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Photochemistry

Intramolecular [2+2] Photocycloaddition of Cyclic Enones: Selectivity Control by Lewis Acids and Mechanistic Implications

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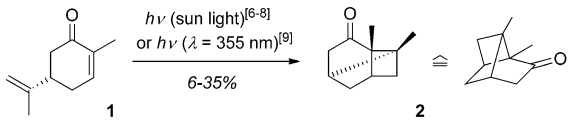
Abstract: The intramolecular [2+2] photocycloaddition of 3-alkenyl-2-cycloalkenones was performed in an enantioselective fashion (nine representative examples, 54–86% yield, 76–96% *ee*) upon irradiation at $\lambda = 366$ nm in the presence of an $AlBr_3$-activated oxazaborolidine as the Lewis acid. An extensive screening of proline-derived oxazaborolidines showed that the enantioface differentiation depends strongly on the nature of the aryl group at the 3-position of the heterocycle. DFT calculations of the Lewis acid–substrate complex indicate that attractive dispersion forces may be responsible for a change of the binding mode. The catalytic [2+2] photocycloaddition was shown to proceed on the triplet hypersurface with a quantum yield of 0.05. The positive effect of Lewis acids on the outcome of a given intramolecular [2+2] photocycloaddition was illustrated by optimizing the key step in a concise total synthesis of the sesquiterpene (±)-italicene.

Introduction

The intramolecular [2+2] photocycloaddition[1] of appropriately substituted 2-cycloalkenones is an enormously powerful transformation which has been extensively used in the total synthesis of natural products.[2] The reaction can be performed by direct irradiation, typically at a wavelength (λ) of 300–370 nm. Since intersystem crossing in enones is fast ($k_{ISC} \cong 10^{11}\ s^{-1}$),[3] the reaction proceeds via the first excited triplet state (T_1) which has π–π^* character. Compared to intermolecular reactions, there is an improved regioselectivity as the internal olefin is enforced to approach the photoexcited enone via an initial cyclization to a 1,4-diradical.[4] Five-membered ring formation is preferred where possible and dictates the regioselectivity of the reaction.[5]

Historically, the reaction belongs to one of the first photochemical transformations known to organic chemists. In 1908, Ciamician and Silber reported on the formation of carvonecamphor (**2**) upon exposure of carvone (**1**) to sunlight (Scheme 1).[6] The same observation was made by Sernagiotto a few years later.[7] In 1957, Büchi and Goldman isolated product **2**—still prepared by sunlight irradiation—and proved its constitution and configuration.[8] Meinwald and Schneider optimized the reaction employing an artificial light source with an emission maximum at $\lambda = 355$ nm and could isolate the desired product with a maximum yield of 35%.[9]



Scheme 1. The conversion of carvone (**1**) into carvonecamphor (**2**) representing the first intramolecular [2+2] photocycloaddition reaction of a cyclic enone.[6–9]

Despite the fact, that the reaction is so powerful, enantioselective variants of the enone [2+2] photocycloaddition have relied, until very recently, on the covalent attachment of a chiral auxiliary.[10] In 2013, our group presented the first enantioselective[11] enone [2+2] photocycloaddition reaction mediated by chiral Lewis acids.[12,13] The substrates were 5,6-dihydro-4-pyridones[14] to which an alkenyl chain was attached at the nitrogen atom. The chiral Lewis acid acts by coordination to the carbonyl carbon atom and lowers the energy difference between the ground state (S_0) and the first excited state (S_1). The chromophore is activated[15] and the allowed π–π^* absorption is red-shifted to absorb at $\lambda \geq 360$ nm. Although there is a weak n–π^* absorption of uncomplexed dihydropyridone at a similar wavelength, the Lewis acid complex has a much higher absorption coefficient and the reaction thus proceeds enantioselectively. Despite the fact that the reaction could be extended to the intramolecular [2+2] photocycloaddition of 3-alkenyloxy-2-cycloalkenones,[16] the intermolecular reaction of simple 2-cycloalkenones, such as 2-cyclohexenone, remained elusive until very recently.[17] In the context of the latter topic, we had performed optimization reactions with 3-alkenyl-2-cycloalke-

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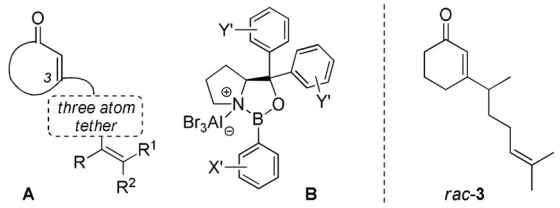
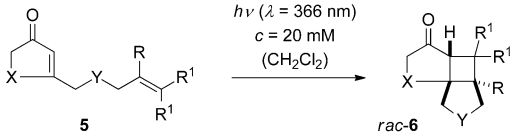


Figure 1. General structure of [2+2] photocycloaddition substrates **A** and of putative chiral catalysts **B**; structure of chiral [2+2] photocycloaddition substrate *rac*-**3**.

nones of general structure **A** (Figure 1) for which there has not yet been a report on an enantioselective variant.

