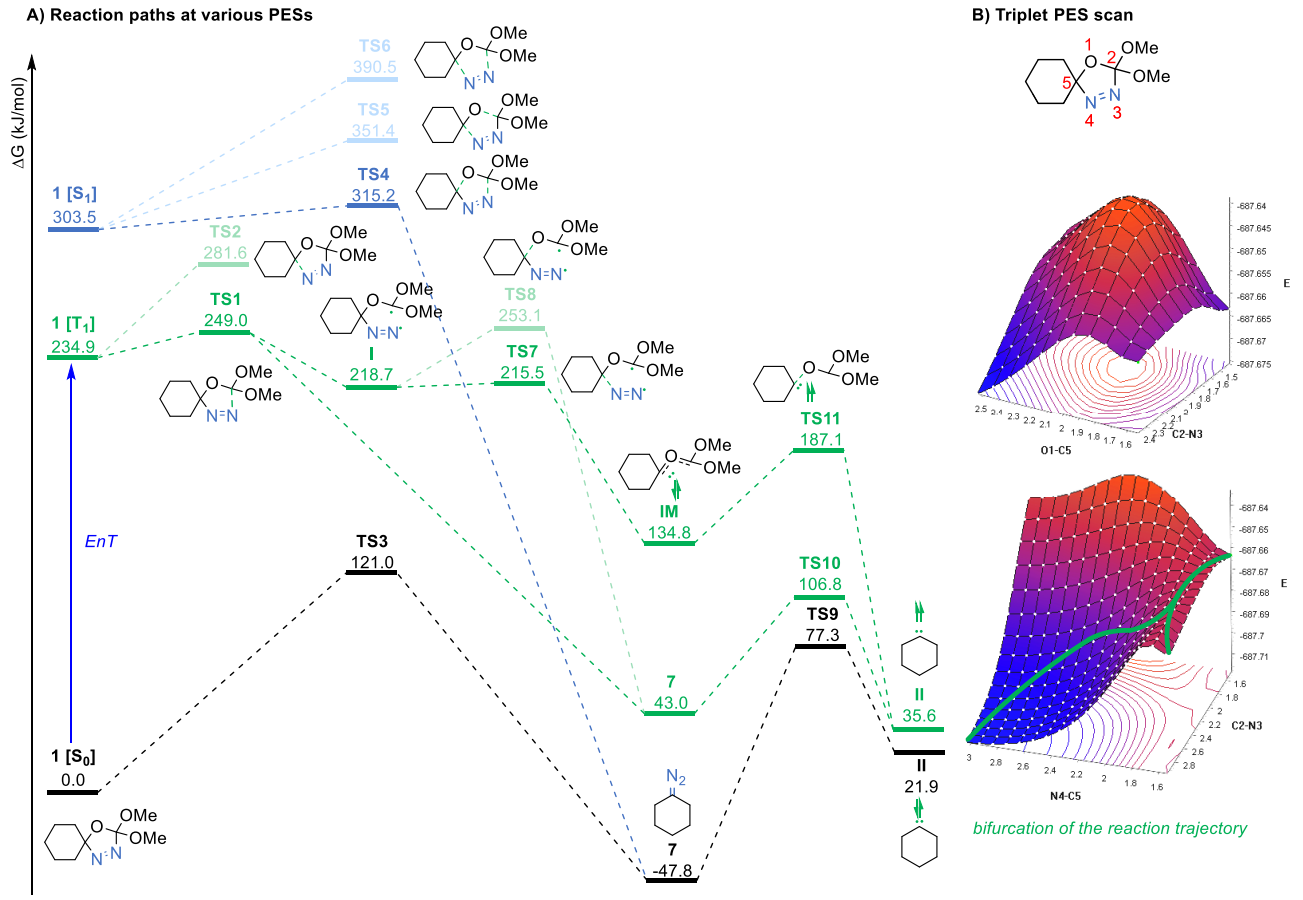
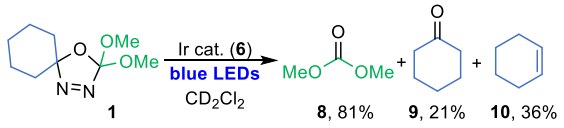


Figure 2. Various decomposition paths of oxadiazoline 1, calculated at the M06/6-311++G(d,p)/SMD(DCM)//B3LYP-D3/6-31G(d) level of theory (TD-DFT for S_1 PES).

Scheme 2. Initial Experiments—Proof of Concept[a]

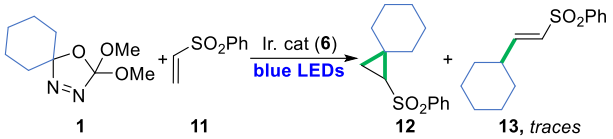


[a]Conditions: {Ir[dF(CF_3)ppy]$_2$(dtbpy)}PF_6 (**6**, 0.5 mol %), oxadiazoline (**1**, 0.1 mmol), CD_2Cl_2 (0.05 M), blue LEDs (450 nm, 25 W, for details see Supporting Information), Ar atmosphere, 17 h. NMR yields, CH_2Br_2 used as internal standard.

