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Hantzsch Ester-Mediated Photochemical Transformations in the Ketone Series: Remote C(sp^3)−H Arylation and Cyclopentene Synthesis through Strain Release

Jan Paternoga, Jonas Kühlborn, Nils Ole Rossdam, and Till Opatz*

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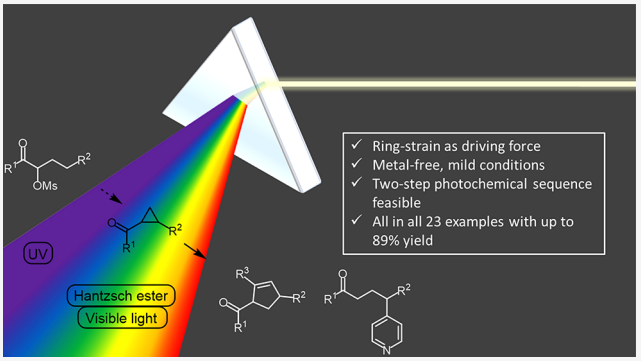
ABSTRACT: A metal-free Hantzsch ester-mediated synthesis of cyclopentenylketones as well as γ-hetarylketones starting from ketocyclopropanes under eco-friendly conditions was developed. The versatility of the developed conditions is shown by reacting ketocyclopropanes in both a formal [3 + 2] cycloaddition with terminal alkynes (further investigated using theoretical calculations) and a radical C−C-coupling with cyanopyridines. The newly developed methodologies were later on utilized as a downstream reaction for photogenerated cyclopropanes combining UV and visible light photochemistry. Following this procedure, a UV-driven Norrish−Yang-type reaction induces the ring strain of the intermediates, which serves as activation energy for the subsequent ring transformation.



INTRODUCTION

The utilization of ring strain as the driving force is a versatile tool in organic synthesis as complex structures can be synthesized from simple precursors ideally under very mild conditions. The incorporation of strained substrates ideally permits traceless transformations, where no low-energy co-products (e.g., metal halides, phosphine oxides, or borate salts) need to be formed simultaneously to effect the formation of new C−C or C−heteroatom bonds.[1] The inherent ring strain energy of small-ring systems, dominantly consisting of angular (Baeyer) strain and torsional (Pitzer) strain, makes them the ideal substrates for such reactions.[1,2] Eco-friendly transformations can be achieved when the ring strain is induced in a previous step by a photochemical valence isomerization or cycloaddition. In terms of green chemistry, light absorption in these cases provides the activation energy for both the synthesis of the strained intermediate and the downstream reaction in a two-step sequence. In the context of the photochemical generation of small-ring systems, the Norrish−Yang cyclization is an attractive methodology and can be used to generate different kinds of highly strained intermediates.[3] While the conventional Norrish−Yang reaction leads to the formation of hydroxycyclobutanes,[4] Wessig reported the formation of cyclopropylketones **2** by installing a leaving group in the α-position of the acyclic ketone substrate (Scheme 1).[5] As such cyclopropylketones contain a carbonyl group, the activation of which can trigger ring opening, they can serve as starting materials for various kinds of strain-releasing reactions.[1,6]

Our laboratory has recently contributed to the field of ring strain-releasing chemistry by developing two-step sequences that employ photogenerated 2-acylazirines in the synthesis of imidazoles[7] and (fused) pyrroles.[8,9] Based on the remarkable work on the Norrish−Yang reactions by Wessig, it appeared attractive to use photogenerated cyclopropanes as the simplest strained carbocycle intermediates in similar sequences. In terms of subsequent reactions of the ketocyclopropanes, several reports on both metal-[10] and photoredox-catalyzed[11] strain-releasing reactions were reported that were able to point out the synthetic potential for remote ring opening of such strained substrates by activation of the carbonyl group. Based on the reported lack of diastereoselectivity for the investigated ketocyclopropanes by Wessig,[5] we aimed at subjecting the photogenerated cyclopropanes to photoredox conditions to achieve a stereoconvergent synthesis via radical intermediates. In terms of single electron transfer (SET)-induced formal [3 + 2] reactions of substrates of this type, ring opening has successfully been triggered using a tandem catalytic system consisting of $[Ru(bpy)_3]^{2+}$ as a photoredox catalyst and the Lewis acid $Gd(OTf)_3$ to lower the redox potential of the carbonyl group.[11a,b] Alternatively, a chiral rhodium-based

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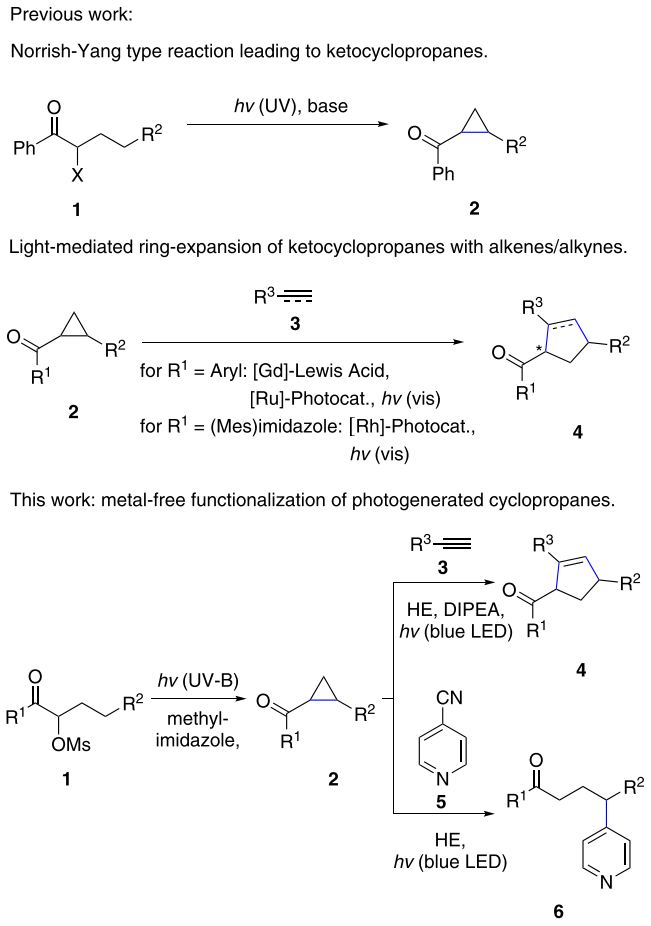
Scheme 1. Previous Work Regarding the Photochemical Synthesis and Related Ring-Opening Reactions of Ketocyclopropanes



photocatalyst that combines both of these functions in a single molecule can be used when the cyclopropane substrate contains an *N*-mesitylimidazole coordination anchor (Scheme 1).[11c]

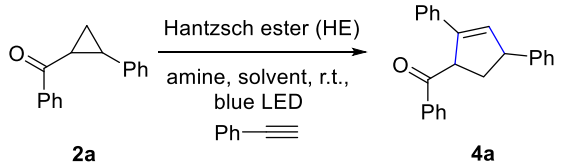
Although these methodologies offer an elegant solution to overcome the highly negative reduction potential of the carbonyl groups of ketones **2**, we sought to identify reaction conditions and a readily available and sustainable photocatalytic system to exploit the "green" aspects of such sequences. Encouraged by recent reports on the use of the strongly reducing photoexcited Hantzsch ester in SET reductions of aldehyde and ketone substrates,[12] it was attempted to first develop a metal-free methodology without additional Lewis acid activation of the carbonyl group or the use of an aiding anchor group starting from conventionally synthesized cyclopropanes. The newly developed methodology should be subsequently applied to cyclopropanes generated by the Norrish–Yang reaction with the spin-center shift described by Wessig.[5]

RESULTS AND DISCUSSION

The initial task of the present study was the identification of suitable reaction conditions for the Hantzsch ester-mediated formal [3 + 2] cycloaddition of cyclopropylketones **2**.

The conditions were optimized on model compound **2a**, as it is easily accessible through the Norrish–Yang cyclization and furnishes a benzyl-stabilized radical intermediate after initial ring opening. Since terminal alkenes have already been extensively studied as reaction partners,[11a−c] we focused on the use of terminal alkynes and phenylacetylene was chosen as the model substrate. The reaction conditions were subsequently optimized with respect to solvent, concentration, as well as equivalents of Hantzsch ester (HE) and amine additive (Table 1). The best results were obtained using

Table 1. Optimization Studies[a]



#	solvent	amine (equiv)	alkyne eq.	HE equiv	yield[b] (%)
1	MeCN	DABCO (2.0)	5.00	2.00	21
2	MTBE	DABCO (2.0)	5.00	2.00	34
3	PhMe	DABCO (2.0)	5.00	2.00	42
4	DMSO	DABCO (2.0)	5.00	2.00	17
5	MeOH	DABCO (2.0)	5.00	2.00	8
6	PhMe	TEA (2.0)	5.00	2.00	35
7	PhMe	Me-Im (2.0)	5.00	2.00	39
8	PhMe	DIPEA (2.0)	5.00	2.00	49
9	PhMe	DIPEA (2.0)	5.00	1.05	50
10	PhMe	DIPEA (2.0)	5.00	0.80	37
11	PhMe	DIPEA (1.1)	5.00	1.05	62
12	PhMe	DIPEA (1.1)	2.00	1.05	40
13	PhMe	DIPEA (1.1)	10.0	1.05	88 (84[c])
14	PhMe		10.0	1.05	48
15	PhMe	DIPEA (1.1)	10.0		0
16	PhMe	DIPEA (1.1)	10.0	1.05	0[d]

[a]Standard conditions: 0.1 mmol scale, 0.05 M, 5 cm distance to blue LED, Me-Im = 1-Methylimidazole. [b]Yields determined using phenanthrene or 1,4-bistrimethylsilylbenzene as internal standard. [c]Isolated yield. [d]Performed in the absence of light.

nonpolar solvents such as methyl *tert*-butyl ether (MTBE) and toluene, in which the HE is poorly soluble and therefore only a low concentration of dihydropyridine is present (entries 1–5). The comparison of different amine additives revealed little influence on the yield (entries 6–8). Nevertheless, the incorporation of diisopropylethylamine (DIPEA) showed the best results among the tested amines. Considering the results of the control reaction without additive which only led to a reduction in yield (entry 14) and the relatively high oxidation potential of methylimidazole (entry 7), the amine presumably only acts as a proton shuttle (*vide infra*). The yield was furthermore found to strongly depend on the concentration of the acetylene (entries 12–13). When the amount of acetylene was lowered, high-performance liquid chromatography/electrospray ionization mass spectrometry (HPLC/ESI-MS) reaction control qualitatively showed a higher percentage of ring-opened dimerization and hydrogenation products. Control reactions showed the reaction to selectively occur via the excited HE as both the reaction without the dihydropyridine and without light showed no conversion of the cyclopropane starting material (entries 15–16).

To investigate the robustness of the developed methodology, several terminal alkynes (cyclopentenes **4a–e**) and cyclopropanes (cylopentenes **4i–n**) were subjected to the optimized reaction procedure.

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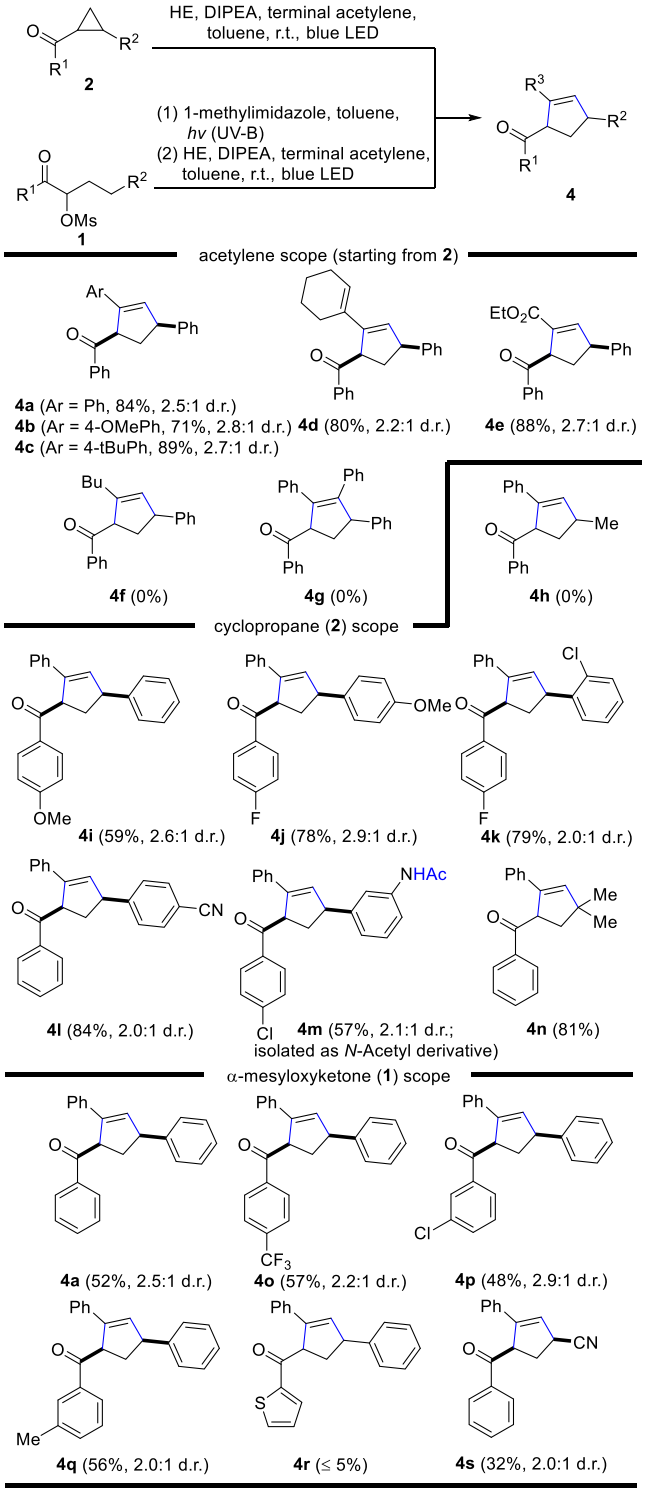
As shown in Table 2, terminal alkynes containing radical stabilizing aryl, alkenyl, and alkoxycarbonyl substituents furnished the corresponding cyclopentenes in high yields (71−89%) with a moderate diastereomeric ratio in the range of 2:1 to 3:1. In all of the investigated examples, the 1,4-*cis* configuration was found to be favored over the 1,4-*trans* configuration (determined using NOESY correlations on the diastereomeric mixtures). Both internal and terminal alkynes without stabilizing substituents (cyclopentenes **4f−g**) were found to give no [3 + 2] adducts, and only dimerized and hydrogenated products of the ring-opened cyclopropane were detected by HPLC/ESI-MS. The decoration of both the R^1 and R^2 aryl substituents in the cyclopropane with halogen, cyano, or methoxy substituents (cyclopentenes **4i−m**) as well as the incorporation of a *gem*-dimethyl group in the position of R^2 (cyclopentene **4n**) were tolerated well. Nevertheless, the higher reduction potential of the carbonyl accompanied with the increased electron density of the conjugated aromatic system in the synthesis of methoxy derivative **4i** resulted in longer reaction times and lower yield. Additionally, no product formation was observed when a cyclopropane with a monomethylated R^2 group (cyclopentene **4h**) was incorporated in the cyclization. The incorporation of a nitro-substituted arene as R^2 (cyclopentene **4m**) gave the amino-substituted cyclopropane first (as judged by HPLC/ESI-MS; see Figures S4 and S5 in the Supporting Information (SI)), which could be further reacted to the corresponding cyclopentene by increasing the amount of HE to 2.5 equiv. Although recent examples already showed the potential of the Hantzsch ester in deoxygenation reactions of nitroaromatics,[13] to the best of our knowledge, no photoreduction with the HE of an aromatic nitro group to the aniline has been described so far. For reasons of purification, the aniline was quantitatively transformed into the acetanilide derivative **4m**, which was obtained in 57% over two steps.

After a brief optimization of the Norrish−Yang reaction with spin-center shift toward higher yields and eco-friendliness for the investigated substrates (see Table S1 in the SI), a two-step telescoped methodology for the synthesis of cyclopentenes **4** starting from α-mesyloxyketones **1** was developed and investigated (cyclopentenes **4o−s**). Initially, a one-pot procedure was envisioned by adding the reactants of the formal [3 + 2] cycloaddition to the reaction mixture after the photoisomerization. However, as the precipitated imidazolium methanesulfonate salt was found to interfere with the downstream reaction, the salt was removed by simple filtration before performing the ring enlargement. As shown in Table 2, electronic variation of the aromatic R^1 moiety by introducing halogen, trifluoromethyl, or methyl groups was tolerated well and gave the corresponding cyclopentenes **4a+o−q** in moderate yields (48−57%) over two steps. Although HPLC/ESI-MS predictably showed diastereomeric mixtures for the photogenerated cyclopropane intermediates, the final products were formed with the same diastereoselectivity when starting from the pure *trans*-configurated cyclopropanes **2**.

To elucidate the symmetrizing effect of the radical intermediate **7** (*vide infra*), the diphenyl-substituted cyclopentene **4a** was both synthesized starting from α-mesyloxyketone **1a** and from pure 1,2-*trans*-configurated cyclopropane **2a** (Scheme 2). The photoisomerization of α-mesyloxyketone **1a** was previously found to give the cyclopropane **2a** in a diastereomeric ratio of 1.6:1 (Table S1 in the SI). The two-step protocol gave the cyclopentene **4a** in a similar diastereomeric ratio of 2.5 to 1 as the single-step reaction, confirming the symmetrizing effect of radical intermediate **7** (Scheme 3). Consequently, the formal cycloaddition was found to occur via a stereoselective mechanism, where the

Table 2. Substrate Scope of the Metal-Free Formal [3 + 2] Cycloaddition



Standard procedures:
2 to **4** (0.4 mmol scale): 0.40 mmol of **2**, 1.05 eq. HE, 1.10 eq. DIPEA, 10.0 eq. alkyne, 8.00 mL toluene, blue LED, r.t., 58-144h
1 to **4** (0.4 mmol scale):(1) 0.40 mmol of **1**, 2.00 eq. 1-methylimidazole, 40.0 mL toluene, UV-B, r.t., 0.5-2h
(2) 1.05 eq. HE, 1.10 eq. DIPEA, 10.0 eq. alkyne, 8.00 mL toluene, blue LED, r.t., 48-89h

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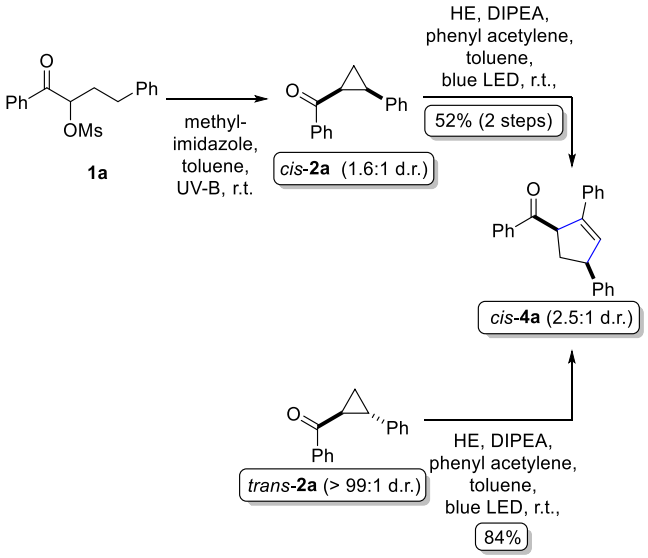
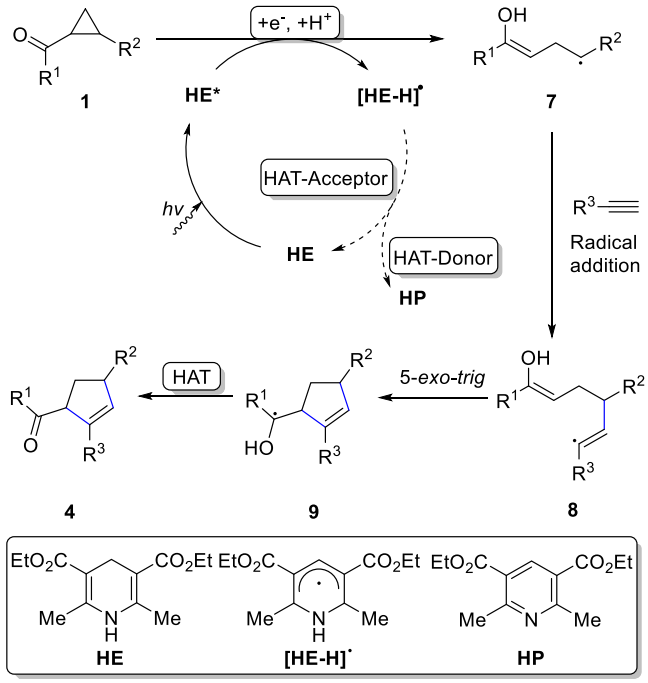
Scheme 2. Comparison between Single-Ring Expansion Reaction and Strain Induce/Strain Release Sequence with respect to Yield and Diastereomeric Ratio of the Cyclization Product and Intermediate



Scheme 3. Proposed Mechanism for the Hantzsch Ester-Mediated Synthesis of Cyclopentenes 4



stereoinformation of the cyclopropane **2** is obviously not transferred to cyclopentene **4** and the outcome of the reaction in terms of diastereoselctivity is solely based on the kinetics of the cyclization itself (see Figure 2). The 2-thienyl derivative **4r** as a model substrate for five-membered heteroaromatics as substituent R^1 only gave trace amounts of the respective product. Based on HPLC/ESI-MS, the limitation for this substrate likely results from an ineffective photoisomerization rather than from a problem in the formal [3 + 2] cycloaddition. Other radical stabilizing groups such as a nitrile group as R^2 (**4s**) were also tolerated but gave the cyclopentene in lower yield due to a higher tendency of the ring-opened radical **7** toward H-atom transfer (HAT) from HE. Such hydrogenation products were only found in traces for the other substrates.