The reaction was studied with a broad variety of chiral oxazaborolidine Lewis acids[18] **B** (variation of X′ and Y′) and the results of this study are disclosed in this Full Paper. In addition, we could show with chiral substrate *rac*-**3** that Lewis acid coordination lends a significantly improved selectivity to the reaction. This reaction was used in the total synthesis of italicene and isoitalicene. Mechanistic studies confirm the fact that the reaction proceeds on the triplet surface and computational studies offer an explanation for an unexpected reversal in the enantioselectivity of the process.

Table 1. Racemic [2+2] photocycloaddition reactions of enones **5**: Substitution patterns, reaction times and yields.



Substrate[a]	X	Y	R	R^1	*t* [h]	Yield [%]
5a	CH_2CH_2	CH_2	H	H	8	91
5b	CH_2CH_2	CMe_2	H	H	3	87
5c	CH_2CH_2	O	H	H	5	87
5d	CMe_2CH_2	CH_2	H	H	5	79
5e	CH_2	CH_2	H	H	47	56
5f	CH_2CH_2	CH_2	Me	H	5	68
5g	CH_2CH_2	CH_2	H	Me	5.5	51[b]
5h	CH_2CH_2	O	Me	H	8	80
5i	CMe_2CH_2	CH_2	Me	H	5	88
5j	CH_2	CH_2	Me	H	8	63[c]

[a] Unless noted otherwise, the reactions were performed under anhydrous and oxygen-free conditions at an irradiation wavelength of $\lambda =$ 366 nm (emission maximum of the light source) and at a substrate concentration of 20 mM in CH_2Cl_2 as the solvent at ambient temperature. [b] Olefinic by-products were removed by ozonolysis. [c] An irradiation wavelength of $\lambda = 350$ nm (emission maximum of the light source) was used.

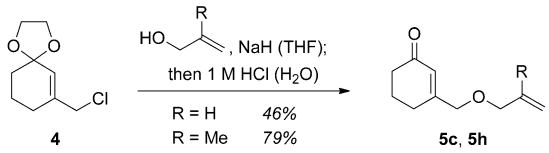
Results and Discussion

Synthesis of starting materials and racemic [2+2] photocycloaddition

Our experiments focussed on 2-cyclopentenones and 2-cyclohexenones, which carry an alkenyl chain at position C-3. To the best of our knowledge, the first intramolecular [2+2] photocycloaddition of a 3-alkenyl-substituted 2-cycloalkenone was mentioned in a communication by Corey and Sestanj.[19] Since then, this compound class has been extensively used and there are a plethora of examples for their intramolecular [2+2] photocycloaddition.[1]

The precursors are typically prepared from 3-ethoxy-2-cycloalkenones by addition of the respective alkenyl metal reagent and subsequent hydrolysis.[20] The previously unknown compounds **5c** and **5h** were synthesized from the chloromethyl-substituted olefinic acetal **4** which was obtained by a known procedure[21] and which underwent nucleophilic substitution by an allylic alcohol (Scheme 2).

Table 1 lists the substrates **5** and racemic products *rac*-**6** which were investigated in the present study. Irradiation was performed with fluorescent lamps which exhibit an emission

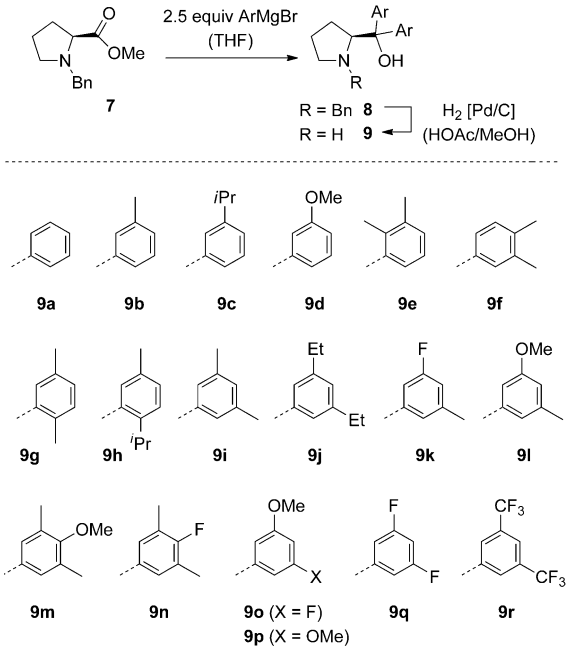


Scheme 2. Preparation of photocycloaddition substrates **5c** and **5h** from allylic chloride **4**.

maximum at $\lambda = 366$ nm.[22] Typically, full conversion of 2-cyclohexenones (**5a**–**5d**, **5f**–**5i**) was achieved after a maximum irradiation time of 8 h. The blue-shifted absorption of cyclopentenones **5e** and **5j** required for substrate **5e** a longer irradiation time of 47 h while in the case of enone **5j** a short-wavelength emitter ($\lambda = 350$ nm) was used to complete the reaction in a reasonable period of time.