6). In contrast, the reaction exposed to UV irradiation without the catalyst added yielded compound **12** in only 10%, regardless of almost full conversion of the starting materials (entry 7), thus corroborating the significance of the triplet−triplet energy transfer process for the reaction selectivity.

We evaluated the influence of the substitution pattern at the position C_2 on the reaction yield by testing oxadiazolines **2**−**5** under the developed conditions (Scheme 3). Within all analogues tested, only reagent **1** proved to be an adequate substrate and efficiently furnished desired cyclopropane **12**. Thioalkoxy derivative **2** with a triplet state energy level almost equal to oxadiazoline **1** brought only 18% yield within a multitude of byproducts, along with dibenzyl sulfide. Although the calculated emission maxima for derivatives **3** and **4** are comparable, the reaction outcomes differ significantly. Oxadiazoline **3** yielded product **12** in 40% yield despite full conversion of olefin **11**. In this case, we cannot exclude the

Table 1. Background and Optimization Studies of Visible-Light-Induced Cyclopropanation



entry	deviation from standard conditions[a]	yield of **12** (%)[b]
1	none	41
2	no catalyst **6**	0
3	no light	0
4	no light, no catalyst **6**, in toluene, 110 °C	0
5	2.0 equiv of **1**	71
6[c]	0.25 mol % of catalyst **6**, 2.0 equiv of **1**, 1 h, 25 °C	81
7[cd]	UV light, no catalyst **6**, 2.0 equiv of **1**, 1 h, 25 °C	10

[a]Conditions: {Ir[dF(CF_3)ppy]$_2$(dtbpy)}PF_6 (**6**, 1 mol %), oxadiazoline (**1**, 0.5 mmol, 5.0 equiv), phenyl−vinyl sulfone (**11**, 0.1 mmol), DCM_{anh} (0.05 M), blue LEDs (450 nm, 25 W), 17 h, 18 °C. [b]Isolated yields. [c]DCM p.a. grade was used. [d]365 nm light was used.

formation of other reaction intermediates, since 2-methyl-2-methoxy derivatives are known to fragment unselectively upon thermolysis.[45,46] When oxadiazoline **4** was used, a complex mixture of products formed with only traces of the desired product and cyclohexyl benzoate, the latter presumably originating from a diradical species—an intermediate postulated for 2-phenyl derivatives.[47] Oxadiazoline **5**, which proved

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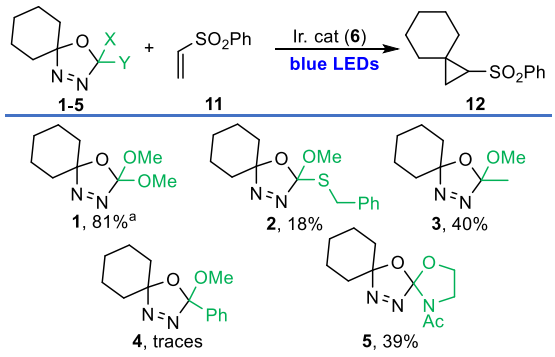
Scheme 3. Cyclopropanation with Various Oxadiazolines[b]



[a]Isolated yield. [b]Conditions: {Ir[dF(CF$_3$)ppy]$_2$(dtbpy)}PF$_6$ (**6**, 0.25 mol %), oxadiazoline (**1**−**5**, 0.4 mmol, 2.0 equiv), PVS (**11**, 0.2 mmol), DCM (0.05 M), blue LEDs (450 nm, 25 W), 1 h, 25 °C, GC yields.

unstable under electrochemical conditions (see SI Section 6.3), provided cyclopropane **12** with only a moderate yield.

These findings demonstrate that an appropriate E_T value is not the only prerequisite required for ensuring the reaction efficiency. Among crucial factors are also the stability, as well as reactivity, of generated intermediates, which we shall take into consideration.

Mechanistic Investigations. Various experiments were performed to investigate the reaction mechanism. The Stern−Volmer analysis confirmed the interaction between the excited state of photocatalyst **6** and oxadiazolines, revealing the correlation between the E_T value of the latter and their Ir fluorescence quenching ability (Figure 3). For oxadiazolines

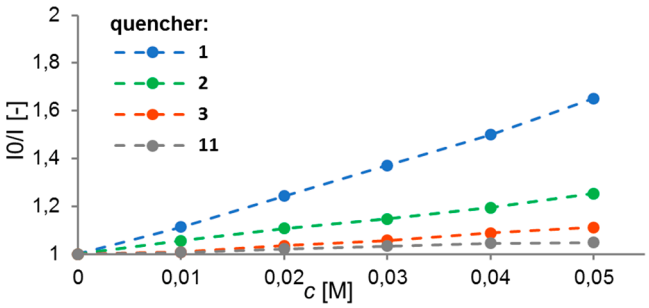


Figure 3. Stern−Volmer (SV) Analysis for Photocatalyt **6**.