Subsequently, the mechanism of the developed reaction was investigated. Since the Norrish–Yang reaction with spin-center shift has already been intensively studied,[5] we focused on the photoredox-mediated downstream reaction using the Hantzsch ester as a photoreductant. Initially, the ring opening of the cyclopropane was investigated by radical trapping experiments. The addition of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) to the reaction mixture of the formal [3 + 2] cycloaddition under standard conditions both inhibited the cyclization and gave the TEMPO adduct of ring-opened radical **7**, which could be verified with high-resolution mass spectrometry (HR-MS) and HPLC by comparing it with an authentic sample synthesized differently (see the SI for procedure and chromatograms).[14] Additionally, we were not able to observe any product formation by directly exciting the cyclopropane **2a** with UV-B irradiation, suggesting no energy transfer pathway to be present. Subsequently, we investigated the existence of an electron donor–acceptor (EDA) complex between the HE and the other reaction partners by UV/Vis titration experiments. Such experiments revealed characteristic charge transfer absorption bands in other HE-related reactions.[12c,13,15] Although we are unable to unambiguously rule out the presence of an EDA complex at present, no such CT bands could be found in our experiments (Figure 1, top; for detailed UV spectra with all reaction partners, see the SI). The light on/off experiment showed no product formation in the dark phases. During these studies, the aromatized Hantzsch pyridine **HP** was found to be formed in substoichiometric amounts with ratios of around three molecules of cyclopentene **4a** per molecule of pyridine (Figure 1, middle). The optimization studies also showed full conversion of the cyclopropane **2a** with substoichiometric amounts of HE (Table 1, entry 10), indicating the dihydropyridine to act as a catalyst to some extent. However, these reaction conditions were discarded due to lower yields and prolonged reaction times (see Table S2 in the SI). The SET-oxidized Hantzsch ester is rather known as an H-atom donor in HAT processes than for its reductive regeneration, which would be required in the redox-neutral reaction sequence. Moreover, no oxidizing agent was present in the reaction mixture so that the ketyl radical **9** is likely to be transformed into cyclopentene **4** through an HAT pathway involving the radical **9** as an H-atom donor. Possible HAT acceptors are the terminal acetylene **3** or the [HE-H] radical (*vide infra*). As the group of Yoon has challenged the significance of light on/off experiments in the investigation of radical chain mechanisms, an HAT to cyclopropane **2** cannot be excluded.[16] Evidence for HAT processes involving the acetylene used in excess were found during the purification of cyclopentene **4c**, where the nonvolatile 4-(*tert*-butyl)phenylacetylene could be reisolated to find a consumption of around 3.5 equiv based on the cyclopropane starting material. Accordingly, the cyclopentene formation is likely to proceed via the following mechanism (Scheme 3).

The ring-opened key intermediate **7** is generated by SET from the excited Hantzsch ester ($E_{1/2,calc.}(HE^{\bullet+}/HE^*) = -2.28$ V vs SCE)[12c] to the carbonyl of cyclopropane **2** ($E_{1/2,MeCN}(\mathbf{2a}/\mathbf{2a}^{\bullet-}) = -2.01$ V vs SCE) followed by proton transfer and ring opening. The assumption was further confirmed by Stern–Volmer studies showing the cyclopropane to quench the

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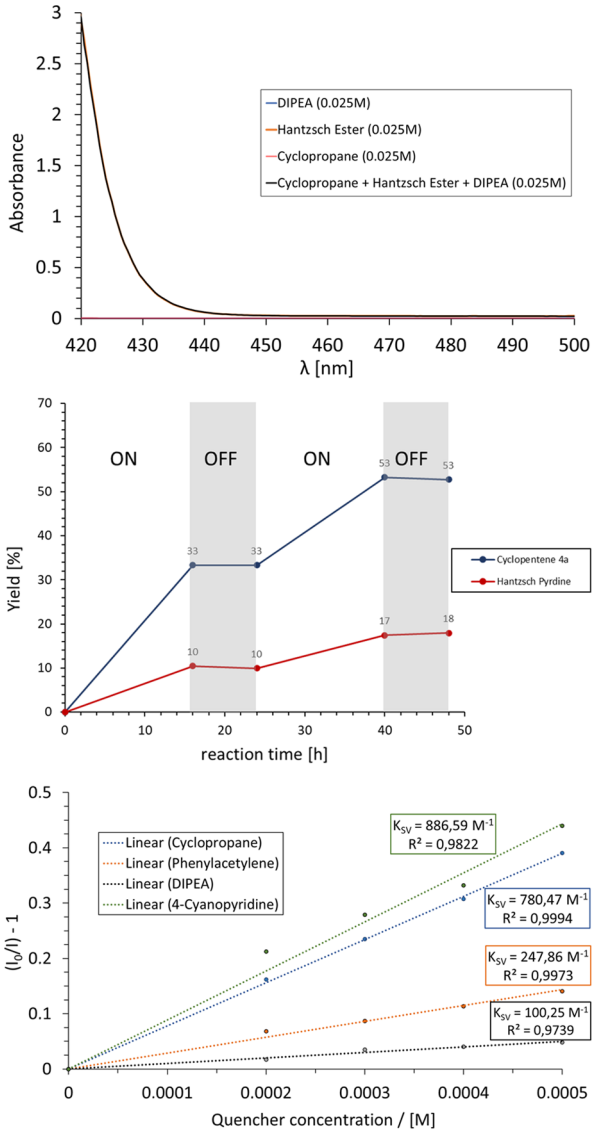

Figure 1. UV/Vis titration experiment (top), light on/off experiment (middle), and fluorescence quenching studies of Hantzsch ester (5×10^{-4} M in degassed $CHCl_3$) by 4-cyanopyridine **5** (green), cyclopropane **2a** (blue), phenylacetylene (orange) and DIPEA (black) (bottom).

fluorescence of the HE with the highest rate within the reaction components (Figure 1, bottom). The order and mechanism of the proton and the electron transfer were not investigated and might either involve sequential steps or a concerted mechanism, which was proposed for other HE-mediated reactions generating ketyl radicals.[12d,f,17] In this regard, the amine additive might act as a proton shuttle for the poorly soluble Hantzsch ester. Radical addition into the triple bond of the alkyne regioselectively leads to the more stabilized radical **8** that undergoes *5-exo-trig* cyclization forming ketyl radical **9**. The already discussed HAT finally yields cyclopentene **4**.

To gain insight into the origin of the preference for the 1,4-*cis* diastereomers during the *5-exo-trig* cyclization, DFT calculations on the uM06-2X-D3/6-31+G(d,p)/SMD-(toluene) level of theory[18] on the related transition states leading to the two possible diastereomers in the synthesis of model cyclopentene **4a** were performed (Figure 2).

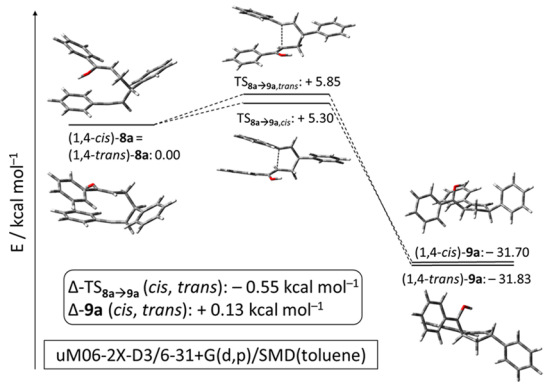

Figure 2. Elucidation of the preferred formation of the 1,4-*cis* isomers on model cyclopentene **4a** during the *5-exo-trig* cyclization based on the energy difference of the crucial transition states by density functional theory (DFT) calculations.

We opted for the use of the M06-2X functional[18a] (unrestricted formalism due to the open-shell system) in combination with the D3BJ dispersion correction,[18f,g] which was found to be the best hybrid functional for computing reaction energies by Grimme and Goerigk.[19] The unrestricted formalism was chosen rather than a restricted open-shell formalism since it has a lower computational cost and proved to be reasonably accurate for various applications.[20] The calculated results nicely matched the experimental observations in our case as well. The energies of the radicals **8a** with a geometrical preorientation leading to the two possible diastereomers were found to be identical. The energy of the transition states ($TS_{8a/9a}$), on the other hand, matches well with the observed d.r. values. Assuming the cyclization to be kinetically controlled, the energy difference of 0.55 kcal/mol favoring the transition state of the 1,4-*cis* over the 1,4-*trans* diastereomer translates into a calculated d.r. value of 2.5:1 at 298 K,[21] which matches exactly the experimental value (see Scheme 2). Further evidence for a kinetic control in the cyclization was found experimentally. An attempt of a subsequent thermodynamically driven equilibration of the diastereomeric mixture of cyclopentene **4a** toward higher d.r. values by activation of the carbonyl with Al_2O_3 only led to an ablation of the diastereoselectivity (see Figure S20 in the SI), indicating only little difference between the energies of the two diastereomers of cyclization product **4a**.

Next, the reactivity of the ring-opened radical **7** towards other reaction partners was investigated. Our lab has positive experience with reductively generated persistent radical anions of cyanopyridines in photoredox-mediated reactions.[22] Additionally, the Chu Lab demonstrated the Hantzsch ester to be able to reductively generate such radical anions via excited-state SET reduction.[15] As a test case and based on the relatively long lifetime of these radical anions, it was attempted to incorporate them in a radical−radical recombination with the HE-generated ring-opened radical **7**. In this reaction, the photoexcited HE serves as a single electron donor for the generation of both the cyanopyridine radical anion and the radical **7**. Gratifyingly, the C−C-coupling product **6a** between model cyclopropane **2a** and 4-cyanopyridine **5** was already formed in the first attempt. After conducting optimization experiments (Table S3 in the SI), the developed methodology was applied to a series of cyanopyridines (**6a−c**), cyclopropanes (**6d−f**), and α-mesyloxyketones (**6a+g−h**) to

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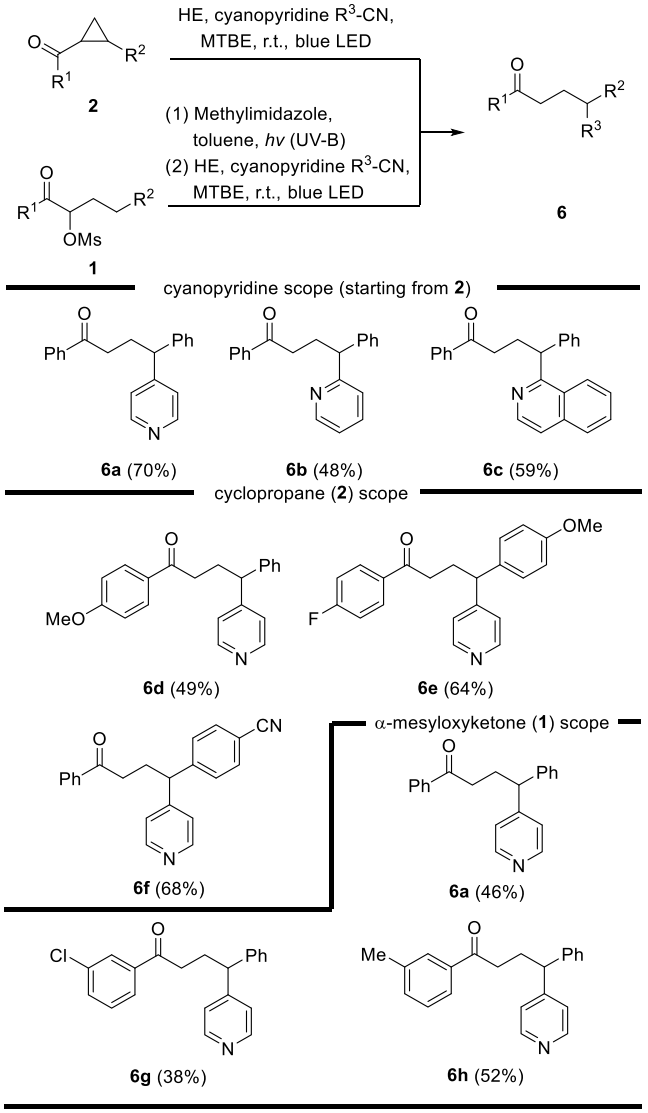
demonstrate the scope of the procedure (Scheme 4). The reaction of 4-cyanopyridine and model cyclopropane **2a** gave

Scheme 4. Substrate Scope of the Metal-Free Functionalization of Cyclopropanes with Cyanopyridines



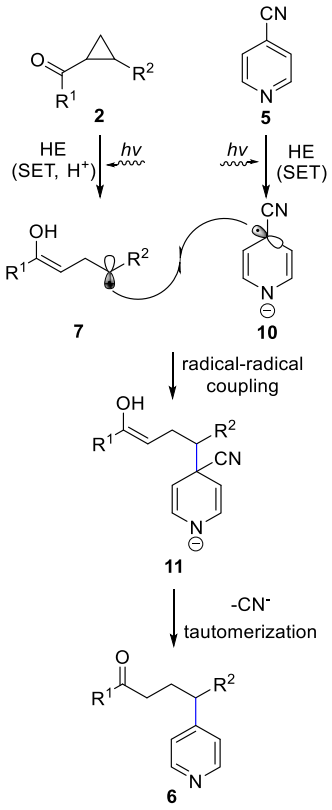
Standard procedures:
2 to **6** (0.30 mmol scale): 0.30 mmol of **2**, 2.30 eq. HE, 1.30 eq. cyanopyridine, 10.0 mL MTBE, blue LED, r.t., 24-78h
1 to **6** (0.30 mmol scale):(1) 0.30 mmol of **1**, 2.00 eq. 1-methylimidazole, 30.0 mL toluene, UV-B, r.t., 0.5-2h
(2) 2.30 eq. HE, 1.30 eq. cyanopyridine, 10.0 mL MTBE, blue LED, r.t., 24-48h

the 4-pyridinylated product in 70% yield. The 2-pyridinylated analogue **6b** was isolated in a moderate yield of 48%. Preliminary work showed the radical anion of 2-cyanopyridines not only to have significant electron density in the *ipso*-position but also in the 5-position, frequently resulting in lower yields.[22a] When the 5-position is blocked, for example, in 1-cyanoisoquinoline as a benzo-annulated 2-cyanopyridine analogue, the yield of the corresponding product **6c** increased to 59%.

A variation of the cyclopropane precursor again demonstrated the tolerance of methoxy-, halogen-, and cyano-substituted aromatics as R^1 and R^2 furnishing the γ-pyridinylated ketones **6d–f** in moderate yields (49–68%). Once again, the incorporation of an electron-rich substituent in the aromatic R^1 resulted in longer reaction times and lower yields. The developed methodology could also be transformed into a telescoped procedure starting from α-mesyloxyketones **1**, formally leading to a dual-wavelength double photochemical remote reductive hetarylation of these substrates. Comparable to the results of the formal [3 + 2] cycloaddition sequence, the pyridinylated products **6a+g–h** were obtained in moderate yield over two steps (38–52%).

Based on the previous results, the mechanism of the pyridinylation of the cyclopropane is assumed to be straightforward (Scheme 5). Both the ring-opened radical **7**

Scheme 5. Proposed Mechanism for the Synthesis of γ-Pyridinylated Ketones 6



and the radical anion of the cyanopyridine **5** ($E_{1/2}$ (**5**/**5**$^{\bullet-}$) = −1.87 V vs SCE)[23] are reductively generated by the excited HE. This assumption was further confirmed as cyclopropane **2a** and 4-cyaonpyridine **5** were found to quench the fluorescence of HE in a similar magnitude (Figure 1, bottom). Radical–radical coupling as a consequence of the higher concentration of the long-lived cyanopyridine radical anion **10** (persistent radical effect)[24] followed by elimination of cyanide subsequently give the γ-pyridinylated ketone **6**. While the generation of the ring-opened radical **7** was verified in the radical trapping experiments, the ability of the HE to generate the persistent radical anions of 4-cyanopyridine was demonstrated in the literature.[15]

CONCLUSIONS

In summary, a metal-free photochemical synthesis of ketocyclopentenes and γ-hetarylated ketones was developed starting from conventionally synthesized ketocyclopropanes. Furthermore, the methodology could be implemented into a

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facile metal-free two-step double photochemical synthesis of such products combining a strain-inducing UV-driven step for the generation of a strained cyclopropane intermediate with the downstream visible light photoredox-catalyzed strain-releasing reactions. To emphasize the sustainability aspects of the sequences, the use of benign solvents as well as the readily available Hantzsch ester as a photoreductant was implemented for the two reactions.

EXPERIMENTAL SECTION

Materials and Methods. Acetonitrile (MeCN), dichloromethane (DCM), 1,2-dichloroethane (DCE), and cyclohexane were distilled from calcium hydride under a nitrogen atmosphere. Solvents were degassed using freeze−pump−thaw cycles or by bubbling argon through the liquid in an ultrasonic bath. Deuterochloroform was stored over basic alumina (Brockmann activity I). All reagents were purchased from commercial suppliers and used without further purification. Water- or oxygen-sensitive reactions were performed under an atmosphere of nitrogen in oven-dried glassware using standard Schlenk techniques. Photochemical reactions using UV light were performed in quartz tubes using a photochemical reactor equipped with a circular array of 16 UV lamps (Ushio G8T5E (7.2 W, λ_{max} = 306 nm)), a magnetic stirrer, and a cooling fan. Visible light photochemical reactions were performed using blue LEDs (Kessil A150W Deep Ocean Blue, 34 W, $\lambda_{max} \approx$ 460 nm) that were placed next to the reaction mixture in a 10 mL Schlenk tube (distance, 5 cm). For more information and the emission spectra of the lamps, see the Supporting Information. Thin-layer chromatography was carried out on silica gel 60 F_{254} plates and visualized using UV light. Preparative normal-phase chromatography was carried out on silica gel (35−70 μm) using manual flash chromatography or an automatic flash purification system. Preparative reversed-phase chromatography was performed on an HPLC system with a C_{18}PFP or H-Tec column (pore size: 5 μm, length: 15 cm, diameter: 30 mm) or on an automatic flash purification system with C_{18}-modified silica gel columns and using mixtures of acetonitrile and water as eluent. Melting points were determined in open capillary tubes and are not corrected. NMR spectra were recorded on a 300, 400, or 600 MHz instrument at 23 °C using standard pulse sequences. The ^{1}H and ^{13}C{H} chemical shifts (δ) were referenced to the residual solvent signal as an internal standard ($CDCl_3$: δ = 7.26 and 77.16 ppm).[25] The ^{19}F NMR were referenced to an external standard (^{19}F: α,α,α-trifluorotoluene in $CDCl_3$, δ = −63.9 ppm). Structural assignments were made with additional information from gCOSY, gHSQC, gNOESY, and gHMBC experiments. FT-IR spectra (given in cm^{-1}) were recorded using a diamond ATR unit. HPLC/ESI-MS spectra were recorded using an HPLC system with a UV diode array detector coupled with an LC/MSD ion trap. Mixtures of water (with 0.1% formic acid) and acetonitrile were used as an eluent at a total flow rate of 1.0 mL/min. High-resolution masses (APCI-MS and ESI-MS) were recorded using a Q-ToF instrument with dual source and suitable external calibrant.