Oxazaborolidine Lewis acids of general formula **B** (Figure 1) were prepared from the respective amino alcohols[23] by oxazaborolidine formation and subsequent complexation with $AlBr_3$ as the activating Lewis acid. Other activators did not match the enantioselectivity achieved with this Lewis acid neither did other amino alcohol skeletons. In the optimization experiments, we thus focussed on amino alcohols derived from proline. Accordingly, the synthesis commenced with known L-proline methyl ester **7**[23] which was converted to amino alcohols **8** by treatment with an excess (2.5 equiv) of the respective Grignard reagent (Scheme 3). The latter in turn was formed from aryl (Ar) bromide by direct magnesiation in the presence of catalytic amounts of iodine. Yields were high (>80%) both for the formation of the alcohols and for the subsequent hydrogenolysis of the *N*-benzyl group to the target compounds (see the Supporting Information for more details).

There was some concern regarding a possible racemization at the stereogenic center of proline during the Grignard addition which is the reason we attempted to determine the enantiomeric excess (*ee*) of the amino alcohols after deprotection. However, a satisfactory separation of the enantiomers by chiral HPLC could not be achieved and an unambiguous *ee* determination was impossible. Two representative amino alcohols were hence converted into the respective oxazolidinones **10a** and **10b** which were amenable to HPLC separation (Figure 2).



Scheme 3. Synthesis of various diaryl-substituted prolinols **9** from *N*-benzyl proline methyl ester (**7**).

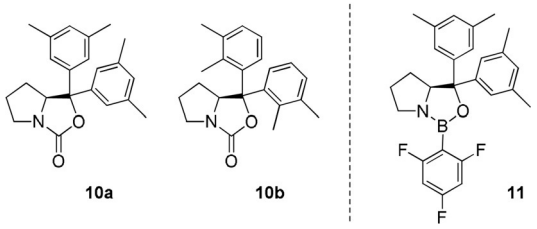


Figure 2. Structures of oxazolidinones **10** and of oxazaborolidine **11**.

Both compounds turned out to be essentially enantiopure (98.8% *ee* for **10a**, 99.9% *ee* for **10b**). Oxazaborolidine **11** was prepared from aminoalcohol **9i** by condensation with 2,4,6-trifluorophenyl boronic acid and it was characterized by NMR analysis (^{1}H, ^{11}B, ^{13}C, ^{19}F). The NMR data matched reported data of other previously synthesized oxazaborolidines.[24] In the ^{11}B NMR there was a single signal for the oxazaborolidine boron atom at 30.2 ppm[24a] (for further details, see the Supporting Information). In the catalytic experiments, the oxazaborolidines were freshly prepared but not individually characterized. After thorough removal of water they were directly activated by addition of $AlBr_3$.

Enantioselective [2+2] photocycloaddition

As mentioned in the introduction, Lewis acids display a profound influence on the absorption properties of enones.[15] Figure 3 shows the absorption spectrum of enone **5a** in dichloromethane solution ($c = 0.5$ mM). The strong π–π^* absorption of the compound appears at short wavelength with an absorption maximum at $\lambda_{max} = 234$ nm ($\varepsilon = 17010\ M^{-1}cm^{-1}$).

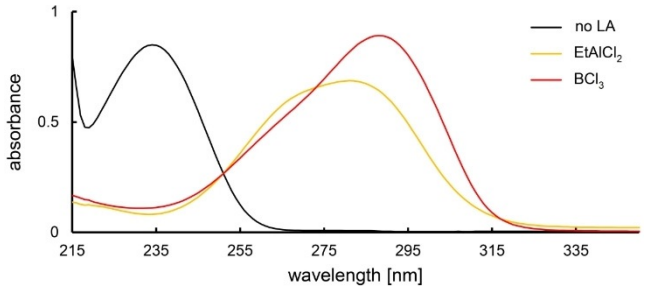


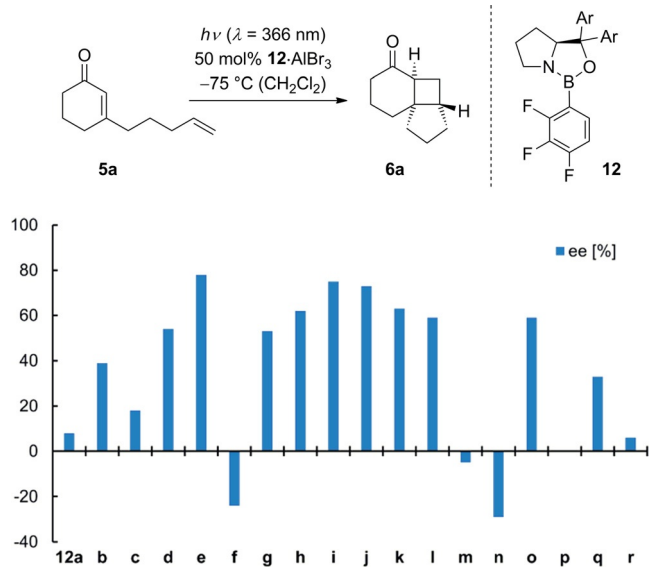
Figure 3. UV/Vis spectra of cyclic alkenone **5a** in the absence (black line) and in the presence of 20 equivalents of either $EtAlCl_2$ (yellow) or BCl_3 (red) ($c = 0.5$ mM in CH_2Cl_2).