1−**3**, the higher the E_T value is, the lower the quenching rate constant is [**1** (256.0 kJ/mol) < **2** (256.2 kJ/mol) < **3** (264.4 kJ/mol), and **1** (5.42×10^6 s^{-1} M^{-1}) > **2** (2.20×10^6 s^{-1} M^{-1}) > **3** (9.35×10^5 s^{-1} M^{-1})]. Thus, the lower the E_T is for oxadiazoline, the more intensive the quencher of the Ir catalyst luminescence is. In contrast, no significant influence of substrate **11** was observed on the fluorescence intensity of catalyst **6**.

Furthermore, the formation of product **12** via a competitive single electron transfer (SET) process was ruled out because oxadiazoline **1** exhibits oxidation and reduction potentials (for details see SI Section 6.3) significantly exceeding those of the examined photocatalysts (Table 2). Expectedly, sensitizers with low E_T values were not effective in catalyzing the cyclopropanation reaction (catalysts **14**−**16**). Although iridium catalysts **17** and **18** with triplet energy levels comparable with those of oxadiazoline **1** catalyzed the reaction, they were less efficient. Interestingly, the model reaction in the presence of a common organic triplet sensitizer, thioxanthone (**19**, λ_{max} = 360 nm),[50] which exhibits remarkably long-lived and highly energetic triplet species, provided cyclopropane **12** in diminished yield (63%), even upon increased catalyst loading and the use of violet light. The application of short-lived xanthone (**20**, λ_{max} = 340 nm)[50] also gave desired product **12** but in much lower yield (25%); pyrazoline **21** was isolated (70%) instead, similarly to the catalyst-free reaction performed under violet LEDs (Table 3, entries 1, 2).

The 1,3-dipolar cycloaddition of sulfone **11** to diazoalkane **7** leads to compound **22**, which isomerases to isolated heterocycle **21** (NMR analysis, see SI Section 6.7). The generation of the diazo compound from oxadiazoline **1** via direct photolysis exhibits slow kinetics because only traces of product **21** formed within 1 h in the catalyst-free conditions (entry 3). In contrast, the Ir-photosensitized cyclopropanation efficiently yields cyclopropane **12** after 1 h of irradiation (entry 4). The distinct distribution of products upon direct photolysis and in the Ir-catalyzed reaction unambiguously indicates that these processes operate via different mechanisms involving various reactive intermediates. While direct absorption of violet light by reagent **1** slowly leads to diazoalkane **7**, a triplet sensitization presumably gives fast access to dialkyl carbenes. If accessed in that way, as is typical for the triplet energy transfer process, they should possess triplet multiplicity and undergo stepwise addition to olefin **11**, thereby generating a diradical species. Overall, these studies reveal a high absorption coefficient and long excited state lifetime of a catalyst, together with its triplet energy level comparable with the E_T value of a substrate, as prerequisites for the reaction efficacy.

The radical nature of the mechanism was verified with experiments in the presence of TEMPO (Scheme 4A). The reaction was halted completely once the radical trap was added prior to exposure to light. When added just 2 min after the start of the reaction, cyclopropane **12** formed, though in a diminished yield along with pyrazoline **21**. ESI-MS analysis of the reaction mixture revealed the presence of a peak corresponding to TEMPO adduct **23**, formed from a radical generated upon the addition of triplet carbene to olefin **11**. The observation of pyrazoline **21** in the radical trapping experiment suggests the parallel diazoalkane **7** formation under the developed conditions. This was further supported by the isolation of heterocycle **21** when the reaction was stopped after 2 min (Scheme 4B). Because this compound is not observed under optimal conditions, one can conclude that 1-pyrazoline **22** converts to cyclopropane **12** during the reaction course. In fact, preprepared compound **22** efficiently transformed into cyclopropane **12** when exposed to blue LED irradiation in the presence of catalyst **6** (Scheme 4C). These results directly point to compound **22** and, therefore, diazoalkane **7** as intermediates involved along with carbene in the reaction mechanism.

Alkylidene carbenes, especially those with a cyclic structure, are extremely reactive species with short lifetimes (0.1−0.7 ns in C_6H_{12} for cyclohexylidene),[33] so for EPR measurements, DMPO (5,5-dimethyl-1-pyrroline *N*-oxide) and MNP (2-methyl-2-nitrosopropane) as spin traps were used, the latter being a typical carbene trapping agent.