Ketone Synthesis. Ketones **12** were synthesized using an optimized method of Van Aerschot and co-workers:[26] To a solution of 1-bromo-3-phenylpropane (1.40 equiv) and magnesium (1.40 equiv) in dry THF (c = 0.60 mmol/mL) was added a catalytic amount of iodine, and the suspension was refluxed for 0.5 h. The reaction mixture was cooled to room temperature, and the corresponding nitrile (1.00 equiv) in THF (c = 2.00 mmol/mL) was added dropwise. The solution was stirred at 70 °C until thin-layer chromatography (TLC) or HPLC/ESI-MS showed full consumption of the starting material (2−16 h). The reaction mixture was cooled to room temperature, and saturated ammonium chloride solution (50 mL) was slowly added to quench the excess of Grignard reagent. The phases were separated, and the aqueous phase was further extracted with ethyl acetate (3 × 50 mL). The organic phase was dried over $NaHCO_3$, and the solvent was removed *in vacuo*. The crude products were purified by automatic flash column chromatography (eluent: cyclohexane/ethyl acetate) to afford the ketones **12**.

*1,4-Diphenylbutan-1-one (**12a**).* Following the general procedure using benzonitrile (3.06 mL, 30.0 mmol, 0.98 mL, 1.00 equiv) after column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 95:5 → 80:20) afforded the title compound (6.10 g, 27.2 mmol, 91%) as a colorless solid. R_f = 0.51 (4:1 cyclohexane/ethyl acetate). Mp: 54−55 °C (cyclohexane/ethyl acetate), lit.[27] mp: 54−57 °C. IR/cm^{-1} (ATR): 3061, 2936, 3026, 1684, 1597, 1496, 1407, 1226, 744, 691. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95−7.90 (m, 2H), 7.58−7.52 (m, 1H), 7.48−7.41 (m, 2H), 7.36−7.24 (m, 2H), 7.24−7.17 (m, 3H), 2.99 (t, J = 7.5 Hz, 1H), 2.73 (t, J = 7.5 Hz, 1H), 2.15−2.03 (m, 2H). ^{13}C{H} NMR (75 MHz, $CDCl_3$) δ 200.1, 141.7, 137.0, 132.9, 128.6, 128.5, 128.4, 128.0, 125.9, 37.7, 35.2, 25.7. MS (ESI): m/z = 225.1 $[M + H]^+$. The spectroscopic data are in accordance with the literature.[27]

*1-(4-Trifluoromethylphenyl)-4-phenylbutan-1-one (**12b**).* Following the general procedure using 4-trifluoromethylbenzonitrile (20.0 mmol, 2.68 mL, 1.00 equiv) after column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 95:5 → 80:20) afforded the title compound (3.09 g, 10.60 mmol, 53%) as a colorless solid. R_f = 0.41 (4:1 cyclohexane/ethyl acetate). Mp: 69−71 °C (cyclohexane/ethyl acetate), lit.[28] mp: 74−75 °C. IR/cm^{-1} (ATR): 2942, 1686, 1410, 1328, 1161, 1115, 1069, 827, 748, 703. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04−7.98 (m, 2H), 7.75−7.68 (m, 2H), 7.35−7.27 (m, 2H), 7.25−7.18 (m, 3H), 3.00 (t, J = 7.4 Hz, 2H), 2.74 (t, J = 7.4 Hz, 2H), 2.19−2.03 (m, 2H). ^{13}C{H} NMR (75 MHz, $CDCl_3$) δ 199.0, 141.4, 139.6, 134.3 (q, J = 32.7 Hz), 128.51, 128.47, 128.3, 126.1, 125.7 (q, J = 3.8 Hz), 123.6 (q, J = 272.7 Hz), 37.9, 35.0, 25.4. MS (ESI): m/z = 293.1 $[M + H]^+$. The spectroscopic data are in accordance with the literature.[28]

*1-(3-Chlorophenyl)-4-phenylbutan-1-one (**12c**).* Following the general procedure using 3-chlorobenzonitrile (20.0 mmol, 2.41 mL, 1.00 equiv) after column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 95:5 → 80:20) afforded the title compound (3.65 g, 14.1 mmol, 71%) as a yellow oil. R_f = 0.47 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3026, 1688, 1571, 1241, 1222, 1196, 786, 752, 700, 680. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 7.88 (t, J = 1.6 Hz, 1H, H-2′), 7.78 (dt, J = 7.8, 1.6 Hz, 1H, H-6′), 7.55−7.49 (m, 1H, H-4′), 7.39 (t, J = 7.8 Hz, 1H, H-5′), 7.34−7.27 (m, 2H, H-3″ + H-5″), 7.24−7.16 (m, 3H, H-2″ + H-4″ + H-6″), 2.95 (t, J = 7.5 Hz, 2H, H-2), 2.72 (t, J = 7.5 Hz, 2H, H-4), 2.08 (p, J = 7.5 Hz, 2H, H-3). ^{13}C{H} NMR, HSQC, HMBC (75 MHz, $CDCl_3$) δ 198.8 (C-1), 141.5 (C-1″), 138.5 (C-1′), 134.9 (C-3′), 132.9 (C-4′), 129.9 (C-5′), 128.5 (C-3″ + C-5″), 128.5 (C-2″ + C-6″), 128.2 (C-2′), 126.1 (C-6′), 126.0 (C-4″), 37.7 (C-2), 35.1 (C-4), 25.5 (C-3). MS (ESI): m/z = 259.1 $[M + H]^+$. HRMS (APCI-ToF) m/z: $[M + H]^+$ calcd for $C_{16}H_{16}ClO$ 259.0884, found 259.0883.

*1-(3-Methylphenyl)-4-phenylbutan-1-one (**12d**).* Following the general procedure using 3-methylbenzonitrile (20.0 mmol, 2.40 mL, 1.00 equiv) after column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 97:3 → 85:15) afforded the title compound (4.38 g, 18.4 mmol, 66%) as a colorless solid. R_f = 0.60 (4:1 cyclohexane/ethyl acetate). Mp: 39−40 °C (cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2924, 1683, 1604, 1454, 1270, 745, 699. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75−7.69 (m, 2H), 7.38−7.32 (m, 2H), 7.32−7.27 (m, 2H), 7.24−7.17 (m, 3H), 2.97 (t, J = 7.5 Hz, 2H), 2.73 (t, J = 7.5 Hz, 2H), 2.40 (s, 3H), 2.09 (p, J = 7.5 Hz, 2H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 200.4, 141.7, 138.3, 137.0, 133.7, 128.6, 128.5, 128.42, 128.39, 125.9, 125.3, 37.7, 35.2, 25.8, 21.4. MS (ESI): m/z = 239.1 $[M + H]^+$. The spectroscopic data are in accordance with the literature.[29]

*1-(2-Thienyl)-4-phenylbutan-1-one (**12e**).* Following the general procedure using 2-cyanothiophene (20.0 mmol, 1.86 mL, 1.00 equiv) after column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 95:5 → 80:20) afforded the title compound (1.69 g, 7.30 mmol, 37%) as a yellow oil. R_f = 0.38 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2937, 1660, 1416, 1236, 857, 725, 700. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 7.65 (dd, J = 3.8, 1.1 Hz, 1H, H-3′), 7.62 (dd, J = 5.0, 1.1 Hz, 1H, H-5′), 7.33−7.26 (m, 2H, H-3″ + H-5″),

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7.24−7.16 (m, 3H, H-2″ + H-4″ + H-6″), 7.11 (dd, J = 5.0, 3.8 Hz, 1H, H-4′), 2.92 (t, J = 7.5 Hz, 2H, H-2), 2.72 (t, J = 7.5 Hz, 2H, H-4), 2.16−2.03 (m, 2H, H-3). ^{13}C{H} NMR, HSQC, HMBC (75 MHz, $CDCl_3$) δ 193.1 (C-1), 144.4 (C-2′), 141.5 (C-1″), 133.4 (C-5′), 131.7 (C-3′), 128.5 (C-2″ + C-6″), 128.4 (C-3″ + C-5″), 128.0 (C-4′), 126.0 (C-4″), 38.5 (C-2), 35.2 (C-4), 26.1 (C-3). MS (ESI): m/z = 231.0 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{14}H_{15}OS$ 231.0838, found 231.0838.

*4-Cyano-1-phenylbutan-1-one (**12f**).* The title compound was synthesized using a procedure of the Streuff group.[30] The spectroscopic data are in accordance with the literature.[30]

α-Mesyloxyketone synthesis. The α-mesyloxyketones **1** were synthesized applying a modified method of Wessig:[5] To a solution of the corresponding ketone **12** (1.00 equiv) in MeCN (c = 0.40 M) was added [hydroxy(mesyloxy)iodo]benzene (1.20 equiv), and the solution was stirred at 70 °C until TLC or HPLC/ESI-MS showed full consumption of the starting material (16−40 h). The excess of hypervalent iodine reagent was quenched with saturated sodium thiosulfate solution (20 mL), and the mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4, and the solvent was removed *in vacuo*. The residue was purified by automatic flash column chromatography (eluent: cyclohexane/ethyl acetate) to afford the α-mesyloxyketones **1**.

*1,4-Diphenyl-2-mesyloxybutan-1-one (**1a**).* Following the general procedure using 1,4-diphenylbutan-1-one (2.24 g, 10.0 mmol, 1.00 equiv) after 16 h, column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 95:5 → 60:40) afforded the title compound (2.23 g, 7.00 mmol, 70%) as a slightly yellow solid. R_f = 0.21 (4:1 cyclohexane/ethyl acetate). Mp: 40−42 °C (cyclohexane/ethyl acetate), lit.[5] mp: 52−57 °C. IR/cm^{-1} (ATR): 3028, 2938, 1699, 1597, 1450, 1352, 1173, 883, 697, 525. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75−7.67 (m, 2H), 7.65−7.55 (m, 1H), 7.48−7.38 (m, 2H), 7.39−7.29 (m, 2H), 7.31−7.17 (m, 3H), 5.92−5.85 (m, 1H), 3.17 (s, 3H), 2.97−2.77 (m, 2H), 2.28−2.15 (m, 2H). ^{13}C{H} NMR (75 MHz, $CDCl_3$) δ 195.2, 139.7, 134.3, 133.9, 129.1, 128.9, 128.6, 126.8, 80.2, 39.6, 34.3, 31.3. MS (ESI): m/z = 341.1 $[M + Na]^+$. The spectroscopic data are in accordance with the literature.[5]

*1-(4-Trifluoromethylphenyl)-2-mesyloxy-4-phenylbutan-1-one (**1b**).* Following the general procedure using 4-phenyl-1-(4-trifluormethylphenyl)-butan-1-one (5.00 mmol, 1.46 g, 1.00 equiv) after 16 h at 70 °C, column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 95:5 → 70:30) afforded the title compound (1.45 g, 3.70 mmol, 75%) as a colorless solid. R_f = 0.13 (4:1 cyclohexane/ethyl acetate). Mp: 108−110 °C. IR/cm^{-1} (ATR): 1706, 1323, 1168, 1128, 1067, 932, 820, 701, 524. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 7.80−7.76 (m, 2H, H-2′ + H-6′), 7.70−7.66 (m, 2H, H-3′ + H-5′), 7.38−7.32 (m, 2H, H-3′ + H-5″), 7.30−7.25 (m, 1H, H-4″), 7.24−7.20 (m, 2H, H-2″ + H-6″), 5.87−5.80 (m, 1H, H-2), 3.18 (s, 3H, SO_2CH_3), 2.97−2.78 (m, 2H, H-4), 2.25−2.15 (m, 2H, H-3). ^{13}C{H} NMR, HSQC, HMBC (75 MHz, $CDCl_3$) δ 194.4 (C-1), 139.31 (C-1″), 136.5 (C-1′), 135.3 (q, $^2J_{CF}$ = 33.0 Hz, C-4′), 128.9 + 128.2 (C-2′ + C-6′ + C-3″ + C-5″), 128.8 (C-2″ + C-6″), 126.8 (C-4″), 126.0 (q, $^3J_{CF}$ = 3.7 Hz, C-3′ + C-5′), 123.30 (q, $^1J_{CF}$ = 273.0 Hz, C-4′-CF_3), 79.6 (C-2), 39.4 (SO_2CH_3), 33.8 (C-3), 31.1 (C-4). ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.34 (s, CF_3). MS (ESI): m/z = 409.1 $[M + Na]^+$. HRMS (ESI-ToF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{17}F_3O_4SNa$ 409.0692, found 409.0692.

*1-(3-Chlorophenyl)-2-mesyloxy-4-phenylbutan-1-one (**1c**).* Following the general procedure using 4-phenyl-1-(3-chlorophenyl)-butan-1-one (5.00 mmol, 1.29 g, 1.00 equiv) after 18 h at 70 °C, column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 95:5 → 70:30) afforded the title compound (1.38 g, 3.90 mmol, 78%) as a colorless solid. R_f = 0.25 (4:1 cyclohexane/ethyl acetate). Mp: 107−108 °C. IR/cm^{-1} (ATR): 3065, 1703, 1351, 1240, 1172, 938, 753, 701, 525. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 7.67 (t, J = 1.9 Hz, 1H, H-2′), 7.58−7.51 (m, 2H, H-4′ + H-6′), 7.39−7.28 (m, 4H, H-5′ + H-3″-5″), 7.28−7.19 (m, 2H, H-2″ + H-6″), 5.79 (t, J = 6.2 Hz, 1H, H-2), 3.17 (s, 3H, SO_2CH_3), 2.97−2.76 (m, 2H, H-4), 2.25−2.15 (m, 2H, H-3). ^{13}C{H} NMR, COSY, HSQC (75 MHz, $CDCl_3$) δ 194.0 (C-1), 139.3 (C-1″), 135.4 + 135.2 (C-1′ + C-3′), 134.1 (C-4′), 130.3 (C-5′), 128.9 (C-3″ + C-5″), 128.8 (C-2″ + C-6″), 128.5 (C-2′), 126.8 (C-4″), 126.4 (C-6″), 79.6 (C-2), 39.5 (SO_2CH_3), 33.9 (C-3), 31.1 (C-4). MS (ESI): m/z = 375.0 $[M + Na]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{17}H_{18}ClO_4S$ 353.0609, found 353.0606.

*1-(3-Methylphenyl)-2-mesyloxy-4-phenylbutan-1-one (**1d**).* Following the general procedure using 1-(3-methylphenyl)-4-phenylbutan-1-one (3.00 mmol, 0.71 g, 1.00 equiv) after 16 h at 70 °C, column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 95:5 → 60:40) afforded the title compound (789 mg, 2.38 mmol, 79%) as a colorless oil. R_f = 0.22 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2937, 1696, 1348, 1260, 1170, 937, 846, 681, 525. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 7.55−7.49 (m, 1H, H-6′), 7.46−7.43 (m, 1H, H-2′), 7.42−7.36 (m, 1H, H-4′), 7.36−7.28 (m, 3H, H-5′ + H-2″ + H-6″), 7.27−7.20 (m, 3H, H-3″-5″), 5.94−5.85 (m, 1H, H-2), 3.17 (s, 3H, SO_2CH_3), 2.97−2.77 (m, 2H, H-3), 2.39−2.32 (m, 3H, C-3′-CH_3), 2.28−2.14 (m, 2H, H-4). ^{13}C{H} NMR, HSQC, HMBC (75 MHz, $CDCl_3$) δ 195.3 (C-1), 139.8 (C-1″), 139.0 (C-3′), 135.1 (C-4′), 133.8 (C-1′), 129.1−128.9 (6C, C-2′ + C-5′ + C-2″-3″ + C-5″-6″), 126.7 (C-4″), 125.7 (C-6″), 80.1 (C-2), 39.6 (SO_2CH_3), 34.3 (C-4), 31.2 (C-3), 21.4 (C-3′-CH_3). MS (ESI): m/z = 333.1 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{20}O_4SNa$ 355.0974, found 355.0971.

*1-(2-Thienyl)-2-mesyloxy-4-phenylbutan-1-one (**1e**).* Following the general procedure using 4-phenyl-1-(2-thienyl)-butan-1-one (3.00 mmol, 0.69 g, 1.00 equiv) after 18 h at 70 °C, column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 95:5 → 70:30) afforded the title compound (640 mg, 2.00 mmol, 66%) as a yellow solid. R_f = 0.15 (4:1 cyclohexane/ethyl acetate). Mp: 68−70 °C (cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3028, 1673, 1413, 1353, 1251, 1173, 969, 922, 854, 731, 525. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 7.72 (dd, J = 5.0, 1.1 Hz, 1H, H-5′), 7.48 (dd, J = 3.9, 1.1 Hz, 1H, H-3′), 7.37−7.30 (m, 2H, H-3″ + H-5″), 7.28−7.20 (m, 3H, H-2″ + H-4″ + H-6″), 7.11 (dd, J = 5.0, 3.9 Hz, 1H, H-4′), 5.66−5.60 (m, 1H, H-2), 3.14 (s, 3H, SO_2CH_3), 3.00−2.76 (m, 2H, H-4), 2.35−2.23 (m, 2H, H-3). ^{13}C{H} NMR, HSQC, HMBC (75 MHz, $CDCl_3$) δ 187.8 (C-1), 140.0 (C-2′), 139.6 (C-1″), 135.5 (C-5′), 133.2 (C-3′), 128.8 (C-3″ + C-5″), 128.7 (C-2″ + C-6″), 128.6 (C-4′), 126.6 (C-4″), 80.3 (C-2), 39.4 (SO_2CH_3), 34.8 (C-4), 31.1 (C-3). MS (ESI): m/z = 325.1 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}O_4S_2Na$ 347.0382, found 347.0382.

*4-Cyano-2-mesyloxy-1-phenylbutan-1-one (**1f**).* Following the general procedure using 4-cyano-1-phenylbutan-1-one (4.00 mmol, 0.69 g, 1.00 equiv) after 18 h at 70 °C, column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 92:8 → 50:50) afforded the title compound (850 mg, 3.20 mmol, 80%) as a colorless solid. R_f = 0.17 (2:1 cyclohexane/ethyl acetate). Mp: 57−58 °C (cyclohexane/ethyl acetate), lit.[5] mp: 60−62 °C. IR/cm^{-1} (ATR): 2940, 1699, 1354, 1174, 1056, 1001, 930, 698, 524. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.89 (m, 2H), 7.72−7.62 (m, 1H), 7.59−7.48 (m, 2H), 6.11−6.00 (m, 1H), 3.18 (s, 3H), 2.71−2.52 (m, 2H), 2.43−2.34 (m, 1H), 2.27−2.17 (m, 1H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 193.5, 134.8, 133.3, 129.3, 128.6, 118.0, 77.9, 39.4, 28.3, 13.4. MS (ESI): m/z = 268.0 $[M + H]^+$. The spectroscopic data are in accordance with the literature.[5]

Cyclopropane synthesis. The corresponding cyclopropanes were synthesized using an optimized procedure of Yoon and coworkers.[11b] The α,β-unsaturated ketones were commercially available or previously synthesized in our group using standard conditions.[31] To a mixture of trimethylsulfoxonium iodide (1.20 equiv) and NaH (60% in mineral oil, 1.20 equiv), dimethyl sulfoxide (DMSO) (c = 0.60 M) was added dropwise. After the hydrogen evolution ended, the corresponding chalcone (1.00 equiv) was added (portion-wise in case of solids, or dropwise in case of liquids as solution in DMSO (c = 2.00 M)). The mixture was stirred at room temperature until TLC or HPLC/ESI-MS showed full consumption of the starting material. The reaction was carefully quenched with water (50 mL) and extracted with Et_2O (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4, and the solvent was removed *in vacuo*. The crude

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product was purified by automatic flash column chromatography (eluent: cyclohexane/ethyl acetate) to afford cyclopropanes **2**.