The n–π^* absorption that is responsible for the observed photocycloaddition reaction (Table 1) could not be identified due to its low absorbance but it was clearly detectable at higher concentration ($c = 50$ mM, see Supporting Information). Its absorption maximum was found at $\lambda_{max} = 324$ nm ($\varepsilon = 50\ M^{-1}cm^{-1}$). Addition of Lewis acids led to a bathochromic shift of the allowed π–π^* transition (Figure 3). Assuming full complexation to occur with 20 equivalents of Lewis acid, the respective UV/Vis absorption data are for **5a**·$EtAlCl_2$ $\lambda_{max} = 281$ nm ($\varepsilon = 13750\ M^{-1}cm^{-1}$) and for **5a**·$BCl_3$ $\lambda_{max} = 288$ nm ($\varepsilon = 17830\ M^{-1}cm^{-1}$). In both cases, there is a significant absorption at longer wavelength that exceeds in terms of quantitative absorbance the n–π^* absorption of the uncomplexed substrate **5a**. In the presence of a Lewis acid there is no n–π^* transition.[15]

The above-mentioned scenario is typical for enones[15] and is the prerequisite for the use of chiral Lewis acids in a subsequent intramolecular [2+2] photocycloaddition reaction. The higher absorption coefficient of the Lewis acid-substrate complex allows this complex to harvest the respective long wavelength photons and to suppress the racemic background reaction that occurs upon excitation of the uncomplexed substrates via their n–π^* transition. Indeed, it was found for the reaction of compound **5a** that several $AlBr_3$-activated oxazaborolidines derived from 2,3,4-trifluoroboronic acid and amino alcohols **9** promoted an enantioselective intramolecular [2+2] photocycloaddition to product **6a** (Scheme 4).

Upon diastereoselective reduction to the respective secondary alcohol, the absolute configuration of the major enantiomer **6a** was elucidated by Mosher analysis.[25] The selection of the aryl boronic acid was based on a preliminary screen performed with the 3,5-dimethylphenyl-substituted alcohol **9i** and various boronic acids. In this first set of experiments, the 2,3,4-trifluorophenyl boronic acid performed the best (see Supporting Information). Surprisingly, we found that the enantioface differentiation in the reaction **5a**→**6a** was not consistent but that it depended strongly on the aryl group Ar in catalyst **12**. In some cases, there was even a slight preference for the other enantiomer *ent*-**6a** which is presented in Scheme 4 as a negative enantiomeric excess (*ee*).

The highest enantioselectivity (78% *ee*) was recorded for oxazaborolidine **12e** derived from amino alcohol **9e** (Ar = 2,3-dimethylphenyl). Several other oxazaborolidines **12** with alkyl-



Scheme 4. Evaluation of various oxazaborolidines **12** in the enantioselective intramolecular [2+2] photocycloaddition to tricyclic product **6a**.

and methoxy-substituted aryl groups also led to selectivities >50% *ee* (**12d**, **12g**–**12l**, **12o**). A substitution in *para*-position of the aryl group and fluorine substituents led to low or negative enantioselectivities (**12f**, **12m**, **12n**, **12p**, **12r**).

When searching for ways to optimize the enantioselectivity of the intramolecular [2+2] photocycloaddition we initially turned towards the irradiation conditions. The emission source that we employed exhibits an emission maximum at $\lambda =$ 366 nm (Figure 4) but has a notable emission in the short wavelength ($\lambda < 360$ nm) region. It was speculated that this emission might lead to a direct excitation of substrate **5a** and might favor the racemic transformation by direct excitation. We could show that an $Fe_2(SO_4)_3$ filter solution[26] indeed suppresses the short wavelength emission and the effect on the enantioselectivity was clearly notable. Upon direct irradiation at $\lambda = 366$ nm the reaction with Lewis acid **12e**·$AlBr_3$ had provided product **6a** (Table 1) in 62% yield and with 78% *ee*. When the light was filtered by an $Fe_2(SO_4)_3$ solution ($c =$ 600 mg L^{-1}) the yield increased to 80% and the enantioselectivity increased to 84% *ee*.