Simulations performed with the EasySpin package in Matlab revealed EPR spectra of the reaction mixture as a superposition of multiple components when DMPO was applied, which predominantly arose from capturing the diazenyl radical **I**

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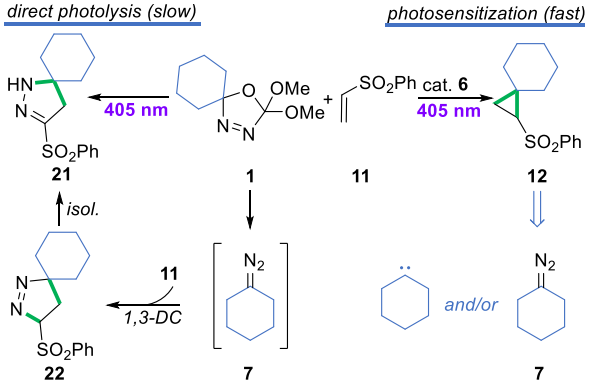
Table 2. Photophysical Properties of Commonly Used Photocatalysts

photocatalyst[a]	E_T [kJ/mol]		τ [ns]	yield of **12** [%][b,c]
$Ru(bpy)_3Cl_2$ (**14**)	205	increasing E_T	1100	0
$Ir[(dtbbpy)(ppy)_2]PF_6$ (**15**)	206		557	traces
fac-$Ir(ppy)_3$ (**16**)	231		1900	traces
$Ir[dF(Me)ppy)_2(dtbbpy)]PF_6$ (**17**)	252		1221	50
$[Ir(dFCF_3ppy)_2(bpy)]PF_6$ (**18**)	253		2280	49
$Ir[dF(CF_3)ppy)_2(dtbpy)]PF_6$ (**6**)	258		2300	(71)
thioxantone (**19**)	265		73000	63[d,e]
xanthone (**20**)	310		20	25[d,e]

[a]Photophysical properties of listed photocatalyst from reported data.[42,48,49] [b]Conditions: photocatalyst (1 mol %), oxadiazoline (**1**, 0.5 mmol, 5.0 equiv), phenyl−vinyl sulfone (**11**, 0.1 mmol), $DCM_{anh.}$ (0.05 M), blue LEDs (450 nm, 25 W), 17 h, 18 °C. [c]GC yields, isolated yields in parentheses. [d]Irradiation with violet LEDs (405 nm, 25 W). [e]2.5 mol % of catalyst loading.

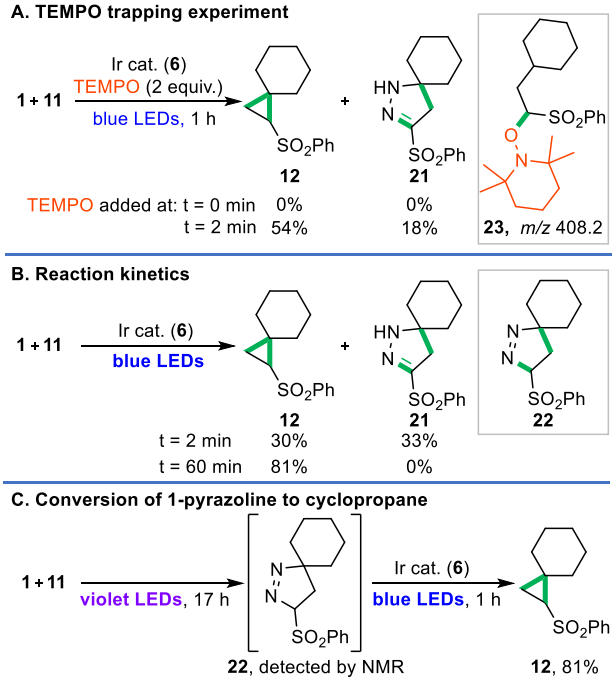
Table 3. Oxadiazoline Reactivity under Violet Light Irradiation



entry	conditions[a]	yield of **12** [%][b]	yield of **21** [%][b]
1	xanthone (**20**, 2.5 mol %), 17 h	25	70
2	catalyst-free, 17 h	15	62
3	catalyst-free, 1 h	0	traces
4	catalyst **6** (0.25 mol %), 1 h	84	0

[a]Conditions: oxadiazoline (**1**, 0.5 mmol, 5.0 equiv), phenyl−vinyl sulfone (**11**, 0.1 mmol), $DCM_{anh.}$ (0.05 M), violet LEDs (405 nm, 25 W), 18 °C. [b]Isolated yields.

Scheme 4. Mechanistic Experiments



(Figure 4A, for details, see SI Section 6.9). However, one of the signals could be tentatively ascribed to a biradical species, which correlates well with carbene−DMPO adduct **c1** [Figure 4A, hyperfine couplings (HFCs): a_N = 1.22 mT, a_H = 2.27 mT for the nitroxide moiety and a_N = 0.31 mT, $a_{H(nitroxide)}$ = 1.87 mT, and $a_{H(CH_2)}$ = 1.45 mT for the cyclohexane moiety with rather fast spin exchange (J = 6.55 mT)]. The formation of carbene was further implied in an experiment with the MNP spin trap because a weak signal between the DTBN peaks (di-*tert*-butyl nitroxide) of parameters matching to a biradical adduct **c2** appeared (Figure 4B; for details see SI Section 6.9).

For better insight into the reaction mechanism, putative intermediates resulting from the reactivity of diazoalkane **7** toward olefin **11** were investigated computationally in both singlet (black) and triplet (green) spin states (Figure 5). At a singlet PES, the concerted cycloaddition of diazocyclohexane **7**, which provides product **22**, should proceed more feasibly (**TS12** with $\Delta G‡$ = 82.5 kJ/mol) than its prior denitrogenation through **TS9** that leads to singlet carbene **II** ($\Delta G‡$ = 125.1 kJ/mol).