*Phenyl-[phenylcyclopropyl]methanone (**2a**).* Following the general procedure using (2*E*)-1,3-diphenyl-2-propen-1-one (36.0 mmol, 7.50 g, 1.00 equiv) after stirring at room temperature for 16 h, flash column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 80:20) afforded the title compound (5.78 g, 26.0 mmol, 72%) as a colorless solid. R_f = 0.30 (50:1 cyclohexane/ethyl acetate). Mp: 44−46 °C (cyclohexane/ethyl acetate), lit.[5] mp: 45−47 °C. IR/cm^{-1} (ATR): 1667, 1449, 1398, 1343, 1223, 987, 925, 697. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02−7.99 (m, 2H), 7.57 (m, 1H), 7.49−7.45 (m, 2H), 7.35−7.30 (m, 2H), 7.26−7.22 (m, 1H), 7.20−7.18 (m, 2H), 2.92 (m, 1H), 2.71 (m, 1H), 1.94 (m, 1H), 1.57 (m, 1H). ^{13}C{H} NMR (151 MHz, $CDCl_3$) δ 198.6, 140.5, 137.7, 133.0, 128.6, 128.1, 126.6, 126.2, 30.1, 29.4, 19.3. MS (ESI): m/z = 223.1 [M + H]$^+$. The spectroscopic data are in accordance with the literature.[5]

*(4-Methoxyphenyl)-[2-phenylcyclopropyl]methanone (**2b**).* Following the general procedure using (2*E*)-3-phenyl-1-(4-methoxyphenyl)prop-2-en-1-one (10.0 mmol, 2.38 g, 1.00 equiv) after stirring for 18 h at room temperature, flash column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 97:3 → 75:25) afforded the title compound (2.07 g, 8.20 mmol, 82%) as a colorless solid. R_f = 0.47 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3006, 1656, 1599, 1260, 1228, 1168, 1027, 986, 742, 697. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−7.96 (m, 2H), 7.33−7.28 (m, 2H), 7.25−7.20 (m, 1H), 7.20−7.16 (m, 2H), 6.97−6.91 (m, 2H), 3.87 (s, 3H), 2.90−2.82 (m, 1H), 2.71−2.63 (m, 1H), 1.94−1.84 (m, 1H), 1.55−1.48 (m, 1H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 196.9, 163.4, 140.7, 130.7, 130.4, 128.5, 126.5, 126.2, 113.7, 55.5, 29.5, 28.9, 18.9. MS (ESI): m/z = 253.1 [M + H]$^+$. The spectroscopic data are in accordance with the literature.[32]

*(4-Fluorophenyl)-[2-(4-methoxyphenyl)cyclopropyl]methanone (**2c**).* Following the general procedure using (2*E*)-3-(4-methoxyphenyl)-1-(4-fluorophenyl)prop-2-en-1-one (8.20 mmol, 2.10 g, 1.00 equiv) after stirring at room temperature for 16 h, flash column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 96:4 → 80:20) afforded the title compound (1.87 g, 6.90 mmol, 84%) as a colorless solid. R_f = 0.36 (4:1 cyclohexane/ethyl acetate). Mp: 74−75 °C (cyclohexane/ethyl acetate), lit.[33] mp: 74−75 °C. IR/cm^{-1} (ATR): 1666, 1598, 1516, 1250, 1223, 1156, 1033, 834, 596. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05−7.98 (m, 2H), 7.16−7.08 (m, 4H), 6.88−6.83 (m, 2H), 3.80 (s, 3H), 2.80−2.74 (m, 1H), 2.69−2.62 (m, 1H), 1.92−1.86 (m, 1H), 1.55−1.49 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ −(105.93−107.61) (m). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 197.0, 165.7 (d, J = 254.4 Hz), 158.5, 134.2 (d, J = 3.2 Hz), 132.3, 130.7 (d, J = 9.3 Hz), 127.4, 115.6 (d, J = 21.8 Hz), 114.0, 55.3, 29.7, 29.1, 19.0. MS (ESI): m/z = 271.1 [M + H]$^+$. The spectroscopic data are in accordance with the literature.[33]

*(4-Fluorophenyl)-[2-(2-chlorophenyl)cyclopropyl]methanone (**2d**).* Following the general procedure using (2*E*)-3-(2-chlorophenyl)-1-(4-fluorophenyl)prop-2-en-1-one (7.50 mmol, 1.95 g, 1.00 equiv) after stirring at room temperature for 18 h, flash column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 97:3 → 80:20) afforded the title compound (1.96 g, 7.20 mmol, 95%) as a colorless oil. R_f = 0.52 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2925, 1669, 1599, 1509, 1224, 1156, 1031, 754. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 8.10−8.02 (m, 2H, H-2′ + H-6′), 7.41−7.35 (m, 1H, H-3‴), 7.28−7.09 (m, 5H, H-3′ + H-5′ + H-4‴-6‴), 2.98−2.85 (m, 1H, H-2″), 2.79−2.67 (m, 1H, H-1″), 1.96−1.87 (m, 1H, H-3″a), 1.68−1.53 (m, 1H, H-3″b). ^{19}F NMR (282 MHz, $CDCl_3$) δ −106.78 (tt, J = 8.6, 5.4 Hz). ^{13}C{H} NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ 197.2 (CO), 165.85 (d, $^1J_{CF}$ = 254.4 Hz), 137.9 (C-1‴), 136.0 (C-2‴), 134.2 (d, $^4J_{CF}$ = 3.0 Hz, C-1′), 130.9 (d, $^3J_{CF}$ = 9.3 Hz, C-2′ + C-6′), 129.6 (C-3‴), 128.2 (C-4‴), 127.6 (C-6‴), 127.0 (C-5‴), 115.8 (d, $^2J_{CF}$ = 21.9 Hz, C-3′ + C-5′), 28.3 (C-2″), 27.5 (C-1″), 17.7 (C-3″). MS (ESI): m/z = 275.1 [M + H]$^+$. HRMS (ESI-ToF) m/z: [M + H]$^+$ calcd for $C_{16}H_{13}ClFO$ 275.0634, found 275.0636.

*(Phenyl)-[2-(4-cyanophenyl)cyclopropyl]methanone (**2e**).* Following the general procedure using (2*E*)-3-phenyl-1-(4-cyanophenyl)prop-2-en-1-one (3.50 mmol, 820 mg, 1.00 equiv) after stirring at room temperature for 18 h, flash column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 97:3 → 90:10) afforded the title compound (685 mg, 2.80 mmol, 79%) as a colorless solid. R_f = 0.25 (4:1 cyclohexane/ethyl acetate). Mp: 85−86 °C (cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3058, 2227, 1667, 1608, 1450, 1396, 1340, 1224, 988, 821, 713, 559. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01−7.96 (m, 2H), 7.62−7.56 (m, 3H), 7.51−7.45 (m, 2H), 7.30−7.23 (m, 2H), 2.97−2.92 (m, 1H), 2.77−2.70 (m, 1H), 2.01−1.93 (m, 1H), 1.61−1.55 (m, 1H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ = 197.8, 146.4, 137.5, 133.4, 132.5, 128.8, 128.3, 127.0, 110.4, 29.7, 29.3, 19.9. MS (ESI): m/z = 248.1 [M + H]$^+$. The spectroscopic data are in accordance with the literature.[34]

*(4-Chlorophenyl)-[2-(3-nitrophenyl)cyclopropyl]methanone (**2f**).* Following the general procedure using (2*E*)-3-(4-chlorophenyl)-1-(3-nitrophenyl)prop-2-en-1-one (3.5 mmol, 1.01 g, 1.00 equiv) after stirring for 20 h at room temperature, flash column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 97:3 → 90:10) afforded the title compound (0.75 g, 2.48 mmol, 71%) as a yellow solid. R_f = 0.28 (4:1 cyclohexane/ethyl acetate). Mp: 102−103 °C (cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 1668, 1572, 1407, 1349, 1221, 1092, 1004, 734, 680. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 8.12−8.05 (m, 1H, H-4‴), 7.98 (t, J = 2.0 Hz, 1H, H-2‴), 7.96−7.91 (m, 2H, H-2′ + H-6′), 7.56−7.52 (m, 1H, H-6‴), 7.49 (d, J = 7.9 Hz, 1H, H-5‴), 7.47−7.43 (m, 2H, H-3′ + H-6′), 2.94−2.88 (m, 1H, H-1″), 2.85−2.78 (m, 1H, H-2″), 2.02−1.92 (m, 1H, H-3″$_a$), 1.68−1.59 (m, 1H, H-3″$_b$). ^{13}C{H} NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ 196.5 (CO), 148.6 (C-3‴), 142.6 (C-1‴), 139.8 (C-4′), 135.6 (C-1′), 133.0 (C-6‴), 129.6 (C-2′ + C-6′), 129.5 (C-5‴), 129.0 (C-3′ + C-5′), 121.7 (C-4‴), 120.5 (C-2‴), 29.2 (C-1″), 28.7 (C-2″), 19.7 (C-3″). MS (ESI): m/z = 302.1 [M + H]$^+$. HRMS (ESI-ToF) m/z: [M + H]$^+$ calcd for $C_{16}H_{13}ClNO_3$ 302.0579, found 302.0587.

*(2,2-Dimethylcyclopropyl)(phenyl)methanone (**2g**).* Following the general procedure using 3,3-dimethyl-1-phenylprop-2-en-1-one (10.0 mmol, 1.60 g, 1.00 equiv) after stirring at room temperature for 18 h, flash column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 90:10) afforded the title compound (1.46 g, 8.40 mmol, 84%) as a yellow oil. R_f = 0.45 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2959, 1711, 1604, 1290, 1245, 766, 753, 530. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.92 (m, 2H), 7.58−7.51 (m, 1H), 7.50−7.43 (m, 2H), 2.51−2.45 (m, 1H), 1.55−1.50 (m, 1H), 1.36 (s, 3H), 1.09 (s, 3H), 0.98−0.93 (m, 1H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 198.6, 139.1, 132.4, 128.5, 128.0, 32.9, 27.1, 27.0, 22.0, 18.5. MS (ESI): m/z = 175.1 [M + H]$^+$. The spectroscopic data are in accordance with the literature.[34]

Cyclopentene Synthesis. *Method **A**.* In an oven-dried Schlenk tube (10 mL) under nitrogen atmosphere, cyclopropanes **2** (0.40 mmol, 1.00 equiv) and Hantzsch ester (0.42 mmol, 106 mg, 1.05 equiv) were suspended in dry toluene (8.00 mL, c = 0.05 M). DIPEA (0.44 mmol, 75.0 μL, 1.10 equiv) and the corresponding alkyne (4.00 mmol, 10.0 equiv) were added, and the mixture was degassed and then placed in front of a blue LED (see the materials section) at a distance of 5 cm. The vessel was irradiated until TLC or HPLC/ESI-MS indicated full consumption of the starting material (58−144 h). The solvent was removed *in vacuo*, and the residue was purified by flash chromatography to afford the cyclopentenes **4**. The d.r. was calculated by comparison of the ^{1}H NMR signals (H-3 of the cyclopentenes) of the corresponding diastereomers. The relative configuration was determined using NOESY contacts (see the SI). Some of the products were further purified using preparative HPLC with mixtures of water and acetonitrile as eluent.

*Method **B**.* In an oven-dried quartz tube under nitrogen atmosphere, α-mesyloxyketones **1** (0.40 mmol, 1.00 equiv) and 1-methylimidazole (0.80 mmol, 64.0 μL, 2.00 equiv) were dissolved in dry toluene (40.0 mL, c = 0.01 M). The reaction tube was degassed and placed in a Rayonet photoreactor. The vessel was irradiated (λ_{max} = 300 nm, 16 × 8 W) at room temperature until TLC or HPLC/ESI-MS indicated full consumption of the starting material (0.5−2.0 h). The precipitated imidazolium methanesulfonate was filtered, washed with toluene, and the solvent was removed *in vacuo*. The residue was

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dissolved in dry toluene (8.00 mL, c = 0.05 M) and transferred to a 10 mL Schlenk tube charged with Hantzsch ester (0.42 mmol, 106 mg, 1.05 equiv). DIPEA (0.44 mmol, 75.0 μL, 1.10 equiv) and phenylacetylene (4.00 mmol, 439 μL, 10.0 equiv) were added, the mixture was degassed, and afterward placed in front of a blue LED (see the materials section) with a distance of 5 cm. The vessel was irradiated until TLC or HPLC/ESI-MS indicated full consumption of the starting material (48−89 h). The solvent was removed *in vacuo*, and the residue was purified by flash chromatography to afford the cyclopentenes **4**. The d.r. was calculated by integration of the ^{1}H NMR signals (H-3 of the cyclopentenes) of the diastereomers in the crude mixture. The relative configuration was determined using NOESY correlations (see the SI). Some of the products were further purified using preparative HPLC with mixtures of water and acetonitrile as an eluent.

*(2,4-Diphenylcyclopent-2-en-1-yl)(phenyl)methanone (**4a**).* Following general procedure **A**, a mixture of phenyl-[phenylcyclopropyl]-methanone (0.40 mmol, 88.8 mg, 1.00 equiv) and phenylacetylene (4.00 mmol, 439 μL, 10.0 equiv) was irradiated for 86 h with a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 75:25), the title compound (108 mg, 0.34 mmol, 84%, 2.5:1 d.r.) was obtained as a colorless solid.

Following general procedure **B**, 1,4-diphenyl-2-mesyloxybutan-1-one (0.40 mmol, 127 mg, 1.00 equiv) was irradiated for 1 h using UV-B irradiation and 72 h using a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 96:4 → 70:30), the title compound (67.4 mg, 0.21 mmol, 52%, 2.5:1 d.r.) was obtained as a colorless solid. In an up-scaled batch reaction, 1,4-diphenyl-2-mesyloxybutan-1-one (2.00 mmol, 636 mg, 1.00 equiv) was irradiated for 1.5 h using UV-B irradiation and 96 h using two blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 96:4 → 70:30), the title compound (285 mg, 0.88 mmol, 44%, 2.5:1 d.r.) was obtained as a colorless solid.

R_f = 0.35 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3058, 3026, 1681, 1597, 1493, 1447, 1210, 697. ^{1}H NMR, COSY, NOESY (400 MHz, $CDCl_3$) δ 8.10−8.07 (m, 0.8H, H-2‴ + H-6‴, minor), 8.06−8.04 (m, 2.0H, H-2‴ + H-6‴, major), 7.63−7.60 (m, 0.4H, H-4‴, minor), 7.60−7.57 (m, 1.0H, H-4‴, major), 7.54−7.50 (m, 1.0H, H-3‴ + H-5‴, minor), 7.50−7.46 (t, 2.0H, H-3‴ + H-5‴, major), 7.40−7.17 (m, 13.0H, H-2′-6′ + H-2″-6″, major + minor), 6.56−6.53 (m, 0.4H, H-3, minor), 6.40 (t, J = 2.1 Hz, 1.0H, H-3, major), 5.17−5.13 (m, 0.4H, H-1, minor), 5.13−5.08 (m, 1.0H, H-1, major), 4.27−4.23 (m, 0.4H, H-4, minor), 4.23−4.19 (m, 1.0H, H-4, major), 3.16−3.10 (m, 1.0H, H-5a, major), 2.67−2.62 (m, 0.4H, H-5a, minor), 2.48−2.42 (m, 0.4H, H-5b, minor), 2.05−2.00 (m, 1.0H, H-5b, major). ^{13}C{H} NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ 201.2 (CO, major), 200.6 (CO, minor), 145.0 (C-1″, minor), 144.9 (C-1″, major), 142.8 (C-2, major), 142.6 (C-2, minor), 136.5 (C-1‴, major), 136.3 (C-1‴, minor), 135.4 (C-1′, major), 135.0 (C-1′, minor), 133.33 + 133.31 (C-3 + C-4‴, minor), 133.2 (C-4‴, major), 133.1 (C-3, major), 128.8 (C-3‴ + C-5‴, minor), 128.72 (C-3‴ + C-5‴, major), 128.70 (C-2‴ + C-6‴, minor), 128.66 (C-2‴ + C-6‴, major;, C-3″ + C-5″, minor), 128.6 (C-3″ + C-5″, major), 128.52 (C-3′ + C-5′, minor), 128.46 (C-3′ + C-5′, major), 127.7 (C-2″ + C-6″, major), 127.6 (C-4′, minor), 127.4 (C-4′, major; C-2″ + C-6″, minor), 126.6 (C-4″, minor), 126.5 (C-4″, major), 126.02 (C-2′ + C-6′, major), 125.96 (C-2′ + C-6′, minor), 53.5 (C-1, major), 53.4 (C-1, minor), 51.4 (C-4, major), 50.8 (C-4, minor), 40.4 (C-5, minor), 39.7 (C-5, major). MS (ESI): m/z = 347.3 [M + Na]$^+$. HRMS (APCI-ToF) m/z: [M + H]$^+$ calcd for $C_{24}H_{21}O$ 325.1587, found 325.1583.

*(2-(4-Methoxyphenyl)-4-phenylcyclopent-2-en-1-yl)(phenyl)-methanone (**4b**).* Following general procedure **A**, a mixture of phenyl-[phenylcyclopropyl]methanone (0.40 mmol, 88.8 mg, 1.00 equiv) and 4-methoxyphenylacetylene (4.00 mmol, 519 μL, 10.0 equiv) was irradiated for 96 h with a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 75:25), the title compound (100 mg, 0.28 mmol, 71%, 2.8:1 d.r.) was obtained as a colorless solid. R_f = 0.35 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3025, 1671, 1509, 1493, 1315, 1261, 1214, 1169, 1028, 842, 699. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ 8.09−8.06 (m, 0.6H, H-2‴ + H-6‴, minor), 8.06−8.03 (m, 2.0H, H-2‴ + H-6‴, major), 7.63−7.59 (m, 0.3H, H-4‴, minor), 7.59−7.56 (m, 1.0H, H-4‴, major), 7.52 (d, J = 7.8 Hz, 0.8H, H-3‴ + H-5‴, minor), 7.48 (t, J = 7.8 Hz, 2.0H, H-3‴ + H-5‴, major), 7.35−7.23 (m, 8.8H, H-2′ + H-6′ + H-2″-3″ + H-5″-6″, major; H-2′ + H-6′ + H-2″-6″, minor), 7.22−7.18 (m, 1.0H, H-4″, major), 6.81 (d, J = 7.1 Hz, 0.6H, H-3′ + H-5′, minor), 6.80−6.78 (m, 2.0H, H-3′ + H-5′, major), 6.41−6.40 (m, 0.3H, H-3, minor), 6.29−6.26 (m, 1.0H, H-3, major), 5.13−5.09 (m, 0.3H, H-1, minor), 5.08−5.03 (m, 1.0H, H-1, major), 4.25−4.21 (m, 0.3H, H-4, minor), 4.21−4.17 (m, 1.0H, H-4, major), 3.77 (s, 1.0H, OCH_3, minor), 3.76 (s, 3.0H, OCH_3, major), 3.19−3.05 (m, 1.0H, H-5a, major), 2.68−2.59 (m, 0.3H, H-5a, minor), 2.48−2.38 (m, 0.4H, H-5b), 2.06−1.94 (m, 1.1H, H-5b, major). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 201.4 (CO, major), 200.8 (CO, minor), 159.1 (C-4′, minor), 158.9 (C-4′, major), 145.3 (C-1″, minor), 145.2 (C-1″, major), 142.2 (C-2, major), 142.0 (C-2, minor), 136.6 (C-1‴, major), 136.3 (C-1‴, minor), 133.3 (C-4‴, minor), 133.2 (C-4‴, major), 131.3 (C-3, minor), 131.1 (C-3, major), 128.8 (C-3‴ + C-5‴, minor), 128.73 (C-3‴ + C-5‴, major), 128.70 (C-2‴ + C-6‴, minor), 128.68 (C-2‴ + C-6‴, major), 128.64 (C-3″ + C-5″, minor), 128.57 (C-3″ + C-5″, major), 128.2 (C-1′, major), 127.8 (C-1′, minor), 127.7 (C-2″ + C-6″, major), 127.4 (C-2″ + C-6″, minor), 127.3 (C-2′ + C-6′, major), 127.2 (C-2′ +C-6′, minor), 126.6 (C-4″, minor), 126.5 (C-4″, major), 113.92 (C-3′ + C-5′, minor), 113.88 (C-3′ + C-5′, major), 55.29 (OCH_3, minor), 55.26 (OCH_3, major), 53.7 (C-1, major), 53.6 (C-1, minor), 51.4 (C-4, major), 50.8 (C-4, minor), 40.4 (C-5, minor), 39.7 (C-5, major). MS (ESI): m/z = 355.1 [M + Na]$^+$. HRMS (ESI-ToF) m/z: [M + H]$^+$ calcd for $C_{25}H_{23}O_2$ 355.1693, found 355.1694.