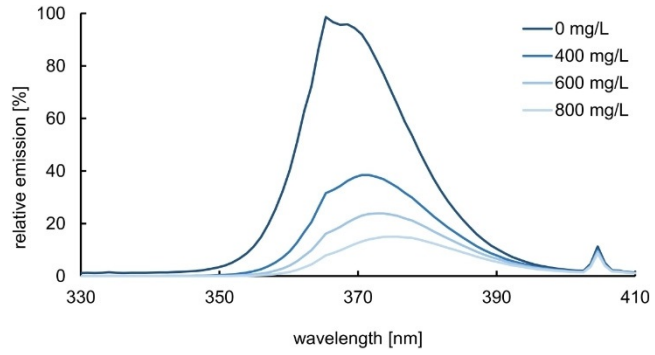
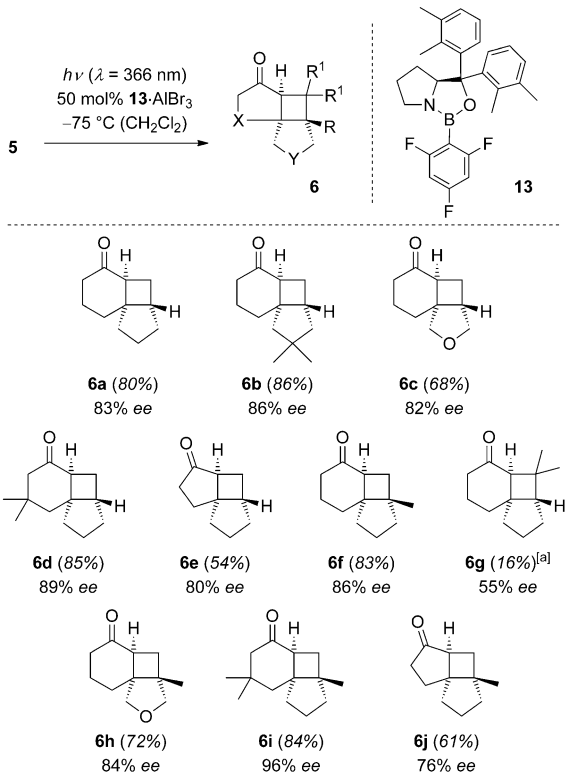


Figure 4. Calculated emission profile of a 366 nm fluorescent lamp tuned by an $Fe_2(SO_4)_3$ filter solution (in 0.01 M HCl) of varying concentration.

Simultaneously to the emission experiments, we revisited the aryl boronic acids and performed another screening of their influence on the enantioselectivity now employing prolinol **9e** (Ar = 2,3-dimethylphenyl) as the amino alcohol. It was found that 2,4,6-trifluorophenyl boronic acid led to an improvement that parallels the improvement achieved with the filter solution. When catalyzed by $AlBr_3$-activated oxazaborolidine **13**, the yield for the reaction **5a**→**6a** improved as compared to the reaction promoted by catalyst **12e** to 80% and the enantioselectivity to 83% *ee* (Scheme 5). Since direct irradiation at $\lambda = 366$ nm is operationally easier than irradiation through a filter solution, alkenones **5a**-**5j** were subsequently subjected to the former conditions. Substrate consumption was complete after 24 h and the products were—with a single exception (vide infra)—obtained in good to high yields (54–86%). More importantly, the enantiocontrol was high and exceeded in eight out of ten examples a level of 80% *ee*. Upon Lewis acid-promoted conversion of enone **5g**, a significant amount of olefinic side products were identified which had to be removed from the product by ozonolysis.



Scheme 5. Enantioselective intramolecular [2+2] photocycloaddition of enones **6** in the presence of $AlBr_3$-activated oxazaborolidine **13**.[a]Olefinic side-products were removed by ozonolysis prior to purification.

This method thus paves—for the first time—an enantioselective route to access typical intramolecular [2+2] photocycloaddition products of 2-cyclohexenones (**6a**–**6d**, **6f**, **6h**, **6i**) and 2-cyclopentenones (**6e**, **6j**). The product configuration was assigned in analogy to major enantiomer **6a** which was dextrorotatory ($[\alpha]_D = +156$). Likewise, all other cyclobutane

products showed a high positive specific rotation in CH_2Cl_2 solution ($[\alpha]_D = +98$ to $[\alpha]_D = +292$).