In contrast, triplet **7** (calculated E_T = 195.8 kJ/mol, see SI Table T8), would preferentially lose the N_2 molecule rather than enter a stepwise addition to olefin **11** (**TS10** and **TS13**, $\Delta G‡$ = 63.8 and 77.9 kJ/mol). If a stepwise process occurs, the subsequent intermediate **IM1** is prone to dinitrogen elimination along a practically barrierless path leading to biradical **III**.

The alternative cyclization of **IM1** to heterocycle **22** through a **TS16** is hardly accessible ($\Delta G‡$ = 104.6 kJ/mol), while the

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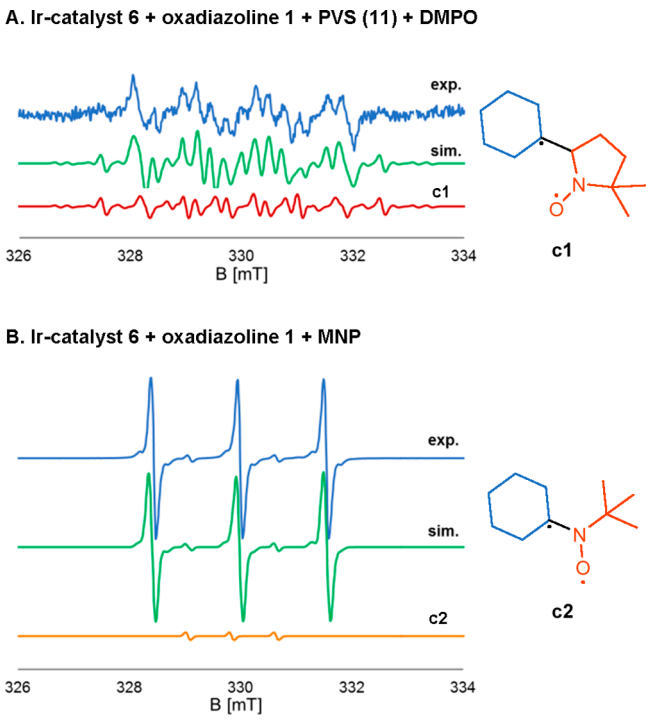


Figure 4. EPR spectra of selected reagents with (A) DMPO and (B) MNP used as the spin trap (spin traps added 15 s after irradiation); whole spectra (exp., experimental; sim., simulated) and selected components with plausible structures attached.

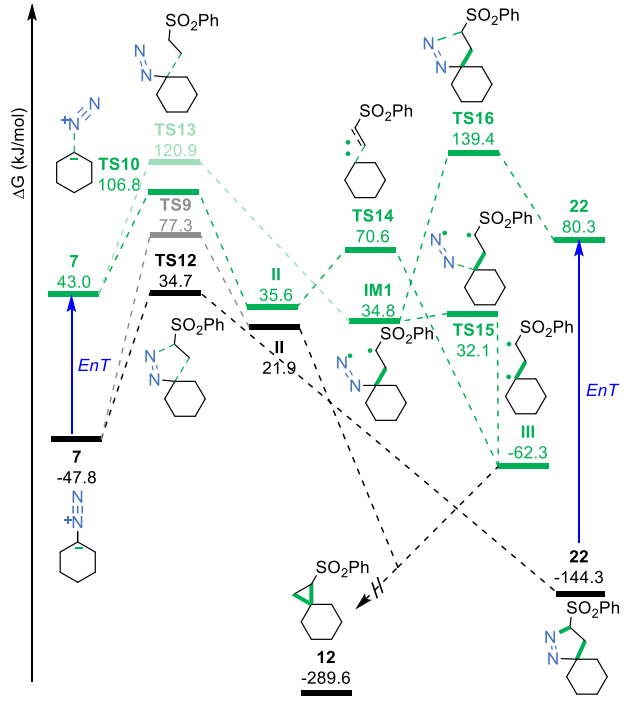
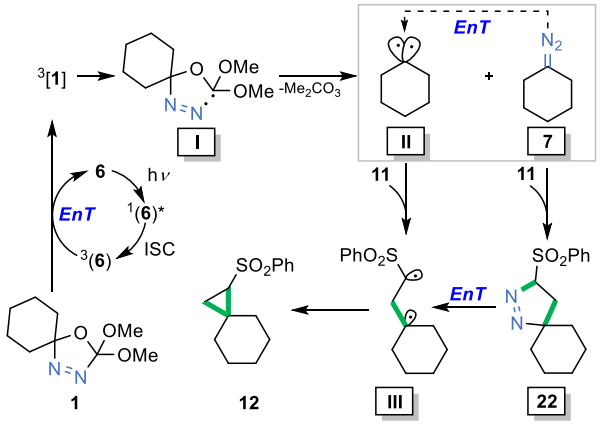


Figure 5. Plausible reaction paths calculated at the M06/6311++G(d,p) /SMD(DCM)//B3LYP-D3/6-31G(d) level of theory.

reverse decomposition process of triplet pyrazoline **22** (accessed via *E*nT from sensitizer **6**) ultimately leading to biradical **III** seems a viable reactivity channel ($\Delta G‡$ = 59.1 kJ/mol). Conversely, the extrusion of nitrogen from compound **22** in a close-shell process is sluggish ($\Delta G‡$ = 147.2 kJ/mol) but would lead to olefin **13**, which may also originate from the insertion of a singlet carbene **II** into the C−H bond of sulfone **11** ($\Delta G‡$ = 81.5 kJ/mol).