*(2-(4-tert-Butylphenyl)-4-phenylcyclopent-2-en-1-yl)(phenyl)-methanone (**4c**).* Following general procedure **A**, a mixture of phenyl-[phenylcyclopropyl]methanone (0.40 mmol, 88.8 mg, 1.00 equiv) and 4-(*tert*-butyl)phenylacetylene (4.00 mmol, 722 μL, 10.0 equiv) was irradiated for 58 h with a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 75:25), the title compound (126 mg, 0.36 mmol, 89%, 2.7:1 d.r.) was obtained as a colorless solid. Additionally, 457 mg (2.89 mmol, 72%) acetylene were reisolated. R_f = 0.47 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3027, 2962, 1682, 1492, 1448, 1269, 1209, 1006, 830, 701. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ 8.09−8.07 (m, 0.8H, H-2‴ + H-6‴, minor), 8.07−8.04 (m, 2.0H, H-2‴ + H-6‴, major), 7.63−7.60 (m, 0.4H, H-4‴, minor), 7.60−7.57 (m, 1.1H, H-4‴, major), 7.53−7.51 (m, 0.8H, H-3‴ + H-5‴, minor), 7.49 (t, $^3J_{HH}$ = 7.7 Hz, 2.1H, H-3″ + H-5″, major), 7.34−7.27 (m, 10.4H, H-2′-3′ + H-5′-6′ + H-2″-3″ + H-5″-6″, major + minor), 7.25−7.22 (m, 0.7H, H-4″, minor), 7.22−7.18 (m, 1.1H, H-4″, major), 6.51 (dd, J = 2.2, 1.1 Hz, 0.4H, H-3, minor), 6.37 (t, J = 2.1 Hz, 1.1H, H-3, major), 5.16−5.11 (m, 0.5H, H-1, minor), 5.10−5.05 (m, 1.1H, H-1, major), 4.26−4.21 (m, 0.5H, H-4, minor), 4.21−4.17 (m, 1.1H, H-4, major), 3.16−3.08 (m, 1.2H, H-5a, major), 2.66−2.60 (m, 0.5H, H-5a, minor), 2.46−2.39 (m, 0.5H, H-5b, minor), 2.03−1.96 (m, 1.2H, H-5b, major), 1.28 (s, 3.2H, $C(CH_3)_3$, minor), 1.27 (s, 9.0H, $C(CH_3)_3$, major). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 201.4 (CO, major), 200.8 (CO, minor), 150.5 (C-4′, minor), 150.3 (C-4′, major), 145.2 (C-1″, minor), 145.1 (C-1″, major), 142.5 (C-2, major), 142.3 (C-2, minor), 136.6 (C-1‴, major), 136.3 (C-1‴, minor), 133.3 (C-4‴, minor), 133.1 (C-4‴, major), 132.5 (C-3, minor), 132.4 (C-1′, major), 132.2 (C-3, major), 132.1 (C-1′, minor), 128.8 (C-3‴ + C-5‴, minor), 128.71 (C-3‴ + C-5‴, major), 128.69 (minor), 128.67 (C-2‴ + C-6‴, major), 128.63 (minor), 128.55 (C-3″ + C-5″,major), 127.8 (major, C-2″ + C-6″), 127.4 (C-2″ + C-6″, minor), 126.6 (C-4″, minor), 126.5 (C-4″, major), 125.7 + 125.4 (C-2′-3′ + C-5′-6′, major), 125.6 + 125.5 (C-2′-3′ + C-5′-6′, minor), 53.38 (C-1, major), 53.4 (C-1, minor), 51.4 (C-4, major), 50.8 (C-4, minor), 40.4 (C-5, minor), 39.6 (C-5, major), 34.53 ($C(CH_3)_3$, minor), 34.50 ($C(CH_3)_3$, major), 31.2 ($C(CH_3)_3$). MS (ESI): m/z = 381.2 [M + H]$^+$. HRMS (ESI-ToF) m/z: [M + H]$^+$ calcd for $C_{28}H_{29}O$ 381.2213, found 381.2219.

*(2-(Cyclohex-1-en-1-yl)-4-phenylcyclopent-2-en-1-yl)(phenyl)-methanone (**4d**).* Following general procedure **A**, a mixture of

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phenyl-[phenylcyclopropyl]methanone (0.40 mmol, 88.8 mg, 1.00 equiv) and 1-ethynylcyclohexene (4.00 mmol, 470 μL, 10.0 equiv) was irradiated for 82 h with a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 75:25), the title compound (105 mg, 0.32 mmol, 80%, 2.2:1 d.r.) was obtained as a colorless oil. R_f = 0.42 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2929, 1682, 1597, 1493, 1447, 1338, 1209, 759, 701. ^{1}H NMR, COSY, TOCSY, NOESY (400 MHz, $CDCl_3$) δ 8.09−7.98 (m, 2.8H, H-2‴ + H-6‴, major + minor), 7.62−7.53 (m, 1.5H, H-4‴, major + minor), 7.52−7.44 (m, 3.1H, H-3‴ + H-5‴, major + minor), 7.35−7.24 (m, 6.5H, H-2′-3′ + H-5′-6′, major; H-2′ + H-.6′, minor), 7.24−7.15 (m, 2.5H, H-4″, major; H-3″-5″, minor), 6.02 (s, 0.5H, H-3, minor), 5.94−5.92 (m, 1.0H, H-3, major), 5.46−5.39 (m, 1.5H, H-2′, major + minor), 4.90−4.85 (m, 0.5H, H-1, minor), 4.82−4.76 (m, 1.0H, H-1, major), 4.16−4.11 (m, 0.5H, H-4, minor), 4.11−4.05 (m, 1.0H, H-4, major), 3.02−2.92 (m, 1.1H, H-5a, major), 2.52−2.44 (m, 0.6H, H-5a, minor), 2.42−2.28 (m, 3.1H, H-3′, major + minor), 2.26−2.21 (m, 0.6H, H-5b, minor), 2.06−1.97 (m, 3.4H, H-6′, major + minor), 1.91−1.83 (m, 1.1H, H-5b, major), 1.76−1.41 (m, 6.8H, H-4′-5′, major + minor). ^{13}C{H} NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ 201.8 (CO, major), 201.0 (CO, minor), 145.4 (C-1″, major + minor), 144.72 (C-2, minor), 144.67 (C-2, major), 136.8 (C-1‴, major), 136.5 (C-1‴, minor), 133.1 (C-4‴, minor), 132.9 (C-4‴, major), 132.5 (C-1′, minor), 132.2 (C-1′, major), 131.0 (C-3, minor), 130.5 (C-3, major), 128.7 (C-3‴ + C-5‴, minor), 128.6 (C-3‴ + C-5‴, major), 128.54 (C-3″ + C-5″, minor), 128.52 (C-2‴ + C-6‴, major + minor), 128.4 (C-3″ + C-5″, major), 127.7 (C-2″ + C-6″, major), 127.4 (C-2″ + C-6″, minor), 126.40 (C-2′, minor), 126.37 (C-2′, major), 126.3 (C-4″, major), 126.2 (C-4″, minor), 52.7 (C-1, major), 52.4 (C-1, minor), 51.3 (C-4, major), 50.5 (C-4, minor), 40.2 (C-5, minor), 39.1 (C-5, major), 26.4 (C-6′, major), 26.2 (C-6′, minor), 25.8 (C-3′, minor), 25.7 (C-3′, major), 22.59 (C-5′, major), 22.56 (C-5′, minor), 22.2 (C-4′, major + minor). MS (ESI): m/z = 329.2 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ Calcd. for $C_{24}H_{25}O$ 329.1900, found 329.1905.

*(2-Ethoxycarbonyl-4-phenylcyclopent-2-en-1-yl)(phenyl)-methanone (**4e**).* Following general procedure **A**, a mixture of phenyl-[phenylcyclopropyl]methanone (0.40 mmol, 88.8 mg, 1.00 equiv) and ethyl propiolate (4.00 mmol, 405 μL, 10.0 equiv) was irradiated for 58 h with a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 75:25), the title compound (113 mg, 0.35 mmol, 88%, 2.7:1 d.r.) was obtained as a colorless oil. R_f = 0.30 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2980, 1713, 1681, 1448, 1257, 1214, 1100, 1024, 701. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ = 8.08−8.02 (m, 2.9H, H-2″ H-6″, major + minor), 7.62−7.57 (m, 1.5H, H-4″, major + minor), 7.53−7.47 (m, 2.9H, H-3″ + H-5″, major + minor), 7.38−7.35 (m, 0.7H, H-3′ + H-5′, minor), 7.35−7.31 (m, 2.3H, H-3′ + H-5′, major), 7.30−7.27 (m, 2.9H, H-2′ + H-6′, major + minor), 7.26−7.21 (m, 1.8H, H-4′, major + minor), 7.09−7.06 (m, 0.3H, H-3, minor), 6.99−6.95 (m, 1.0H, H-3, major), 5.05−4.99 (m, 0.4H, H-1, minor), 4.94−4.88 (m, 1.1H, H-1, major), 4.31−4.26 (m, 0.4H, H-4, minor), 4.25−4.13 (m, 4.1H, H-4, major; OCH_2CH_3, major + minor), 3.07−3.00 (m, 1.2H, H-5a, major), 2.62−2.57 (m, 0.4H, H-5a, minor), 2.44−2.37 (m, 0.4H, H-5b, minor), 2.01−1.95 (m, 1.2H, H-5b, major), 1.24 (t, J = 7.2 Hz, 0.9H, OCH_2CH_3, minor), 1.21 (t, J = 7.2 Hz, 3.2H, OCH_2CH_3, major). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 201.0 (CO, major), 200.7 (CO, minor), 164.39 (CO_2Et, major), 164.35 (CO_2Et, minor), 148.4 (C-3, minor), 147.5 (C-3, major), 143.2 (C-1′, minor), 143.0 (C-1′, major), 137.0 (C-2, major), 136.8 (C-2, minor), 136.5 (C-1″, major), 136.3 (C-1″, minor), 133.3 (C-4″, minor), 133.2 (C-4″, major), 128.84 + 128.76 + 128.69 (C-2″-3″ + C-5″-6″ + C-3′ + C-5′, minor), 128.74 + 128.65 + 128.63 (C-2″-3″ + C-5″-6″ + C-3′ + C-5′, major), 127.7 (C-2′ + C-6′, major), 127.34 (C-2′ + C-6′, minor), 127.0 (C-4′, minor), 126.9 (C-4′, major), 60.7 ($CO_2CH_2CH_3$, minor), 60.6 ($CO_2CH_2CH_3$, major), 51.6 + 51.5 (C-1 + C-4, major; C-1, minor), 51.2 (C-4, minor), 39.4 (C-5, minor), 39.1 (C-5, major), 14.14 ($CO_2CH_2CH_3$, minor), 14.11 ($CO_2CH_2CH_3$, major). MS (ESI): m/z = 321.0 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{20}O_3Na$ 343.1304, found 343.1307.

*(2,4-Diphenylcyclopent-2-en-1-yl)(4-methoxyphenyl)methanone (**4i**).* Following general procedure **A**, a mixture of 4-methoxyphenyl-[phenylcyclopropyl]methanone (0.40 mmol, 101 mg, 1.00 equiv) and phenylacetylene (4.00 mmol, 439 μL, 10.0 equiv) was irradiated for 144 h with two blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 75:25), the title compound (84.0 mg, 0.24 mmol, 59%, 2.6:1 d.r.) was obtained as a colorless solid. R_f = 0.33 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2934, 1672, 1598, 1509, 1262, 1215, 1170, 1028, 843, 699. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ 8.11−8.09 (m, 0.8H, H-2‴ + H-6‴, minor), 8.09−8.06 (m, 2.0H, H-2‴ + H-6‴, major), 7.42−7.20 (m, 14.7H, H-2′-6′ + H-2″-6″, major + minor), 7.03−7.00 (m, 0.8H, H-3‴ + H-5‴, minor), 7.00−6.97 (m, 2.0H, H-3‴ + H-5‴, major), 6.57−6.56 (m, 0.4H, H-3, minor), 6.42−6.40 (m, 1.0H, H-3, major), 5.16−5.12 (m, 0.4H, H-1, minor), 5.11−5.06 (m, 1.0H, H-1, major), 4.30−4.26 (m, 0.4H, H-4, minor), 4.24−4.20 (m, 1.0H, H-4, major), 3.92 (s, 1.2H, OCH_3, minor), 3.90 (s, 3.0H, OCH_3, major), 3.18−3.07 (m, 1.0H, H-5a, major), 2.69−2.62 (m, 0.4H, H-5a, minor), 2.51−2.41 (m, 0.4H, H-5b, minor), 2.04 (dt, J = 13.7, 7.1 Hz, 1.0H, H-5b, major). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 199.8 (CO, major), 199.3 (CO, minor), 163.7 (C-4‴, minor), 163.6 (C-4‴, major), 145.2 (C-1″, minor), 145.0 (C-1″, major), 143.1 (C-2, major), 142.8 (C-2, minor), 135.6 (C-1′, major), 135.2 (C-1′, minor), 133.2 (C-3, minor), 133.0 (C-3, major), 131.03 (C-2‴ + C-6‴, minor), 130.98 (C-2‴ + C-6‴, major), 129.6 (C-1‴, major), 129.3 (C-1‴, minor), 128.7 (C-3″ + C-5″, minor), 128.6 (C-3″ + C-5″, major), 128.52 (C-3′ + C-5′, minor), 128.46 (C-3′ + C-5′, major), 127.8 (C-2″ + C-6″, major), 127.5 (C-4′, minor), 127.43 (C-2″ + C-6″, minor), 127.37 (C-4′, major), 126.6 (C-4″, minor), 126.5 (C-4″, major), 126.03 (C-2′ + C-6′, major), 125.98 (C-2′ + C-6′, minor), 114.0 (C-3‴ + C-5‴, minor), 113.9 (C-3‴ + C-5‴, major), 55.57 (OCH_3, minor), 55.54 (OCH_3, major), 53.2 (C-1, major), 53.1 (C-1, minor), 51.4 (C-4, major), 50.9 (C-4, minor), 40.6 (C-5, minor), 39.9 (C-5, major). MS (ESI): m/z = 377.1 $[M + Na]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{25}H_{23}O_2$ 355.1693, found 355.1693.

*(2-Phenyl-4-(4-methoxyphenyl)cyclopent-2-en-1-yl)(4-fluorophenyl)methanone (**4j**).* Following general procedure **A**, a mixture of 4-fluorophenyl-[(4-methoxyphenyl)cyclopropyl]-methanone (0.40 mmol, 108 mg, 1.00 equiv) and phenylacetylene (4.00 mmol, 439 μL, 10.0 equiv) was irradiated for 64 h with a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 99:1 → 80:20), the title compound (115 mg, 0.32 mmol, 78%, 2.9:1 d.r.) was obtained as a colorless solid. R_f = 0.41 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2921, 2851, 1682, 1511, 1245, 1208, 1034, 831, 759, 695. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ 8.13−8.09 (m, 0.6H, H-2‴ + H-6‴, minor), 8.09−8.06 (m, 2.0H, H-2‴ + H-6‴, major), 7.37−7.35 (m, 0.8H, H-2′ + H-6′, minor), 7.35−7.33 (m, 2.0H, H-2′ + H-6′, major), 7.30−7.26 (m, 2.5H, H-3′ + H-5′, minor + major), 7.25 (d, J = 8.5 Hz, 2.2H, H-2″ + H-6″, major), 7.23−7.20 (m, 1.2H, H-4″, major), 7.20−7.17 (m, 1.5H, H-2‴ + H-6″ + H-3‴ + H-5‴, minor), 7.15 (t, J = 8.5 Hz, 2.2H, H-3‴ + H-5‴), 6.88 (d, J = 8.5 Hz, 0.8H, H-3″ + H-5″, minor), 6.86 (d, J = 8.5 Hz, 2.0H, H-3″ + H-5″, major), 6.53−6.51 (m, 0.3H, H-3, minor), 6.39−6.37 (m, 1.0H, H-3, major), 5.11−5.08 (m, 0.4H, H-1, minor), 5.06−5.00 (m, 1.0H, major), 4.23−4.19 (m, 0.4H, H-4, minor), 4.19−4.14 (m, 1.0H, H-4, major), 3.81 (s, 1.1H, OCH_3, minor), 3.79 (s, 3.0H, OCH_3, major), 3.13−3.06 (m, 1.0H, H-5a, major), 2.63−2.57 (m, 0.4H, H-5a, minor), 2.43−2.37 (m, 0.4H, H-5b, minor), 2.00−1.93 (m, 1.0H, H-5b, major). ^{19}F NMR (282 MHz, $CDCl_3$) δ−106.04 (tt, J = 8.2, 5.3 Hz, minor),−106.21 (tt, J = 8.2, 5.3 Hz, major). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 199.8 (CO, major), 199.3 (CO, minor), 165.95 (d, $^1J_{CF}$ = 255.1 Hz, C-4‴, minor), 165.87 (d, $^1J_{CF}$ = 255.1 Hz, C-4‴, major), 158.5 (OCH_3, minor), 158.4 (OCH_3, major), 142.4 (C-2, major), 142.2 (C-2, minor), 137.1 (C-1″, major), 137.0 (C-1″, minor), 135.5 (C-1′, major), 135.1 (C-1′, minor), 133.9 (C-3, minor), 133.6 (C-3, major), 133.0 (d, $^4J_{CF}$ = 2.9 Hz, C-1‴, major), 132.8 (d, $^4J_{CF}$ = 2.9 Hz,

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C-1‴, minor), 131.43 (d, $^3J_{CF}$ = 9.2 Hz, C-3‴ + C-5‴, minor), 131.39 (d, $^3J_{CF}$ = 9.2 Hz, C-3‴ + C-5‴, major), 128.8 (C-2″ + C-6″, major), 128.64 (C-3′ + C-5′, minor), 128.59 (C-3′ + C-5′, major), 128.4 (C-2″ + C-6″, minor), 127.7 (C-4′, minor), 127.5 (C-4′, major), 126.1 (C-2′ + C-6′, major), 126.0 (C-2′ + C-6′, minor), 116.00 (d, $^2J_{CF}$ = 21.8 Hz, C-3‴ + C-5‴, minor), 115.92 (d, $^2J_{CF}$ = 21.8 Hz, C-3‴ + C-5‴, major), 114.13 (C-3″ + C-5″, minor), 114.05 (C-3″ + C-5″, major), 55.42 (OCH_3, minor), 55.39 (OCH_3, major), 53.53 (C-1, major), 53.46 (C-1, minor), 50.7 (C-4, major), 50.1 (C-4, minor), 40.6 (C-5, minor), 39.8 (C-5, major). MS (ESI): m/z = 395.1 [M + Na]$^+$. HRMS (ESI-ToF) m/z: [M + K]$^+$ calcd for $C_{25}H_{21}FO_2K$ 411.1163, found 411.1161.

*(2-Phenyl-4-(2-chlorophenyl)cyclopent-2-en-1-yl)(4-fluorophenyl)methanone (**4k**).* Following general procedure **A**, a mixture of 4-fluorophenyl-[(2-chlorophenyl)cyclopropyl]methanone (0.40 mmol, 110 mg, 1.00 equiv) and phenylacetylene (4.00 mmol, 439 μL, 10.0 equiv) was irradiated for 64 h with a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 99:1 → 80:20), the title compound (119 mg, 0.32 mmol, 79%, 2.0:1 d.r.) was obtained as a colorless solid. R_f = 0.46 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3060, 1682, 1597, 1505, 1229, 1208, 1156, 1046, 848, 753, 693. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$): δ 8.10−8.07 (m, 1.0H, H-2‴ + H-6‴, minor), 8.06−8.02 (m, 2.0H, H-2‴ + H-6‴,major), 7.48−7.45 (m, 1.0H, H-6″, major), 7.39−7.35 (m, 3.6H, H-2′ + H-6′, major; H-3′ + H-6′ + H-3″, minor), 7.34−7.32 (m, 1.0H, H-3″, major), 7.31−7.27 (m, 3.5H, H-3′ + H-5′, major; H-2′ + H-6′ + H-6″, minor), 7.25−7.21 (m, 2.8H, H-4′ + H-5″, major + minor), 7.20−7.17 (m, 1.3H, H-4″ + H-3‴ + H-5‴, minor), 7.16−7.12 (m, 3.3H, H-4″ + H-3‴ + H-5‴, major), 6.52−6.50 (m, 0.5H, H-3, minor), 6.43−6.40 (m, 1.0H, H-3, major), 5.10−5.07 (m, 0.5H, H-1, minor), 5.07−5.02 (m, 1.0H, H-1, major), 4.72−4.69 (m, 0.5H, H-4, minor), 4.69−4.65 (m, 1.1H, H-5, major), 3.28−3.19 (m, 1.0H, H-5a, major), 2.79−2.72 (m, 0.5H, H-5a, minor), 2.36−2.30 (m, 0.5H, H-5b, minor), 1.90−1.83 (m, 1.0H, H-5b, major). ^{19}F NMR (282 MHz, $CDCl_3$): δ−105.95 (tt, J = 8.3, 5.3 Hz, minor),−106.07 (tt, J = 8.3, 5.3 Hz, major). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 199.3 (CO, major), 199.0 (CO, minor), 165.9 (d, $^1J_{CF}$ = 255 Hz, C-4‴, minor), 165.8 (d, $^1J_{CF}$ = 255 Hz, C-4‴, major), 143.7 (C-2, major), 143.4 (C-2, minor), 142.4 (C-1″, minor), 142.2 (C-1″, major), 135.2 (C-1′, major), 134.9 (C-1′, minor), 133.7 (C-2″, minor), 133.3 (C-2″, major), 132.7 (d, $^4J_{CF}$ = 3.0 Hz, C-1‴, major), 132.6 (d, $^4J_{CF}$ = 3.0 Hz, C-1‴, minor), 131.8 (C-3, minor), 131.4 (d, $^4J_{CF}$ = 8.8 Hz, C-2‴ + C-6‴, minor), 131.3 (d, $^4J_{CF}$ = 8.7 Hz, C-2‴ + C-6‴, major), 129.6 (C-3″, minor), 129.2 (C-3″, major), 129.0 (C-6″, major), 128.6 (C-3′ + C-5′, minor), 128.5 (C-3′ + C-5′, major), 128.0 (C-6″, minor), 127.9 (C-4″, minor), 127.8 (C-4″, major), 127.7 (C-4′, minor), 127.6 (C-4′, major), 127.2 (C-5′, major), 127.1 (C-5′, minor), 126.0 (C-2′ + C-6′, major), 125.9 (C-2′ + C-6′, minor), 115.92 (d, $^2J_{CF}$ = 21.9 Hz, C-3‴ + C-5‴, minor), 115.86 (d, $^2J_{CF}$ = 21.9 Hz, C-3‴ + C-5‴, major), 53.2 (C-1, major), 53.1 (C-1, minor), 47.43 (C-4, minor), 47.35 (C-4, major), 38.4 (C-5, minor), 37.9 (C-5, major). MS (ESI): m/z = 377.1 [M + H]$^+$. HRMS (ESI-ToF) m/z: [M + H]$^+$ calcd for $C_{24}H_{19}ClFO$ 377.1103, found 377.1104.