Computational and mechanistic studies

The coordination of enones to acid-activated oxazaborolidines has been discussed in previous work[27,28] and most commonly a weak non-classical hydrogen bond between the α-hydrogen atom of the enone substrate and the oxygen atom of the oxazaborolidine is invoked. This interaction avoids rotation around the strong coordinating bond between the carbonyl group and the boron atom. In order to visualize the reactive complex, we optimized the structure of model substrate 3-methyl-2-cyclohexenone coordinated to Lewis acid **12i**·$AlBr_3$ (Figure 5). All

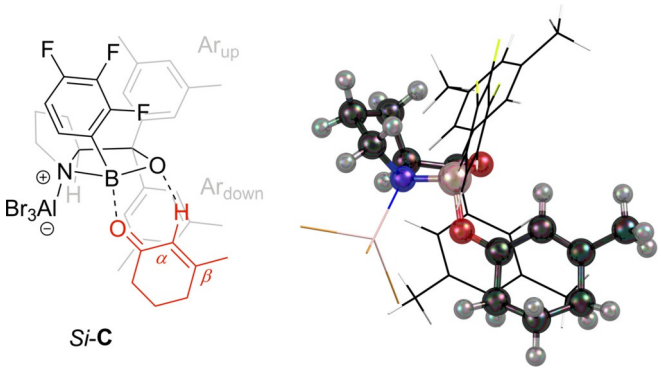


Figure 5. Optimized structure (right) displaying the preferred conformation within the complex of 3-methyl-2-cyclohexenone and Lewis acid **12i**·$AlBr_3$ (*Si*-**C**, left).

computations were carried out with Gaussian 16[29] using the B3LYP-D3BJ functional[30] and the cc-pVTZ basis set.[31] In order to match experimental conditions, computations include thermal corrections at −75 °C and a PCM solvation model for CH_2Cl_2 (for details see the Supporting Information). *Si*-**C** was found to be the most stable conformation of complex **C** with the above-mentioned non-classical hydrogen bond (2.46 Å) clearly visible and the *Si* face of the β-carbon atom being exposed for an intramolecular attack. The lower aryl group (Ar_{down}) is slightly turned with one side pointing towards the enone double bond thereby blocking this enantiotopic face. The 2,3,4-trifluorophenyl group shields the area above the enone α-carbon atom and is very likely responsible for the fact that olefins with terminal substituents (substrate **5g**) react poorly in the intramolecular [2+2] photocycloaddition. Likewise, it was found in the previously studied intermolecular variant of this reaction[17] that tri- and tetrasubstituted olefins reacted sluggishly. A major difference between the former and the latter photocycloaddition is the fact that the first C–C bond formation in the former case will occur exclusively in the β-position ("rule of five")[5] while in the latter case the α-position is likely the position of initial attack. In addition, the intramolecular reaction is faster and thus outcompetes possible degradation pathways of the photoexcited enone. Indeed, Lewis acids **11**·$AlBr_3$ and **12i**·$AlBr_3$ performed poorly in the intermolecular [2+2] photocycloaddition which was ascribed to the fact that they underwent decomposition by hydrogen abstraction from the enone.

The complex of 3-methyl-2-cyclohexenone and Lewis acid **12n**·$AlBr_3$ (complex **D**) was also studied computationally since the latter is the least structurally different from **12i**·$AlBr_3$ but nonetheless had led to an inverted enantioselectivity (Scheme 4, −29% *ee*). Although the *ee* shift from 75% *ee* (**12i**·$AlBr_3$) to −29% *ee* (**12n**·$AlBr_3$) corresponds only to a difference in free enthalpies of approx. 4 kJ mol^{-1} at −75 °C, we were curious whether different conformational properties of the two complexes **C** and **D** could be identified that would rationalize an influence of the rather subtle changes in catalyst aryl group substitution. We first explored enone binding to the opposite concave side of the catalyst which has been discussed in the context of cycloaddition reactions[27,32] and obtained the corresponding conformers for both **C** and **D**. However, both structures were very similar and no apparent characteristics were identified that would explain the strong influence of the aryl *para*-substituent (see Supporting Information for details). In a complimentary approach encouraged by computational studies of complexes without C_{sp^2}H-O contacts but rather π-interactions with Ar_{down}[33] we turned our attention to a coordination pattern in which the substrate is rotated by 180° around the O–B bond between enone and catalyst. This complex would also lead to product of inverse absolute configuration through shielding of the opposite enantiotopic face and, indeed, we identified conformation *Re*-**D** in which the *Re* face of the β-carbon atom is exposed towards an attack.[34] In this conformation, Ar_{down} and enone are perfectly parallel to each other (Figure 6) thereby suggesting attractive dispersion interactions between the two entities. Additionally, the aryl *para*-substituent and the substrate β-substituent are brought in close proximity in *Re*-**D**, which might serve as a plausible hint towards the difference between **C** and **D**. While this result should not be taken in any way as quantitative (the computed ground state energies for *Re*- and *Si*-complexes differ by less than 5 kJ mol^{-1}), it shows qualitatively how cyclic enones can coordinate to certain Lewis acid-activated oxazaborolidines in a way that explains a reversal in enantioselectivity.