On the basis of the above experimental and theoretical findings, a plausible mechanism is featured in Scheme 5. The

Scheme 5. Plausible mechanism



reaction is initiated with light absorption by catalyst **6** that, after intersystem crossing, transfers energy to oxadiazoline **1** in its triplet state. Consequently, the cleavage of the C_2−N_3 bond within oxadiazoline leads to the literature-known[36] diazenyl radical **I**, that decomposing to triplet carbene **II** and diazoalkane **7**. Regardless of the source of species **II**, in the presence of olefin **11**, it furnishes cyclopropane **12** in a stepwise manner with diradical intermediate **III**.

Concurrently, diazoalkane **7** undergoes 1,3-dipolar cycloaddition to olefin **11**, thereby giving pyrazoline **22**, which is an intermediate that upon photosensitization leads to spirocyclopropane **12** through intermediate **III**. Mechanistic experiments confirm both carbene and diazoalkane-mediated pathways; however, at this point, no evidence is known for if any pathway prevails.

Scope and Limitation Studies. The spirocyclopropane scaffold is found in numerous, naturally occurring, bioactive compounds and constitutes a useful building block in the synthesis of carbocycles and heterocycles, etc.[51−54] For this reason, efficient methods for their preparation are highly valued. Therefore, we resolved to evaluate the utility of the developed methodology in the synthesis of structurally diverse spirocyclopropanes (Scheme 6). To this end, reactions with a variety of oxadiazolines substituted variously at the C_5 position were performed. Starting materials bearing cycloalkylidenes of different size are well tolerated giving spirocyclic products **24**−**28** in decent yields (45−76%). Interestingly, the oxadiazoline containing the cyclopropyl moiety furnishes product **29** in 78% with the cyclopropyl group remaining intact. Although no rearrangement occurs, this cannot be recognized as evidence of a nonradical mechanism since diradical species thermally generated from the analogous 2-phenyl-2-methoxy derivative were postulated to undergo reactions that are faster than the cyclopropane ring opening.[47] A modest yield for oxetane **32** (36%) was observed, presumably because of the strain generated upon the formation of the spirocycle or because of the higher reactivity and, therefore, lower selectivity of the generated intermediates. Generally, for reactions leading to compounds **32**−**35**, a decrease in yield was observed; in contrast, *N*-tosyl derivative **36** formed productively (82%). Intrigued by the distinct reactivities displayed by oxadiazolines