*(2-Phenyl-4-(4-cyanophenyl)cyclopent-2-en-1-yl)(phenyl)-methanone (**4l**).* Following general procedure **A**, a mixture of phenyl-[(4-cyanophenyl)cyclopropyl]methanone (0.40 mmol, 98.8 mg, 1.00 equiv) and phenylacetylene (4.00 mmol, 439 μL, 10.0 equiv) was irradiated for 96 h with a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 75:25), the title compound (117 mg, 0.34 mmol, 84%, 2.0:1 d.r.) was obtained as a colorless solid. R_f = 0.28 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2930, 2227, 1682, 1607, 1496, 1448, 1211, 1003, 843, 693. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ 8.10−8.07 (m, 1.0H, H-2‴ + H-6‴, minor), 8.07−8.04 (m, 2.1H, H-2‴ + H-6‴, major), 7.66−7.59 (m, 4.8H, H-3″ + H-5″ + H-4‴, major + minor), 7.57−7.50 (m, 3.2H, H-3‴ + H-5‴, major + minor), 7.49−7.44 (m, 2.1H, H-2″ + H-6″, major), 7.41−7.35 (m, 4.2H, H-2′ + H-6′, major + minor; H-2″ + H-6″, minor), 7.33−7.22 (m, 5.3H, H-3′-5′, major + minor), 6.52−6.47 (m, 0.5H, H-3, minor), 6.39−6.35 (m, 1.0H, H-3, major), 5.21−5.18 (m, 0.5H, H-1, minor), 5.17−5.13 (m, 1.0H, H-1, major), 4.34−4.30 (m, 0.5H, H-4, minor), 4.30−4.25 (m, 1.1H, H-4, major), 3.23−3.15 (m, 1.1H, H-5a, major), 2.71−2.66 (m, 0.5H, H-5a, minor), 2.45−2.37 (m, 0.5H, H-5b, minor), 2.02−1.95 (m, 1.1H, H-5b, major). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 201.1 (CO, major), 200.2 (CO, minor), 150.60 (C-1″, minor), 150.56 (C-1″, major), 144.2 (C-2, major), 144.1 (C-2, minor), 136.3 (C-1‴, major), 136.1 (C-1‴, minor), 134.8 (C-1′, major), 134.6 (C-1′, minor), 133.54 (C-4‴, minor), 133.49 (C-4‴, major), 132.6 (C-3″ + C-5″, minor), 132.5 (C-3″ + C-5″, major), 131.5 (C-3, minor), 131.2 (C-3, major), 128.91 (C-3‴ + C-5‴, minor), 128.87 (C-3‴ + C-5‴, major), 128.70 (C-2‴ + C-6‴, minor), 128.67 (C-2″ + C-6″, major), 128.64 (C-2‴ + C-6‴, major; C-3′ + C-5′, minor), 128.58 (C-3′ + C-5′, major), 128.2 (C-2″ + C-6″, minor), 128.0 (C-4′, minor), 127.8 (C-4′, major), 126.1 (C-2′ + C-6′, major), 126.0 (C-2′ + C-6′, minor), 119.1 (CN, major), 119.0 (CN, minor), 110.5 (C-4″, minor), 110.3 (C-4″, major), 53.2 (C-1, minor), 53.0 (C-1, major), 51.3 (C-4, major), 50.8 (C-4, minor), 40.1 (C-5, minor), 38.9 (C-5, major). MS (ESI): m/z = 372.1 [M + Na]$^+$. HRMS (ESI-ToF) m/z: [M + H]$^+$ calcd for $C_{25}H_{20}NO$ 350.1540, found 350.1543.

*N-Acetyl-(2-phenyl-4-(3-aminophenyl)cyclopent-2-en-1-yl)(4-chlorophenyl)methanone (**4m**).* Following a modified general procedure **A**, a mixture of 4-chlorophenyl-[(3-nitrophenyl)-cyclopropyl]methanone (0.40 mmol, 121 mg, 1.00 equiv), Hantzsch ester (1.00 mmol, 253 mg, 2.50 equiv) and phenylacetylene (4.00 mmol, 439 μL, 10.0 equiv) was irradiated for 120 h with a blue LED (see the materials section). Reversed-phase column chromatography (SiO_2-C_{18}, eluent: water/acetonitrile, 99:1 → 80:20) gave the crude amine (88 mg), which was dissolved in MeCN (5 mL) and reacted with NEt_3 (0.29 mmol, 40.0 μL, 1.20 equiv) and Ac_2O (0.29 mmol, 27.0 μL, 1.20 equiv) for 1 h at room temperature. Ethyl acetate (25 mL) and water (25 mL) were added, the phases were separated, and the aqueous phase was extracted with ethyl acetate (3 ×25 mL). The combined organic extracts were dried over Na_2SO_4, and the solvent was removed under reduced pressure. Preparative HPLC (C_{18}PFP, eluent: water/acetonitrile, 45:55, t_R = 13.6 min) yielded the title compound (94 mg, 0.23 mmol, 57%, 2.1:1 d.r.) as a colorless solid. R_f = 0.13 (2:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3308, 2935, 1672, 1589, 1552, 1488, 1210, 1092, 760, 731, 696. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ 8.00−7.98 (m, 0.8H, H-2‴ + H-6‴, minor), 7.98−7.95 (m, 2.0H, H-2‴ + H-6‴, major), 7.58−7.54 (m, 1.0H, H-4″, major), 7.49−7.47 (m, 0.7H, H-3‴ + H-5‴, minor), 7.47−7.44 (m, 2.0H, H-3‴ + H-5‴, major), 7.43−7.40 (m, 0.4H, H-4″, minor), 7.35−7.33 (m, 1.4H, H-2″ + H-2′ + H-6′, minor), 7.33−7.30 (m, 2.0H, H-2′ + H-6′, major), 7.30−7.23 (m, 5.4H, H-3′ + H-5′ + H-2″ + H-5″, major; H-3′ + H-5′ + H-5″, minor), 7.24−7.18 (m, 2.0H, H-4′, minor + major), 7.03 (dt, J = 7.6, 1.3 Hz, 1.0H, H-6″, major), 6.99 (d, J = 7.6 Hz, 0.4H, H-6″, minor), 6.50−6.48 (m, 0.4H, H-3, minor), 6.39−6.36 (m, 1.0H, H-3, major), 5.09−5.05 (m, 0.4H, H-1, minor), 5.04−5.00 (m, 1.0H, H-1, major), 4.24−4.15 (m, 1.4H, H-4, minor + major), 3.14−3.07 (m, 1.0H, H-5a, major), 2.62−2.56 (m, 0.4H, H-5a, minor), 2.44−2.38 (m, 0.4H, H-5b, minor), 2.16 (s, 3.9H, $COCH_3$, minor + major), 1.97−1.91 (m, 1.0H, H-5b, major). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 200.4 (CO, major), 199.6 (CO, minor), 168.31 ($COCH_3$, major), 168.29 ($COCH_3$, minor), 145.9 (C-1″, minor), 145.8 (C-1″, major), 142.72 (C-2, major), 142.65 (C-2, minor), 139.8 (C-4‴, minor + major), 138.20 (C-3″, major), 138.16 (C-3″, minor), 135.0 (C-1′, major), 134.8 (C-1′, minor), 134.6 (C-1‴, major), 134.5 (C-1‴, minor), 133.0 (C-3, minor), 132.8 (C-3, major), 130.08 (C-2‴ + C-6‴, minor), 130.06 (C-2‴ + C-6‴, major), 129.33 (C-5″, minor), 129.28 (C-5″, major), 129.12 (C-3‴ + C-5‴, minor), 129.10 (C-3‴ + C-5‴, major), 128.6 (C-3′ + C-5′, minor + major), 127.7 (C-4′, minor), 127.6 (C-4′, major), 125.96 (C-2′ + C-6′, major), 125.93 (C-2′ + C-6′, minor), 123.7 (C-6″, major), 123.4 (C-6″, minor), 118.70 (C-2″, major), 118.68 (C-2″, minor), 118.3 (C-4″, minor), 118.2 (C-4″, major), 53.4 (C-1, minor + major), 51.2 (C-4, major), 50.7 (C-4, minor), 40.0 (C-5, minor), 39.3 (C-5, major), 24.68 ($COCH_3$, major), 24.66 ($COCH_3$, minor). MS (ESI): m/z = 416.1 [M + H]$^+$.

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HRMS (ESI-ToF) m/z: $[M + Na]^+$ calcd for $C_{26}H_{22}ClNO_2Na$ 438.1231, found 438.1233.

*(2-Phenyl-4,4-dimethylcyclopent-2-en-1-yl)(phenyl)methanone (**4n**).* Following general procedure **A**, a mixture of (2,2-dimethylcyclopropyl)(phenyl)methanone (0.40 mmol, 69.6 mg, 1.00 equiv) and phenylacetylene (4.00 mmol, 439 μL, 10.0 equiv) was irradiated for 120 h with a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 99:1 → 80:20), the title compound (89.0 mg, 0.32 mmol, 81%) was obtained as a colorless oil. R_f = 0.53 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2953, 2863, 1682, 1445, 1237, 1206, 1012, 751, 706, 691. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ 8.07−8.03 (m, 2H, H-2″ + H-6″), 7.61−7.57 (m, 1H, H-4″), 7.53−7.48 (m, 2H, H-3″ + H-5″), 7.30−7.27 (m, 2H, H-2′ + H-6′), 7.25−7.21 (m, 2H, H-3′ + H-5′), 7.19−7.15 (m, 1H, H-4′), 6.26−6.24 (m, 1H, H-3), 5.06−5.01 (m, 1H, H-1), 2.41 (dd, J = 13.0, 10.2 Hz, 1H, H-5a), 1.96 (dd, J = 13.0, 5.4 Hz, 1H, H-5b), 1.22 + 1.19 (2 × s, 2 × 3H, 2 × CH_3). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 201.5 (CO), 140.1 (C-3), 138.3 (C-2), 136.5 (C-1″), 135.6 (C-1′), 133.1 (C-4″), 128.7 (C-2″-3″ + C-5″-6″), 128.4 (C-3′ + C-5′), 127.1 (C-4′), 125.8 (C-2′ + C-6′), 53.4 (C-1), 45.7 (C-4), 44.7 (C-5), 29.4 + 28.9 (2 × CH_3). MS (ESI): m/z = 277.1 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{20}H_{21}O$ 277.1587, found 277.1587.

*(2,4-Diphenyl-cyclopent-2-en-1-yl)(4-trifluormethylphenyl)-methanone (**4o**).* Following general procedure **B**, 1-(4-trifluoromethylphenyl)-2-mesyloxy-4-phenylbutan-1-one (0.40 mmol, 154 mg, 1.00 equiv) was irradiated for 1 h using UV-B irradiation and 48 h using a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 70:30) and preparative HPLC (C_{18}PFP, eluent: water/acetonitrile, 35:65), the title compound (89.4 mg, 0.23 mmol, 57%, 2.2:1 d.r.) was obtained as a colorless solid. R_f = 0.41 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 1686, 1494, 1409, 1321, 1168, 1128, 1066, 699. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ 8.16 (d, J = 8.1 Hz, 0.9H, H-2‴ + H-6‴, minor), 8.13 (d, J = 8.1 Hz, 2.0H, H-2‴ + H-6‴, major), 7.77 (d, J = 8.1 Hz, 1.0H, H-3‴ + H-5‴, minor), 7.74 (d, J = 8.1 Hz, 2.0H, H-3‴ +H-5‴, major), 7.38−7.18 (m, 13.9H, H-2′-6′ + H-2″-6″, major + minor), 6.55−6.53 (m, 0.4H, H-3, minor), 6.42−6.40 (m, 1.0H, H-3, major), 5.15−5.11 (m, 0.4H, H-1, minor), 5.09−5.05 (m, 1.0H, H-1, major), 4.29−4.19 (m, 1.3H, H-4, major + minor), 3.17−3.10 (m, 1.0H, H-5a, major), 2.66−2.60 (m, 0.4H, H-5a, minor), 2.49−2.43 (m, 0.4H, H-5b, minor), 2.04−1.97 (m, 1.0H, H-5b, major). ^{19}F NMR (282 MHz, $CDCl_3$): δ −64.28 (s, CF_3, minor),−64.29 (s, CF_3, major).^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 200.3 (CO, major), 199.8 (CO, minor), 144.7 (C-1″, minor), 144.6 (C-1″, major), 142.5 (C-2, major), 142.2 (C-2, minor), 139.2 (C-1‴, major), 139.0 (C-1‴, minor), 135.2 (C-1′, major), 134.8 (C-1′, minor), 134.4 (q, $^2J_{CF}$ = 32.7 Hz, C-4‴, major + minor), 133.6 (C-3, minor), 133.3 (C-3, major), 129.00 (C-3‴ + C-5‴, minor), 128.97 (C-3‴ + C-5‴, major), 128.73 (C-2′ + C-6′, minor), 128.67 (C-2′ + C-6′, major), 128.62 (C-3′ + C-5′, minor), 128.57 (C-3′ + C-5′, major), 127.8 (C-4′, minor), 127.7 (C-2″ + C-6″, major), 127.6 (C-4′, major), 127.4 (C-2″ + C-6″, minor), 126.8 (C-4″, minor), 126.7 (C-4″, major), 126.0 (C-3″ + C-5″, major), 125.9 (C-3″ + C-5″, minor), 125.88 (q, $^4J_{CF}$ = 3.7 Hz, C-2‴ + C-6‴, minor), 125.8 (q, $^4J_{CF}$ = 3.7 Hz, C-2‴ + C-6‴, major), 123.6 (C q, $^1J_{CF}$ = 272.9 Hz, CF_3, major + minor), 54.0 (C-1, major), 53.8 (C-1, minor), 51.4 (C-4, major), 50.8 (C-4, minor), 40.0 (C-5, minor), 39.4 (C-5, major). MS (ESI): m/z = 393.1 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{25}H_{20}F_3O$ 393.1461, found 393.1454.

*(2,4-Diphenyl-cyclopent-2-en-1-yl)(3-chlorophenyl)methanone (**4p**).* Following general procedure **B**, 1-(4-chlorophenyl)-2-mesyloxy-4-phenylbutan-1-one (0.40 mmol, 141 mg, 1.00 equiv) was irradiated for 1 h using UV-B irradiation and 48 h using a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 70:30), the title compound (68.8 mg, 0.19 mmol, 48%, 2.9:1 d.r.) was obtained as a colorless solid. R_f = 0.48 (4:1 cyclohexane/ethyl acetate), IR/cm^{-1} (ATR): 3026, 1686, 1571, 1493, 1204, 759, 735, 699. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ 7.97 (t, J = 1.9 Hz, 0.3H, H-2‴, minor), 7.96 (t, J = 1.9 Hz, 1.0H, H-2‴, major), 7.90−7.88 (m, 0.3H, H-6‴, minor), 7.87−7.84 (m, 1.0H, H-3‴, major), 7.53−7.51 (m, 0.3H, H-4‴, minor), 7.51−7.47 (m, 1.0H, H-4‴, major), 7.41−7.38 (m, 0.3H, H-5‴, minor), 7.38−7.35 (m, 1.0H, H-5‴, major), 7.31−7.14 (m, 13.2H, H-2′-6′ + H-2″-6″, minor + major), 6.50−6.48 (m, 0.3H, H-3, minor), 6.36−6.33 (m, 1.0H, H-3, major), 5.05−5.01 (m, 0.3H, H-1, minor), 5.00−4.95 (m, 1.0H, H-1, major), 4.20−4.14 (m, 1.2H, H-4, minor + major), 3.12−3.03 (m, 1.0H, H-5a, major), 2.61−2.54 (m, 0.3H, H-5a, minor), 2.43−2.36 (m, 0.3H, H-5b, minor), 1.98−1.91 (m, 1.0H, H-5b, major). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 199.9 (CO, major), 199.4 (CO, minor), 144.70 (C-1″, minor) 144.66 (C-1″, major), 142.5 (C-2, major), 142.2 (C-2, minor), 137.9 (C-1‴, major), 137.8 (C-1‴, minor), 135.2 (C-1′, major), 135.1 (C-1′, minor), 135.0 (C-3‴, major), 134.8 (C-3‴, minor), 133.5 (C-3, minor), 133.19 (C-4‴, minor), 133.18 (C-3, major), 133.1 (C-4‴, major), 130.1 (C-5‴, minor), 130.0 (C-5‴, major), 128.72 (C-2‴, minor + major), 128.65 (C-3″ + C-5″, minor), 128.6 (C-3″ + C-5″, major), 128.53 (C-3′ + C-5′, minor), 128.48 (C-3′ + C-5′, major), 127.64 (C-2″ + C-6″, major), 127.63 (C-4′, minor), 127.5 (C-4′, major), 127.3 (C-2″ + C-6″, minor), 126.68 (C-6‴, minor), 126.67 (C-4″, major; C-6‴, minor), 126.6 (C-4″, major), 125.94 (C-2′ + C-6′, major), 125.88 (C-2′ + C-6′, minor), 53.7 (C-1, major), 53.5 (C-1, minor), 51.3 (C-4, major), 50.8 (C-4, minor), 40.1 (C-5, minor), 39.5 (C-5, major). MS (ESI): m/z = 359.1 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{24}H_{20}ClO$ 359.1200, found 359.1197.

*(2,4-Diphenyl-cyclopent-2-en-1-yl)(3-methylphenyl)methanone (**4q**).* Following general procedure **B**, 1-(3-methylphenyl)-2-mesyloxy-4-phenylbutan-1-one (0.40 mmol, 133 mg, 1.00 equiv) was irradiated for 1 h using UV-B irradiation and 89 h using a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 70:30), the title compound (75.8 mg, 0.22 mmol, 56%, 2.0:1 d.r.) was obtained as a colorless solid. R_f = 0.48 (4:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3058, 1680, 1601, 1494, 1447, 1244, 1160, 699. ^{1}H NMR, COSY, TOCSY, NOESY (600 MHz, $CDCl_3$) δ 7.89−7.86 (m, 1.0H, H-2‴ + H-6‴, minor), 7.86−7.83 (m, 2.0H, H-2‴ + H-6‴, major), 7.44−7.28 (m, 11.6H, H-2′ + H-6′ + H-2″-3″ + H-5″-6″ + H-4‴-5‴, major; H-2′-3′ + H-5′-6′ + H-3″ + H-5″ + H-4‴-5‴, minor), 7.27−7.22 (m, 3.8H, H-3′ + H-5′, major; H-4′ + H-2″ + H-6″, minor), 7.23−7.18 (m, 2.3H, H-4′ + H-4″, major; H-4″, minor), 6.55−6.53 (m, 0.5H, H-3, minor), 6.40−6.38 (m, 1.0H, H-3, major), 5.16−5.12 (m, 0.5H, H-1, minor), 5.11−5.06 (m, 1.0H, H-1, major), 4.25−4.22 (m, 0.5H, H-4, minor), 4.22−4.18 (m, 1.0H, H-4, major), 3.16−3.08 (m, 1.0H, H-5a, major), 2.66−2.60 (m, 0.5H, H-5a, minor), 2.47−2.42 (m, 0.5H, H-5b, major), 2.44 (s, 1.4H, C-3‴-CH_3, minor), 2.42 (s, 2.9H, C-3‴-CH_3, major), 2.03−1.97 (m, 1.0H, H-5b, minor). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 201.4 (CO, major), 200.8 (CO, minor), 145.04 (C-1″, minor), 144.95 (C-1″, major), 142.9 (C-2, major), 142.7 (C-2, minor), 138.6 (C-3‴, minor), 138.5 (C-3‴, major), 136.5 (C-1‴, major), 136.3 (C-1‴, minor), 135.4 (C-1′, major), 135.0 (C-1′, minor), 134.1 (C-4‴, minor), 134.0 (C-4‴, major), 133.3 (C-3, minor), 133.0 (C-3, major), 129.21 (C-2‴, minor), 129.18 (C-2‴, major), 128.64 (C-3″ + C-5″ + C-5‴, minor), 128.57 (C-3″ + C-5″ + C-5‴, major), 128.49 (C-3′ + C-5′, minor), 128.4 (C-3′ + C-5′, major), 127.7 (C-2″ + C-6″, major), 127.5 (C-4″, minor), 127.40 (C-2″+ C-6″, minor), 127.36 (C-4″, major), 126.6 (C-4′, minor), 126.5 (C-4′, major), 126.02 (C-2′ + C-6′, major), 125.96 (C-2′ + C-6′, minor), 125.89 (C-6‴, minor), 125.86 (C-6‴, major), 53.5 (C-1, major), 53.4 (C-1, minor), 51.4 (C-4, major), 50.8 (C-4, minor), 40.5 (C-5, minor), 39.7 (C-5, major), 21.45 (C-3‴-CH_3, minor), 21.42 (C-3‴-CH_3, major). MS (ESI): m/z = 361.1 $[M + Na]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{25}H_{23}O$ 339.1744, found 339.1748.