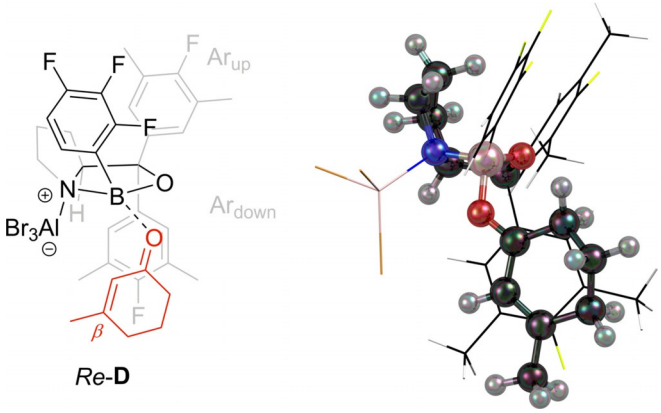


Figure 6. Optimized complex conformer structure (right) of 3-methyl-2-cyclohexenone and Lewis acid **12n**·$AlBr_3$ which displays the *Re* face of the β-carbon atom towards an attack (*Re*-**D**, left).

Due to an efficient symmetry-allowed ISC from the n–π* singlet state,[3,35] cyclic enones undergo [2+2] photocycloaddition reactions from the π–π* triplet state. We determined the quantum yield for the racemic reaction **5a**→*rac*-**6a** at $\lambda = 368$ nm (LED) and at −80 °C to be $\Phi = 0.38$ (±0.02). The high value which compares well with quantum yields previously obtained for this and related [2+2] photocycloaddition reactions[36] is a testimony to the high efficiency with which both ISC and ring closure occur. Under the same conditions it was attempted to determine the quantum yield of the Lewis acid-promoted reaction employing Lewis acid **13**·$AlBr_3$. The high sensitivity of the Lewis acid towards air and moisture made it difficult to take samples at given time intervals and to monitor the progress of the reaction. Instead, the reaction was stopped after 10 min and the conversion was determined (see the Supporting Information for further details). The measurement was performed in triplicate and delivered a quantum yield of $\Phi = 0.052$ (±0.007). Given that ISC occurs in this case from a π–π* singlet the quantum yield is remarkably high. The value seems to support—as earlier suggested by calculations[37]—the hypothesis that the Lewis acids facilitates the forbidden ISC to the π–π* triplet state. An alternative explanation for the efficiency of the Lewis acid-catalyzed process would be a rapid cyclization on the singlet hypersurface prior to ISC. In order to distinguish between the two pathways and to substantiate the fact that the catalyzed reaction proceeds indeed on the triplet hypersurface, we turned to a classical experiment that had been earlier performed with substrates **5k** by Becker and co-workers.[36a] Upon irradiation at $\lambda > 330$ nm (uranium glass filter), it had been found that both diastereoisomers *cis*-**5k** and *trans*-**5k** gave in separate reactions products *rac*-**6k** as a *cis*/*trans* mixture in a ratio of 50:50. The reaction was not stereospecific and implied the intermediacy of triplet diradical **14** which allows for free rotation around the indicated single bond (Figure 7). Likewise, we studied the two substrates *cis*-**5k** and *trans*-**5k** in separate reactions which were performed with the Lewis acid **13**·$AlBr_3$ under the conditions of Scheme 5. The reaction turned out to be also stereoconvergent and led to a mixture of *trans*-**6k** and *cis*-**6k** in an almost identical diastereomeric ratio (d.r.). When starting from *cis*-**5k**, the d.r. was 83:17 whereas the d.r. was 86:14 with *trans*-**5k**. In both reactions, the *trans* compound *trans*-**6k** prevailed and was formed with 79% *ee* in the former and with 86% *ee* in the latter case.

While the stereoconvergency of the reactions **5k**→**6k** supports the intermediacy of 1,4-diradical **14**, the high simple diastereoselectivity is remarkable if compared to the non-existent diastereoselectivity (d.r. = 50:50) observed for the racemic reaction.[36a] The finding seems to indicate that intermediate **14** remains in the coordination sphere of the catalyst which forces the methyl group in the *trans* position of the resulting cyclobutane ring. If intermediate **14** had dissociated from the catalyst prior to ring closure[38] the d.r. should have been similar to the racemic reaction. The observation parallels with the sensitivity of the Lewis acid-mediated [2+2] photocycloaddition towards steric hindrance (substrate **5g**).

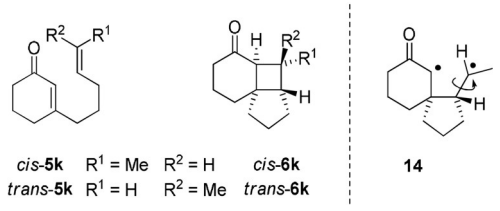
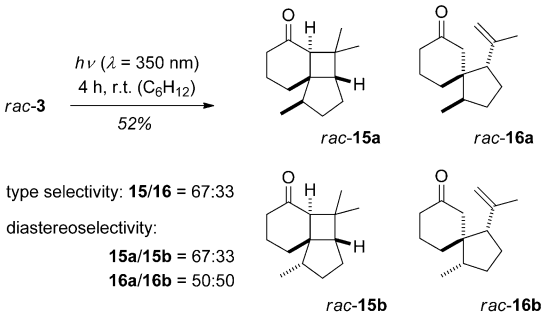


Figure 7. Structures of irradiation precursors *cis*-**5k** and *trans*-**5k**, of photocycloaddition products *cis*-**6k** and *trans*-**6k**, and of putative triplet intermediate **14**.