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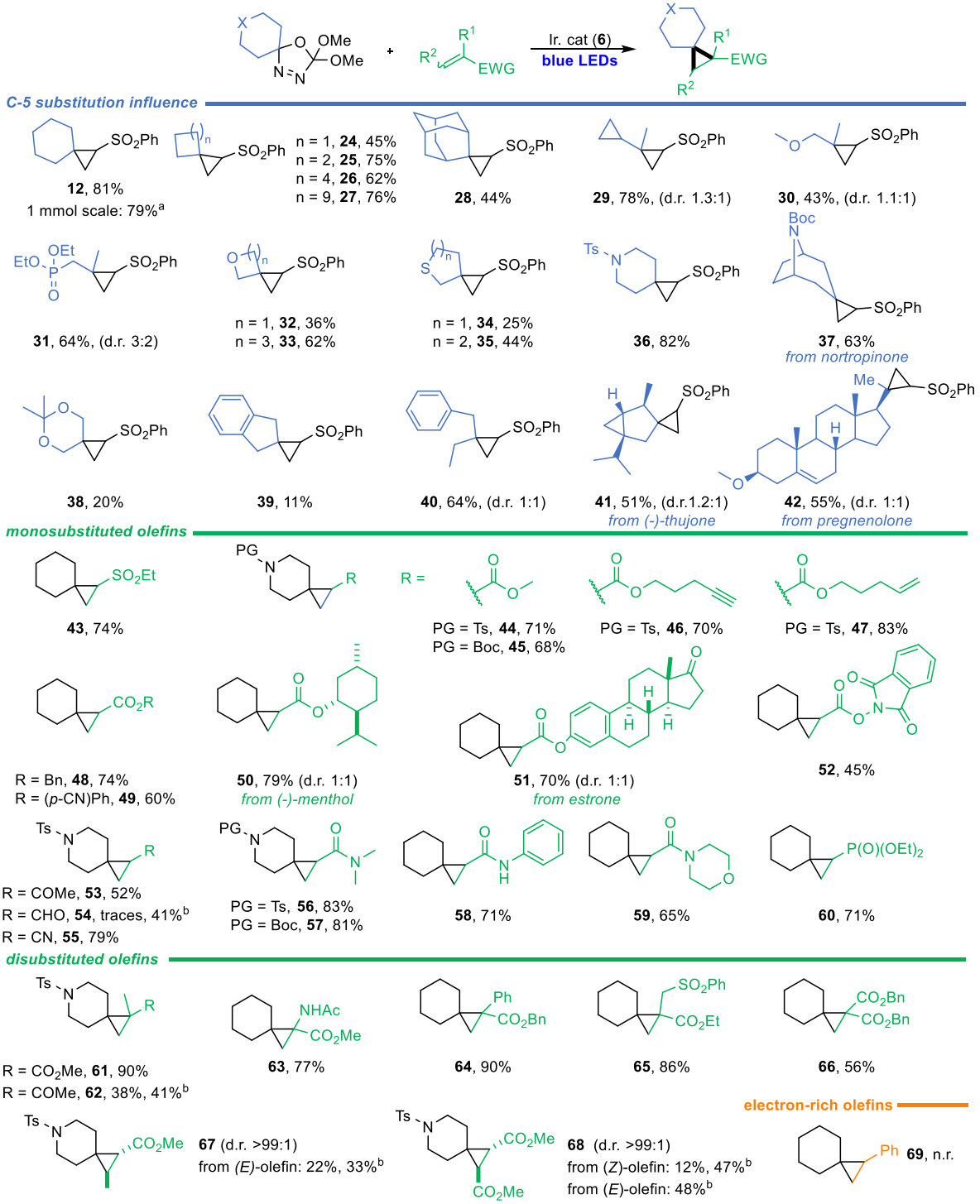
Scheme 6. Spirocyclopropane Synthesis under Visible Light Irradiation[c]



[a]Reaction performed on 10 W LEDs for 5 h. [b]Oxadiazoline used as the limiting substrate (5.0 equiv, 1.0 mmol); n.r. = no reaction. [c]Conditions: $\{Ir[dF(CF_3)ppy]_2(dtbpy)\}PF_6$ (**6**, 0.25 mol %), oxadiazoline (0.4 mmol, 2.0 equiv), olefin (0.2 mmol), DCM (0.05 M), blue LEDs (450 nm, 25 W), 1 h, 25 °C.

S10–**S12**, we estimated their E_T values (see SI Table T8). These are considerably lower than triplet energy levels predicted for 5,5-cyclohexylidene analogues **1**–**5**. The obtained values correspond well with the Stern–Volmer analysis (see SI Section 6.5), which revealed that reagent **S12** (E_T = 247.0 kJ/mol), which has a k_q remarkably higher than all other examined derivatives (1.18×10^7 s^{-1} M^{-1}), affords cyclopropane **36** in high yield (82%). Beneficially, oxadiazolines derived from naturally occurring nortropinone, (−)-α-thujone, and prognenolone efficiently furnished spirocycles **37**, **41**, and **42**, thereby emphasizing the utility of the developed method. Moreover, the reaction can be performed on a larger scale, but prolonged irradiation time is required

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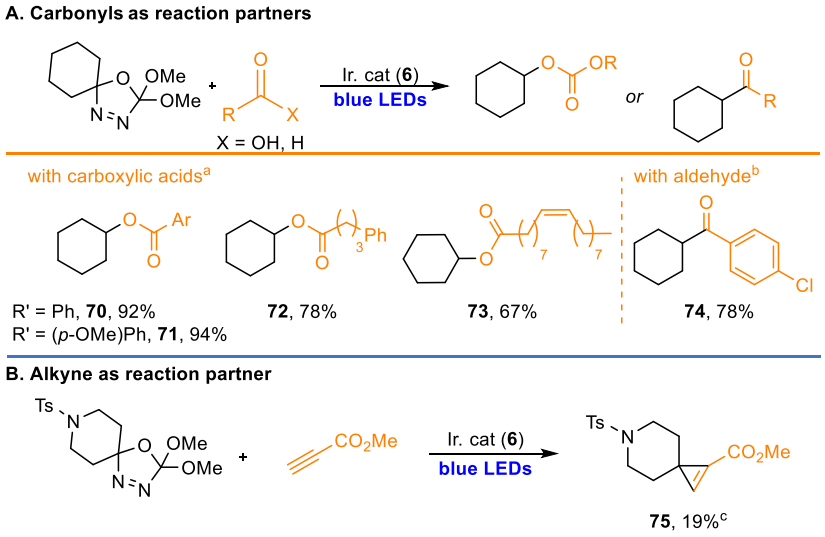
Scheme 7. Preliminary Studies on Other Transformations