*(2-Phenyl-4-cyanocyclopent-2-en-1-yl)(phenyl)methanone (**4s**).* Following general procedure **B**, 4-cyano-2-mesyloxy-1-phenylbutan-1-one (0.40 mmol, 107 mg, 1.00 equiv) was irradiated for 1.5 h using UV-B irradiation and 24 h using a blue LED. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 98:2 → 70:30) and preparative HPLC (H-Tec, eluent: water/acetonitrile, 45:55), the two diastereomers could be isolated as colorless oils (combined 35 mg, 0.13 mmol, 32%, 2.0:1 d.r.).

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*(1,4-cis)(2-Phenyl-4-cyanocyclopent-2-en-1-yl)(phenyl)-methanone (cis-**4s**).* The (1,4-*cis*) diastereomer (23 mg, 0.09 mmol, 22%) was isolated as a colorless oil. R_f = 0.31 (2:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3059, 2238, 1681, 1596, 1447, 1329, 1212, 1002, 761, 693. ^{1}H NMR, COSY, TOCSY, NOESY (400 MHz, $CDCl_3$) δ 8.04−7.99 (m, 2H, H-2″ + H-6″), 7.65−7.60 (m, 1H, H-4″), 7.54−7.48 (m, 2H, H-3″ + H-5″), 7.33−7.21 (m, 5H, H-2′-6′), 6.25−6.22 (m, 1H, H-3), 5.08−5.01 (m, 1H, H-1), 3.94−3.87 (m, 1H, H-4), 3.02−2.92 (m, 1H, H-5a), 2.53−2.41 (m, 1H, H-5b). ^{13}C{H} NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ 198.8 (C-1), 147.1 (C-2), 135.9 (C-1‴), 133.73 (C-1′), 133.67 (C-4‴), 128.9 (C-3‴ + C-5‴), 128.7 (C-2′ + C-6′ + C-2‴ + C-6‴), 128.6 (C-4′), 126.3 (C-3′ + C-5′), 122.8 (C-3), 119.9 (CN), 52.7 (C-1), 34.1 + 34.0 (C-4 + C-5). HRMS (ESI-ToF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{15}NONa$ 296.1046, found 296.1051.

*(1,4-trans)(2-Phenyl-4-cyanocyclopent-2-en-1-yl)(phenyl)-methanone (trans-**4s**).* The (1,4-*trans*) isomer (12 mg, 0.04 mmol, 10%) was isolated as a colorless oil. R_f = 0.49 (2:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3059, 2238, 1681, 1595, 1447, 1212, 989, 946, 691. ^{1}H NMR, COSY, NOESY (400 MHz, $CDCl_3$) δ 8.05−7.98 (m, 2H, H-2″ + H-6″), 7.68−7.61 (m, 1H, H-4″), 7.57−7.49 (m, 2H, H-3″ + H-5″), 7.31−7.23 (m, 5H, H-2′-6′), 6.34−6.27 (m, 1H, H-3), 5.20−5.06 (m, 1H, H-1), 4.00−3.90 (m, 1H, H-4), 2.85−2.73 (m, 1H, H-5a), 2.65−2.52 (m, 1H, H-5b). ^{13}C{H} NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ 199.3 (CO), 146.5 (C-2), 135.7 (C-1″), 133.9 (C-4″), 133.5 (C-1′), 129.0 (C-3″ + C-5″), 128.7 + 128.6 (C-2′ + C-4′ + C-6′ + C-2″ + C-6″), 126.2 (C-3′ + C-5′), 123.6 (C-3), 120.6 (CN), 52.0 (C-1), 34.8 (C-5), 34.3 (C-4). HRMS (ESI-ToF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{15}NONa$ 296.1046, found 296.1051.

Synthesis of γ-Pyridinylated Ketones. *Method **A**.* An oven-dried Schlenk tube (10 mL) was charged with the corresponding cyclopropane **2** (0.30 mmol, 1.00 equiv), cyanopyridine **5** (0.39 mmol, 1.30 equiv), and Hantzsch ester (0.69 mmol, 175 mg, 2.30 equiv) under nitrogen atmosphere. The mixture was suspended in dry MTBE (10.0 mL, c = 0.03 M). The mixture was degassed and then placed in front of a blue LED (see the materials section) at a distance of 5 cm. The vessel was irradiated until TLC or HPLC/ESI-MS indicated full consumption of the starting material (24−72 h). The solvent was removed *in vacuo*, and the residue was purified by flash chromatography to afford the γ-pyridinylated ketones **6**. Some of the products were purified using preparative HPLC with mixtures of water and acetonitrile as an eluent.

*Method **B**.* In an oven-dried quartz tube under nitrogen atmosphere, the α-mesyloxyketones **1** (0.30 mmol, 1.00 equiv) and 1-methylimidazole (0.60 mmol, 47.8 μL, 2.00 equiv) were dissolved in dry toluene (30.0 mL, c = 0.01 M). The reaction tube was degassed and placed into a Rayonet photoreactor. The vessel was irradiated (λ_{max} = 300 nm, 16 × 8 W) until TLC or HPLC/ESI-MS indicated full consumption of the starting material (1.0 h). The precipitated methanesulfonate salt was filtered, washed with toluene, and the solvent was removed *in vacuo*. The residue was dissolved in dry MTBE (10.0 mL, c = 0.03 M) and transferred to a 10 mL Schlenk tube charged with cyanopyridine (0.39 mmol, 1.30 equiv) and Hantzsch ester (0.42 mmol, 1.05 equiv) under nitrogen atmosphere. The suspension was degassed and placed in front of a blue LED at a distance of 5 cm. The vessel was irradiated until TLC or HPLC/ESI-MS indicated full consumption of the starting material (24−48 h). The solvent was removed *in vacuo*, and the residue was purified by flash column chromatography to afford the corresponding γ-pyridinylated ketones **6**. Some of the products were further purified using preparative HPLC with mixtures of water and acetonitrile as an eluent.

*1,4-Diphenyl-4-(pyridine-4-yl)butan-1-one (**6a**).* Following general procedure **A**, phenyl-[phenylcyclopropyl]methanone (0.30 mmol, 66.6 mg, 1.00 equiv) and 4-cyanopyridine (0.39 mmol, 40.6 mg, 1.30 equiv) were irradiated for 48 h at room temperature. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 90:10 → 0:100), the title compound (63 mg, 0.21 mmol, 70%) was obtained as a colorless oil.

Following general procedure **B**, 1,4-diphenyl-2-mesyloxybutan-1-one (0.30 mmol, 95.4 mg, 1.00 equiv) was irradiated for 1 h with UV-B and after mixing with 4-cyanopyridine (0.39 mmol, 40.6 mg, 1.30 equiv) for 48 h with a blue LED at room temperature. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 90:10 → 0:100), the title compound (42.0 mg, 0.14 mmol, 46%) was obtained as a colorless oil.

R_f = 0.33 (2:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3027, 1682, 1596, 1449, 1413, 1181, 992, 752, 701. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 8.53 (s, 2H, H-2‴ + H-6‴), 7.92−7.84 (m, 2H, H-2′ + H-6′), 7.60−7.53 (m, 1H, H-4′), 7.49−7.40 (m, 2H, H-3′ + H-5′), 7.38−7.31 (m, 2H, H-3″ + H-5″), 7.29−7.20 (m, 5H, H-2″ + H-4″ + H-6″ + H-3‴ + H-5‴), 4.04 (t, J = 7.9 Hz, 1H, H-4), 3.00−2.91 (m, 2H, H-2), 2.61−2.45 (m, 2H, H-3). ^{13}C{H} NMR, HSQC, HMBC (75 MHz, $CDCl_3$) δ 199.5 (C-1), 153.5 (C-1‴), 150.1 (C-2‴ + C-6‴), 142.5 (C-1″), 136.9 (C-1′), 133.3 (C-4′), 129.0 (C-3″ + C-5″), 128.7 (C-3′ + C-5′), 128.1 (C-2′ + C-6′ + C-2″ + C-6″), 127.1 (C-4″), 123.3 (C-3‴ + C-5‴), 49.9 (C-4), 36.5 (C-2), 29.1 (C-3). MS (ESI): m/z = 302.2 $[M + H]^+$. The spectroscopic data are in accordance with the literature.[35]

*1,4-Diphenyl-4-(pyridine-2-yl)butan-1-one (**6b**).* Following general procedure **A**, (phenyl)-[2-phenylcyclopropyl]methanone (0.30 mmol, 66.6 mg, 1.00 equiv) and 2-cyanopyridine (0.39 mmol, 37.6 μL, 1.30 equiv) were irradiated for 48 h at room temperature. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 90:10 → 0:100) and preparative HPLC (C_{18}PFP, eluent: water/acetonitrile, 50/50, t_R = 11.8 min), the title compound (43.0 mg, 0.14 mmol, 48%) was obtained as a colorless oil. R_f = 0.49 (2:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3060, 2931, 1682, 1589, 1449, 1433, 749, 701, 523. ^{1}H NMR, COSY, NOESY (600 MHz, $CDCl_3$) δ 8.60−8.56 (m, 1H, H-6‴), 7.91−7.83 (m, 2H, H-2′ + H-6′), 7.62−7.56 (m, 1H, H-4‴), 7.54−7.51 (m, 1H, H-4′), 7.44−7.39 (m, 2H, H-3′ + H-5′), 7.38−7.35 (m, 2H, H-2″ + H-6″), 7.32−7.28 (m, 2H, H-3″ + H-5″), 7.23−7.19 (m, 2H, H-4″ + H-3‴), 7.15−7.10 (m, 1H, H-5‴), 4.22 (t, J = 7.9 Hz, 1H, H-4), 2.98−2.93 (m, 2H, H-2), 2.73−2.65 (m, 1H, H-3a), 2.58−2.49 (m, 1H, H-3b). ^{13}C{H} NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ 200.0 (C-1), 163.1 (C-2‴), 149.0 (C-6‴), 143.0 (C-1″), 136.8 (C-1′ + C-4‴), 133.0 (C-4′), 128.7 (C-3″ + C-5″), 128.5 (C-3′ + C-5′), 128.1 (C-2′ + C-6′ + C-2″ + C-6″), 126.7 (C-4″), 123.0 (C-3‴), 121.6 (C-5‴), 52.6 (C-4), 36.8 (C-2), 29.4 (C-3). MS (ESI): m/z = 302.1 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M+H]^+$ calcd for $C_{21}H_{20}NO$ 302.1547, found 302.1540.

*1,4-Diphenyl-4-(isoquinolin-1-yl)butan-1-one (**6c**).* Following general procedure **A**, (phenyl)-[2-phenylcyclopropyl]methanone (0.30 mmol, 66.6 mg, 1.00 equiv) and 1-cyaonisoquinoline (0.39 mmol, 60.1 mg, 1.30 equiv) were irradiated for 48 h at room temperature. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 90:10 → 50:50), the title compound (62.0 mg, 0.18 mmol, 59%) was obtained as a colorless oil. R_f = 0.54 (2:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2930, 1681, 1598, 1561, 1493, 1232, 825, 746, 701. ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ 8.59 (d, J = 5.7 Hz, 1H, H-8‴), 8.22 (d, J = 8.5 Hz, 1H, H-3‴), 7.92−7.86 (m, 2H, H-2′ + H-6′), 7.81−7.76 (m, 1H, H-6‴), 7.63 7.58 (m, 1H, H-4‴), 7.56 (d, J = 5.7 Hz, 1H, H-7‴), 7.53−7.47 (m, 2H, H-4′ + H-4‴), 7.45−7.34 (m, 4H, H-3′ + H-5′ + H-2″ + H-6″), 7.29−7.20 (m, 2H, H-3″ + H-5″), 7.18−7.12 (m, 1H, H-4″), 5.12−5.03 (m, 1H, H-4), 3.13−3.04 (m, 1H, H-2a), 3.01−2.96 (m, 1H, H-2b), 2.95−2.89 (m, 1H, H-3a), 2.71−2.56 (m, 1H, H-3b). ^{13}C{H} NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ 200.5 (C-1), 161.4 (C-2‴), 143.6 (C-1), 141.5 (C-8‴), 136.9 (C-1′), 136.6 (C-6a‴), 132.9 (C-4′), 129.8 (C-5‴), 128.6 + 128.5 (C-3′ + C-5′), 128.1 (C-2′ + C-6′ + C-2″ + C-6″), 127.4 (C-6‴), 127.3 (C-2a‴), 126.5 (C-4″), 125.2 (C-3‴), 119.8 (C-7‴), 47.7 (C-4), 36.9 (C-2), 30.4 (C-3). MS (ESI): m/z = 352.1 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{25}H_{22}NO$ 352.1696, found 352.1704.

*1-(4-Methoxyphenyl)-4-phenyl-4-(pyridin-4-yl)butan-1-one (**6d**).* Following general procedure **A**, (4-methoxyphenyl)-[2-phenylcyclopropyl]methanone (0.30 mmol, 75.6 mg, 1.00 equiv) and 4-cyanopyridine (0.39 mmol, 40.6 mg, 1.30 equiv) were irradiated for 48 h at room temperature. After column chromatog-

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raphy (SiO_2, eluent: cyclohexane/ethyl acetate, 90:10 → 0:100), the title compound (49.0 mg, 0.15 mmol, 49%) was obtained as a colorless oil. R_f = 0.23 (1:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 1673, 1598, 1415, 1257, 1171, 1029, 984, 702. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 8.54−8.47 (m, 2H, H-2‴ + H-6‴), 7.87−7.77 (m, 2H, H-2′ + H-6′), 7.35−7.28 (m, 2H, H-3″ + H-5″), 7.25−7.19 (m, 5H, H-2″ + H-4″ + H-6″ + H-3‴ + H-5‴), 6.91−6.86 (m, 2H, H-3′ + H-5′), 4.07−3.97 (m, 1H, H-4), 3.84 (s, 3H, OCH_3), 2.93−2.83 (m, 2H, H-2), 2.55−2.43 (m, 2H, H-3). ^{13}C{H} NMR, HSQC, HMBC (75 MHz, $CDCl_3$) δ 198.1 (C-1), 163.6 (C-4′), 154.1 (C-4‴), 149.6 (C-2‴ + C-6‴), 142.4 (C-1″), 130.3 (C-2′ + C-6′), 129.9 (C-1′), 129.0 (C-3″ + C-5″), 128.1 (C-2″ + C-6″), 127.1 (C-4″), 123.4 (C-3‴ + C-5‴), 113.8 (C-3′ + C-5′), 55.6 (OCH_3), 49.9 (C-4), 36.1 (C-2), 29.2 (C-3). MS (ESI): m/z = 332.1 $[M + H]^+$. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{22}H_{22}NO_2$ 332.1645, found 332.1650.

1-(4-Fluorophenyl)-4-(4-methoxyphenyl)-4-(pyridin-4-yl)butan-1-one (**6e**). Following general procedure **A**, (4-fluorophenyl)-[2-(4-methoxyphenyl)cyclopropyl]methanone (0.30 mmol, 81.1 mg, 1.00 equiv) and 4-cyanopyridine (0.39 mmol, 40.6 mg, 1.30 equiv) were irradiated for 48 h at room temperature. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 90:10 → 0:100), the title compound (67.0 mg, 0.19 mmol, 64%) was obtained as a colorless oil. R_f = 0.35 (1:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2935, 1682, 1596, 1509, 1247, 1229, 1156, 809, 560. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 8.50 (s, 2H, H-2‴ + H-6‴), 7.92−7.81 (m, 2H, H-2′ + H-6′), 7.21−7.16 (m, 2H, H-3‴ + H-5‴), 7.16−7.12 (m, 2H, H-2″ + H-6″), 7.12−7.05 (m, 2H, H-3′ + H-5′), 6.90−6.81 (m, 2H, H-3″ + H-5″), 3.95 (t, J = 7.9 Hz, 1H, H-4), 3.78 (s, 3H, OCH_3), 2.89 (t, J = 7.3 Hz, 2H, H-2), 2.56−2.35 (m, 2H, H-3). ^{19}F NMR (282 MHz, $CDCl_3$): δ −105.10 (tt, J = 8.5, 5.3 Hz). ^{13}C{H} NMR, HSQC, HMBC (75 MHz, $CDCl_3$) δ 197.8 (C-1), 165.74 (d, $^1J_{CF}$ = 255.0 Hz, C-4′), 158.5 (C-4″), 153.9 (C-4″), 149.8 (C-2‴ + C-6‴), 134.2 (C-1″), 133.18 (d, $^4J_{CF}$ = 3.0 Hz, C-1′), 130.6 (d, $^3J_{CF}$ = 9.4 Hz, C-2′ + C-6′), 128.9 (C-2″ + C-6″), 123.1 (C-3″ + C-5″), 115.68 (d, $^2J_{CF}$ = 21.8 Hz, C-3′ + C-5′), 114.2 (C-3″ + C-5″), 55.3 (OCH_3), 48.9 (C-4), 36.3 (C-2), 29.1 (C-3). MS (ESI): m/z = 350.1 $[M + Na]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{22}H_{21}FNO_2$ 350.1551, found 350.1558.

1-Phenyl-4-(4-cyanophenyl)-4-(pyridin-4-yl)butan-1-one (**6f**). Following general procedure **A**, (phenyl)-[2-(4-cyanophenyl)-cyclopropyl]methanone (0.30 mmol, 74.1 mg, 1.00 equiv) and 4-cyanopyridine (0.39 mmol, 40.6 mg, 1.30 equiv) were irradiated for 48 h at room temperature. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 90:10 → 0:100), the title compound (67.2 mg, 0.20 mmol, 68%) was obtained as a yellow oil. R_f = 0.21 (1:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 2927, 2228, 1721, 1683, 1596, 1448, 1253, 747, 691, 598. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 8.60−8.48 (m, 2H, H-2‴ + H-6‴), 7.88−7.80 (m, 2H, H-2′ + H-6′), 7.64−7.58 (m, 2H, H-3″ + H-5″), 7.58−7.52 (m, 1H, H-4′), 7.46−7.39 (m, 2H, H-3′ + H-5′), 7.38−7.33 (m, 2H, H-2″ + H-6″), 7.22−7.15 (m, 2H, H-3‴ + H-6‴), 4.12 (t, J = 7.9 Hz, 1H, H-4), 2.96−2.88 (m, 2H, H-2), 2.57−2.45 (m, 2H, H-3). ^{13}C{H} NMR, HSQC, HMBC (75 MHz, $CDCl_3$) δ 198.8 (C-1), 152.1 (C-4‴), 149.9 (C-2‴ + C-6‴), 147.9 (C-1″), 136.5 (C-1′), 133.4 (C-4′), 132.7 (C-3″ + C-5″), 128.8 (C-2″ + C-6″), 128.7 (C-3′ + C-5′), 127.9 (C-2′ + C-6′), 123.3 (C-3‴ + C-5‴), 118.5 (CN), 111.1 (C-4″), 49.6 (C-4), 35.9 (C-2), 28.5 (C-3). MS (ESI): m/z = 327.1 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{22}H_{19}N_2O$ 327.1492, found 327.1498.

1-(3-Chlorophenyl)-4-phenyl-4-(pyridin-4-yl)butan-1-one (**6g**). Following general procedure **B**, 1-(3-chlorophenyl)-2-mesyloxy-4-phenylbutan-1-one (0.30 mmol, 106 mg, 1.00 equiv) was irradiated for 1 h with UV-B and after mixing with 4-cyanopyridine (0.39 mmol, 40.6 mg, 1.30 equiv) for 48 h with a blue LED at room temperature. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 90:10 → 0:100) and preparative HPLC (C_{18}PFP, eluent: water/acetonitrile, 45/55, t_R = 18.0 min), the title compound (38 mg, 0.11 mmol, 38%) was obtained as a colorless oil. A further purification using other HPLC columns was not successful. R_f = 0.33 (1:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3026, 1686, 1595, 1414, 1224, 1202, 995, 768, 744, 701, 558. ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ 8.52 (s, 2H, H-2‴ + H-6‴), 7.82 (t, J = 1.9 Hz, 1H, H-2′), 7.71 (dt, J = 7.9, 1.4 Hz, 1H, H-6′), 7.51 (ddd, J = 7.9, 1.9, 1.4 Hz, 1H, H-4′), 7.40−7.35 (m, 1H, H-5′), 7.35−7.30 (m, 2H, H-3″ + H-5″), 7.25−7.19 (m, 5H, H-2″ + H-4″ + H-6″ + H-3‴ + H-5‴), 4.01 (t, J = 7.9 Hz, 1H, H-4), 2.94−2.86 (m, 2H, H-2), 2.57−2.44 (m, 2H, H-3). ^{13}C{H} NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ 198.1 (C-1), 153.6 (C-4‴), 149.8 (C-2‴ + C-6‴), 142.1 (C-1″), 138.3 (C-1′), 135.0 (C-3′), 133.1 (C-4′), 130.0 (C-5′), 129.0 (C-3″ + C-5″), 128.1 (C-2′), 128.0 (C-2″ + C-6″), 127.1 (C-4″), 126.0 (C-6′), 123.2 (C-3‴ + C-5‴), 49.7 (C-4), 36.5 (C-2), 28.8 (C-3). MS (ESI): m/z = 336.1 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{21}H_{19}ClNO$ 336.1150, found 336.1153.

1-(3-Methylphenyl)-4-phenyl-4-(pyridin-4-yl)butan-1-one (**6h**). Following general procedure **B**, 1-(3-methylphenyl)-2-mesyloxy-4-phenylbutan-1-one (0.30 mmol, 99.6 mg, 1.00 equiv) was irradiated for 1 h with UV-B and after mixing with 4-cyanopyridine (0.39 mmol, 40.6 mg, 1.30 equiv) for 48 h with a blue LED at room temperature. After column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate, 90:10 → 0:100) and preparative HPLC (C_{18}PFP, eluent: water/acetonitrile, 90:10 → 10:90, t_R = 15.3 min), the title compound (49 mg, 0.16 mmol, 52%) was obtained as a colorless oil. R_f = 0.14 (2:1 cyclohexane/ethyl acetate). IR/cm^{-1} (ATR): 3026, 1681, 1595, 1414, 1257, 1178, 993, 770, 701, 558. ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ = 8.53 (s, 2H, H-2‴ + H-6‴), 7.70−7.63 (m, 2H, H-2′ + H-6′), 7.41−7.31 (m, 4H, H-4′-5′, H-3″ + H-5″), 7.30−7.20 (m, 5H, H-2″ + H-4″ + H-6″ + H-3‴ + H-5‴), 4.04 (t, J = 7.9 Hz, 1H, H-4), 2.98−2.90 (m, 2H, H-2), 2.57−2.46 (m, 2H, H-3), 2.40 (s, 3H, C-3′-CH_3). ^{13}C{H} NMR, HSQC, HMBC (75 MHz, $CDCl_3$) δ 199.7 (C-1), 153.6 (C-4‴), 149.9 (C-2‴ + C-6‴), 142.4 (C-1″), 138.4 (C-3′), 136.8 (C-1′), 133.9 (C-2′), 128.9 (C-3″ + C-5″), 128.5 (C-4′ + C-6′), 128.0 (C-2″ + C-6″), 127.0 (C-4″), 125.2 (C-5′), 123.3 (C-3‴ + C-5‴), 49.8 (C-4), 36.5 (C-2), 29.1 (C-3), 21.4 (C-3′-CH_3). MS (ESI): m/z = 316.1 $[M + H]^+$. HRMS (ESI-ToF) m/z: $[M + H]^+$ calcd for $C_{22}H_{22}NO$ 316.1696, found 316.1702.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02591.

Detailed information on light sources and irradiation setup, further information regarding the synthesis of amino-substituted cyclopentene **4m**, reoptimization of the Norrish−Yang as well as optimization of formal [3 + 2] and radical−radical coupling reaction, additional information and procedures of the mechanistic studies, computational data, and copies of the ^{1}H, ^{13}C{H}, and relevant HSQC, HMBC, and NOESY spectra (PDF)

XYZ-coordinates of all calculated structures used for the computation of the energy profile of the ring-closing mechanism (ZIP)

■ AUTHOR INFORMATION

Corresponding Author

Till Opatz − *Department of Chemistry, Johannes Gutenberg University, 55128 Mainz, Germany;* orcid.org/0000-0002-3266-4050; Email: opatz@uni-mainz.de

Authors

Jan Paternoga − *Department of Chemistry, Johannes Gutenberg University, 55128 Mainz, Germany*

Jonas Kühlborn − *Department of Chemistry, Johannes Gutenberg University, 55128 Mainz, Germany*

Nils Ole Rossdam − *Department of Chemistry, Johannes Gutenberg University, 55128 Mainz, Germany*

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Souillart, L.; Cramer, N. Catalytic C−C bond activations via oxidative addition to transition metals. *Chem. Rev.* **2015**, *115*, 9410−9464.

(2) (a) Rotstein, B. H.; Zaretsky, S.; Rai, V.; Yudin, A. K. Small Heterocycles in Multicomponent Reactions. *Chem. Rev.* **2014**, *114*, 8323−8359. (b) Cavitt, M. A.; Phun, L. H.; France, S. Intramolecular donor−acceptor cyclopropane ring-opening cyclizations. *Chem. Soc. Rev.* **2014**, *43*, 804−818. (c) Wang, F.; Yu, S.; Li, X. Transition metal-catalysed couplings between arenes and strained or reactive rings: combination of C−H activation and ring scission. *Chem. Soc. Rev.* **2016**, *45*, 6462−6477.

(3) Hoffmann, N. Photochemical Reactions as Key Steps in Organic Synthesis. *Chem. Rev.* **2008**, *108*, 1052−1103.

(4) Yang, N.; Yang, D.-D. H. Photochemical reactions of ketones in solution. *J. Am. Chem. Soc.* **1958**, *80*, 2913−2914.

(5) Wessig, P.; Muehling, O. Photochemical synthesis of highly functionalized cyclopropyl ketones. *Helv. Chim. Acta* **2003**, *86*, 865−893.

(6) Dudev, T.; Lim, C. Ring strain energies from ab initio calculations. *J. Am. Chem. Soc.* **1998**, *120*, 4450−4458.

(7) Pusch, S.; Opatz, T. A Photochemical One-Pot Three-Component Synthesis of Tetrasubstituted Imidazoles. *Org. Lett.* **2014**, *16*, 5430−5433.

(8) (a) Pusch, S.; Kowalczyk, D.; Opatz, T. A Photoinduced Cobalt-Catalyzed Synthesis of Pyrroles through in Situ-Generated Acylazirines. *J. Org. Chem.* **2016**, *81*, 4170−4178. (b) Pusch, S.; Schollmeyer, D.; Opatz, T. A Light-Induced Vinylogous Nazarov-Type Cyclization. *Org. Lett.* **2016**, *18*, 3043−3045. (c) Paternoga, J.; Opatz, T. A Copper-Catalyzed Synthesis of Pyrroles through Photochemically Generated Acylazirines. *Eur. J. Org. Chem.* **2019**, *2019*, 7067−7078.

(9) Luque, A.; Paternoga, J.; Opatz, T.Release Chemistry of Photogenerated Small-Ring Intermediates *Chem. - Eur. J.* Accepted for publication , DOI: 10.1002/chem.202004178.

(10) For examples of metal-catalyzed formal [3 + 2] cycloadditions of ketocyclopropanes see: (a) Liu, L.; Montgomery, J. Dimerization of cyclopropyl ketones and crossed reactions of cyclopropyl ketones with enones as an entry to five-membered rings. *J. Am. Chem. Soc.* **2006**, *128*, 5348−5349. (b) Ogoshi, S.; Nagata, M.; Kurosawa, H. Formation of nickeladihydropyran by oxidative addition of cyclopropyl ketone. Key intermediate in nickel-catalyzed cycloaddition. *J. Am. Chem. Soc.* **2006**, *128*, 5350−5351. (c) Tamaki, T.; Nagata, M.; Ohashi, M.; Ogoshi, S. Synthesis and Reactivity of Six-Membered Oxa-Nickelacycles: A Ring-Opening Reaction of Cyclopropyl Ketones. *Chem. − Eur. J.* **2009**, *15*, 10083−10091. (d) Tamaki, T.; Ohashi, M.; Ogoshi, S. [3+ 2] Cycloaddition Reaction of Cyclopropyl Ketones with Alkynes Catalyzed by Nickel/Dimethylaluminum Chloride. *Angew. Chem.* **2011**, *123*, 12273−12276. (e) Hao, W.; Harenberg, J. H.; Wu, X.; MacMillan, S. N.; Lin, S. Diastereo-and enantioselective formal [3+ 2] cycloaddition of cyclopropyl ketones and alkenes via Ti-catalyzed radical redox relay. *J. Am. Chem. Soc.* **2018**, *140*, 3514−3517.

(11) For examples of photoredox-catalyzed formal [3 + 2] cycloadditions of ketocyclopropanes, see: (a) Amador, A. G.; Sherbrook, E. M.; Lu, Z.; Yoon, T. P. A general protocol for radical anion [3+ 2] cycloaddition enabled by Tandem lewis acid photoredox catalysis. *Synthesis* **2018**, *50*, 539. (b) Amador, A. G.; Sherbrook, E. M.; Yoon, T. P. Enantioselective photocatalytic [3+ 2] cycloadditions of aryl cyclopropyl ketones. *J. Am. Chem. Soc.* **2016**, *138*, 4722−4725. (c) Huang, X.; Lin, J.; Shen, T.; Harms, K.; Marchini, M.; Ceroni, P.; Meggers, E. Asymmetric [3+ 2] Photocycloadditions of Cyclopropanes with Alkenes or Alkynes through Visible-Light Excitation of Catalyst-Bound Substrates. *Angew. Chem., Int. Ed.* **2018**, *57*, 5454−5458. (d) Feng, L.; Yan, H.; Yang, C.; Chen, D.; Xia, W. Visible-light induced direct synthesis of polysubstituted furans from cyclopropyl ketones. *J. Org. Chem.* **2016**, *81*, 7008−7022. (e) Luis-Barrera, J.; Laina-Martín, V.; Rigotti, T.; Peccati, F.; Solans-Monfort, X.; Sodupe, M.; Mas-Ballesté, R.; Liras, M.; Alemán, J. Visible-Light Photocatalytic Intramolecular Cyclopropane Ring Expansion. *Angew. Chem., Int. Ed.* **2017**, *56*, 7826−7830. (f) Xuan, J.; He, X.-K.; Xiao, W.-J. Visible light-promoted ring-opening functionalization of three-membered carbo-and heterocycles. *Chem. Soc. Rev.* **2020**, *49*, 2546−2556.

(12) For review articles of Hantzsch ester-mediated photoredox chemistry in general and selected publications involving ketones and aldehydes see: (a) Huang, W.; Cheng, X. Hantzsch esters as multifunctional reagents in visible-light photoredox catalysis. *Synlett* **2017**, *28*, 148−158. (b) Wang, P.-Z.; Chen, J.-R.; Xiao, W.-J. Hantzsch esters: an emerging versatile class of reagents in photoredox catalyzed organic synthesis. *Org. Biomol. Chem.* **2019**, *17*, 6936−6951. (c) Jung, J.; Kim, J.; Park, G.; You, Y.; Cho, E. J. Selective Debromination and α-Hydroxylation of α-Bromo Ketones Using Hantzsch Esters as Photoreductants. *Adv. Synth. Catal.* **2016**, *358*, 74−80. (d) Zhu, J.; Yuan, Y.; Wang, S.; Yao, Z.-J. Synthesis of 2,3-Dialkylated Tartaric Acid Esters via Visible Light Photoredox-Catalyzed Reductive Dimerization of α-Ketoesters. *ACS Omega* **2017**, *2*, 4665−4677. (e) Lee, K. N.; Lei, Z.; Ngai, M.-Y. β-Selective reductive coupling of alkenylpyridines with aldehydes and imines via synergistic lewis acid/photoredox catalysis. *J. Am. Chem. Soc.* **2017**, *139*, 5003−5006. (f) Xu, X.; Min, Q.-Q.; Li, N.; Liu, F. Visible light-promoted umpolung coupling of aryl tri-/difluoroethanones with 2-alkenylpyridines. *Chem. Commun.* **2018**, *54*, 11017−11020. (g) Cao, K.; Tan, S. M.; Lee, R.; Yang, S.; Jia, H.; Zhao, X.; Qiao, B.; Jiang, Z. Catalytic enantioselective addition of prochiral radicals to vinylpyridines. *J. Am. Chem. Soc.* **2019**, *141*, 5437−5443.

(13) Konev, M. O.; Cardinale, L.; Jacobi von Wangelin, A. Catalyst-Free N-Deoxygenation by Photoexcitation of Hantzsch Ester. *Org. Lett.* **2020**, *22*, 1316−1320.

(14) Torres-Ochoa, R. O.; Leclair, A.; Wang, Q.; Zhu, J. Iron-Catalysed Remote C(sp3)−H Azidation of O-Acyl Oximes and N-Acyloxy Imidates Enabled by 1,5-Hydrogen Atom Transfer of Iminyl and Imidate Radicals: Synthesis of γ-Azido Ketones and β-Azido Alcohols. *Chem. − Eur. J.* **2019**, *25*, 9477−9484.

(15) Chen, D.; Xu, L.; Long, T.; Zhu, S.; Yang, J.; Chu, L. Metal-free, intermolecular carbopyridylation of alkenes via visible-light-induced reductive radical coupling. *Chem. Sci.* **2018**, *9*, 9012−9017.

(16) Cismesia, M. A.; Yoon, T. P. Characterizing chain processes in visible light photoredox catalysis. *Chem. Sci.* **2015**, *6*, 5426−5434.

(17) (a) Xia, Q.; Dong, J.; Song, H.; Wang, Q. Visible-Light Photocatalysis of the Ketyl Radical Coupling Reaction. *Chem. − Eur. J.* **2019**, *25*, 2949−2961. (b) Warren, J. J.; Tronic, T. A.; Mayer, J. M.

Thermochemistry of Proton-Coupled Electron Transfer Reagents and its Implications. *Chem. Rev.* **2010**, *110*, 6961−7001.
(18) (a) Zhao, Y.; Truhlar, D. G. The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements: two new functionals and systematic testing of four M06-class functionals and 12 other functionals. *Theor. Chem. Acc.* **2008**, *120*, 215−241. (b) Hehre, W. J.; Ditchfield, R.; Pople, J. A. Self—Consistent Molecular Orbital Methods. XII. Further Extensions of Gaussian—Type Basis Sets for Use in Molecular Orbital Studies of Organic Molecules. *J. Chem. Phys.* **1972**, *56*, 2257−2261. (c) Hariharan, P. C.; Pople, J. A. The influence of polarization functions on molecular orbital hydrogenation energies. *Theor. Chim. Acta* **1973**, *28*, 213−222. (d) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. Self-consistent molecular orbital methods. XXIII. A polarization-type basis set for second-row elements. *J. Chem. Phys.* **1982**, *77*, 3654−3665. (e) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. V. R. Efficient diffuse function-augmented basis sets for anion calculations. III. The 3-21+G basis set for first-row elements, Li−F. *J. Comput. Chem.* **1983**, *4*, 294−301. (f) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. A consistent and accurate ab initio parametrization of density functional dispersion correction (DFT-D) for the 94 elements H-Pu. *J. Chem. Phys.* **2010**, *132*, No. 154104. (g) Grimme, S.; Ehrlich, S.; Goerigk, L. Effect of the damping function in dispersion corrected density functional theory. *J. Comput. Chem.* **2011**, *32*, 1456−1465. (h) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378−6396.
(19) Goerigk, L.; Grimme, S. A thorough benchmark of density functional methods for general main group thermochemistry, kinetics, and noncovalent interactions. *Phys. Chem. Chem. Phys.* **2011**, *13*, 6670−6688.
(20) (a) Hait, D.; Haugen, E. A.; Yang, Z.; Oosterbaan, K. J.; Leone, S. R.; Head-Gordon, M. Accurate prediction of core-level spectra of radicals at density functional theory cost via square gradient minimization and recoupling of mixed configurations. *J. Chem. Phys.* **2020**, *153*, No. 134108. (b) Gräfenstein, J.; Kraka, E.; Filatov, M.; Cremer, D. Can unrestricted density-functional theory describe open shell singlet biradicals? *Int. J. Mol. Sci.* **2002**, *3*, 360−394.
(21) Peng, Q.; Duarte, F.; Paton, R. S. Computing organic stereoselectivity−from concepts to quantitative calculations and predictions. *Chem. Soc. Rev.* **2016**, *45*, 6093−6107.
(22) (a) Lipp, B.; Lipp, A.; Detert, H.; Opatz, T. Light-Induced Alkylation of (Hetero) aromatic Nitriles in a Transition-Metal-Free C−C-Bond Metathesis. *Org. Lett.* **2017**, *19*, 2054−2057. (b) Lipp, B.; Kammer, L. M.; Kücükdisli, M.; Luque, A.; Kühlborn, J.; Pusch, S.; Matulevičiūtė, G.; Schollmeyer, D.; Šačkus, A.; Opatz, T. Visible Light-Induced Sulfonylation/Arylation of Styrenes in a Double Radical Three-Component Photoredox Reaction. *Chem. − Eur. J.* **2019**, *25*, 8965−8969.
(23) Mcdevitt, P.; Vittimberga, B. M. The electron transfer reactions of cyano substituted pyridines and quinolines with thermally generated diphenyl ketyl. *J. Heterocycl. Chem.* **1990**, *27*, 1903−1908.
(24) Leifert, D.; Studer, A. The Persistent Radical Effect in Organic Synthesis. *Angew. Chem., Int. Ed.* **2020**, *59*, 74−108.
(25) Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. NMR chemical shifts of common laboratory solvents as trace impurities. *J. Org. Chem.* **1997**, *62*, 7512−7515.
(26) Lagoja, I.; Pannecouque, C.; Griffioen, G.; Wera, S.; Rojasdelaparra, V. M.; Van Aerschot, A. Substituted 2-aminothiazoles are exceptional inhibitors of neuronal degeneration in tau-driven models of Alzheimer's disease. *Eur. J. Pharm. Sci.* **2011**, *43*, 386−392.
(27) Motiwala, H. F.; Gülgeze, B.; Aubé, J. Copper-Catalyzed Oxaziridine-Mediated Oxidation of C−H Bonds. *J. Org. Chem.* **2012**, *77*, 7005−7022.
(28) Sun, W.; Wang, L.; Xia, C.; Liu, C. Dual Functionalization of α-Monoboryl Carbanions through Deoxygenative Enolization with Carboxylic Acids. *Angew. Chem., Int. Ed.* **2018**, *57*, 5501−5505.
(29) Gooßen, L. J.; Mamone, P.; Oppel, C. Catalytic Decarboxylative Cross-Ketonisation of Aryl- and Alkylcarboxylic Acids using Magnetite Nanoparticles. *Adv. Synth. Catal.* **2011**, *353*, 57−63.
(30) Streuff, J.; Feurer, M.; Bichovski, P.; Frey, G.; Gellrich, U. Enantioselective Titanium(III)-Catalyzed Reductive Cyclization of Ketonitriles. *Angew. Chem., Int. Ed.* **2012**, *51*, 8661−8664.
(31) Netz, N.; Díez-Poza, C.; Barbero, A.; Opatz, T. Modular De novo Synthesis of Unsymmetrical BODIPY Dyes Possessing Four Different Aryl Substituents. *Eur. J. Org. Chem.* **2017**, *2017*, 4580−4599.
(32) Cotugno, P.; Monopoli, A.; Ciminale, F.; Milella, A.; Nacci, A. Palladium-Catalyzed Cross-Coupling of Styrenes with Aryl Methyl Ketones in Ionic Liquids: Direct Access to Cyclopropanes. *Angew. Chem., Int. Ed.* **2014**, *53*, 13563−13567.
(33) Sato, M.; Uchimaru, F. Psychotropic Agents. V. Synthesis of 1, 3-Diphenyl-4-(4-substituted piperidinyl)-1-butanones and Related Compounds. *Chem. Pharm. Bull.* **1981**, *29*, 3134−3144.
(34) Allgäuer, D. S.; Jangra, H.; Asahara, H.; Li, Z.; Chen, Q.; Zipse, H.; Ofial, A. R.; Mayr, H. Quantification and theoretical analysis of the electrophilicities of Michael acceptors. *J. Am. Chem. Soc.* **2017**, *139*, 13318−13329.
(35) Bernardi, R.; Caronna, T.; Morrocchi, S.; Ursini, M. Photochemically induced reactions of selected ketones with 4-cyanopyridine in neutral and acidic medium. *J. Heterocycl. Chem.* **1996**, *33*, 1137−1142.

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