[a]Conditions: {Ir[dF(CF$_3$)ppy]$_2$(dtbpy)}PF$_6$ (**6**, 0.25 mol %), oxadiazoline (**1**, 0.2 mmol, 2.0 equiv), acid (0.1 mmol), DCM (0.1 M), blue LEDs (447 nm, 7 W), 1.5 h, 25 °C. [b]Conditions: {Ir[dF(CF$_3$)ppy]$_2$(dtbpy)}PF$_6$ (**6**, 0.25 mol %), oxadiazoline (**1**, 1.0 mmol, 5.0 equiv), aldehyde (0.2 mmol), DCM (0.05 M), blue LEDs (450 nm, 25 W), 2.5 h, 25 °C. [c]Conditions: {Ir[dF(CF$_3$)ppy]$_2$(dtbpy)}PF$_6$ (**6**, 0.25 mol %), oxadiazoline (**S12**, 0.4 mmol, 2.0 equiv), alkyne (0.2 mmol), DCM (0.05 M), blue LEDs (450 nm, 25 W), 1 h, 25 °C, NMR yield with 1,3,5-trimetoxybenzene used as internal standard.

(79% for cyclopropane **12** in the case of 5 h of irradiation with 5 W blue LEDs, Scheme 6).

Next, we explored the scope of olefins in conjunction with oxadiazolines **1** and **S12** (Scheme 6). Numerous olefins that carry various electron-withdrawing groups, including sulfone (**43**), ester (**44**–**52**), ketone (**53**), nitrile (**55**), amide (**56**–**59**), and phosphonate (**60**) moieties, are well tolerated. The reaction proceeds selectively in the presence of unactivated alkenes and alkynes to furnish **46** and **47** with high yields. It is noteworthy that our method is suitable for late-stage functionalizations, as evidenced by the cyclopropanation of olefins bearing menthol and estrone scaffolds (**50** and **51**, 79% and 70%, respectively). Although acrolein initially did not react productively, the modification of a substrate ratio enabled the synthesis of product **54** in decent yield (41%). Additionally, various *N*-protecting groups are well tolerated, thereby providing cyclopropanes **44** and **45**, as well as **56** and **57**, with comparable efficacies. Geminal olefins with either one EDG and one EWG or two EWG groups work similarly to monosubstituted alkenes with yields even up to 90% for **61** and **64**. Products **67** and **68** can be synthesized from vicinal alkenes, albeit in considerably lower yields that can be improved upon by increasing the amount of olefin used.

We could not observe any discrimination between the (*E*)- and (*Z*)-isomers of the starting material, with the more thermodynamically favorable *trans* diastereoisomer furnished solely from olefins of both configurations (products **67** and **68**), which further supports a stepwise, diradical-mediated mechanism. Expectedly, the reaction with styrene did not led to spirocycle **69**, indicating electron-rich olefins as a limitation of the method.

The developed strategy is not limited to the cyclopropanation reaction: preliminary studies also uncovered oxadiazolines as suitable starting materials for O–H insertion into carboxylic acids (Scheme 7A). Both aryl and alkyl carboxylic acids efficiently reacted with oxadiazoline **1**, which led to corresponding cyclohexyl esters **70**–**73** in yields up to 94%. When an aldehyde was applied as the reaction partner, ketone **74** was obtained similarly to the Ley et al. report.[38] Additionally, we were able to proceed a cyclopropenation reaction, albeit with low efficiency, possibly because of the low stability of cyclopropene **75** (Scheme 7B).

CONCLUSIONS

Herein, we have demonstrated that 1,3,4-oxadiazolines — known as extremely stable diazo precursors — give access to reactive dialkyl intermediates when activated by a photosensitizer under visible light irradiation, which we utilized for the efficient synthesis of spirocyclopropanes. The proposed approach not only eliminates the need for the use of highly energetic UV light, thus enabling broader applications, but also alters the reaction pathway. While the developed photosensitized method affords cyclopropanes, violet-light-mediated direct photolysis leads to 2-pyrazolines. The use of UV-light impedes the reaction selectivity. It is, therefore, the visible-light-induced energy transfer event from the excited state of the photocatalyst to 1,3,4-oxadiazolines that makes the reported method compatible with numerous electron-deficient olefins to furnish spirocyclopropanes productively.

Both experimental and theoretical investigations corroborate that alkylidene carbenes, as well as diazoalkanes, are intermediates in the reaction mechanism and reveal the appropriate triplet energy level of a sensitizer as crucial for the reaction efficacy. In addition, preliminary results, including the extension of the scope of the reaction partners to carbonyls and alkynes, are enclosed. Further studies on the reactivity of oxadiazolines under visible light irradiation are ongoing in our laboratories.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscatal.2c05319.

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Supplemental experimental details and procedures, optimization studies, mechanistic experiments, DFT calculations, EPR measurements and simulations, and spectral data for all new compounds (PDF)

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Author Contributions

K.O. and D.G.: methodology design. K.O., J.V.S., P.K., and K.K.: experimental investigations. K.Z.: EPR spectroscopy and simulations. I.D. and W.C.: calculations. K.O., D.G., and W.C.: manuscript writing, editing, reviewing. D.G.: supervision. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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