Total synthesis of (±)-italicene and (±)-isoitalicene

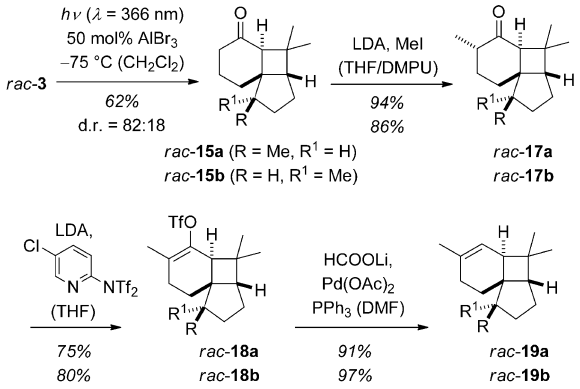
The sesquiterpenes italicene and isoitalicene[39] are the most prominent natural products which feature the octahydrocyclopenta[1,4]cyclobuta[1,2]benzene skeleton that in turn is built up in the intramolecular [2+2] photocycloaddition of 3-(pent-4-enyl)-2-cyclohexenones. Synthetic approaches towards these compounds have been reported[40] and to this date there exist two completed total syntheses.[39,41]

Following a retrosynthetic [2+2] disconnection, 2-cyclohexenone *rac*-**3** seemed to be a reasonable starting material which would allow the implementation of a photochemical key step in the synthesis. Indeed, this reaction had been previously studied by Hoye et al.[42] but the results were somewhat sobering (Scheme 6). At ambient temperature, not a single selectivity parameter was satisfactorily controlled and the reaction delivered four isomeric products in relative proportions of almost unity. Optimization of the intramolecular [2+2] photocycloaddition in our study rested on three parameters: choice of the irradiation wavelength, temperature, and Lewis acid. There was a minor improvement in yield at $\lambda = 366$ nm but the d.r. (*rac*-**15a**/*rac*-**15b**) remained low (67:33) and the formation of compounds *rac*-**16** was not suppressed. As already found by Hoye et al., a decrease of the reaction temperature to −75 °C enhanced the d.r. to 78:22 but olefins *rac*-**16** remained present. Eventually, we discovered that with $AlBr_3$ as the (achiral) Lewis acid there was a perfect type selectivity and even an increase of the d.r. to 82:18 (Scheme 7).



Scheme 6. Low-type selectivity and facial diastereoselectivity in the [2+2] photocycloaddition of substrate *rac*-**3**.[42]

The diastereomeric photocycloaddition products *rac*-**15** were separable and the relative configuration of the major



Scheme 7. Total synthesis of (±)-italicene (*rac*-**19a**) and (±)-isoitalicene (*rac*-**19b**) via a selective Lewis-acid promoted [2+2] photocycloaddition.

isomer *rac*-**15a** was confirmed.[42] Its preferred formation can be explained by a chair-like transition state in which the methyl group at the stereogenic center is in an equatorial position.[43] While it was initially attempted to perform the α-methylation and to follow a known route towards italicene and isoitalicene,[39] we failed to separate the isomers at the stage of the natural products. In addition, the final dehydration step yielded repeatedly several product isomers apart from the two natural products. As an alternative, we decided to process the diastereoisomers separately and devised an alternative sequence for the introduction of the olefinic double bond. The α-methylation proceeded smoothly and with high diastereoselectivity for both epimers *rac*-**15a** and *rac*-**15b**. The ketones *rac*-**17a** and *rac*-**17b** were converted via the respective enolates into unstable triflates[44] *rac*-**18a** and *rac*-**18b** which had to be purified on deactivated neutral alumina. The reduction was eventually performed with lithium formate employing $Pd(OAc)_2$ (10 mol%) as the catalyst.[45] The conditions were found to be superior to other reported procedures which led to the formation of inseparable nonpolar side products.[46] Starting from 4-bromoanisole as precursor for enone *rac*-**3**,[42] (±)-italicene (*rac*-**19a**) was synthesized in seven steps with an overall yield of 14%. The Lewis acid was responsible for a significant improvement in the selectivity of the photochemical stey step which accounts for the high overall yield. (±)-Isoitalicene (*rac*-**19b**) was obtained via the minor photocycloaddition diastereoisomer *rac*-**15b** with an overall yield of 3%.

Given that the starting alkene *rac*-**3** is doubly substituted at the terminal carbon atom, the chances were low to process the compound in a kinetic photochemical resolution (cf. substrate **5g**). Still, it was attempted to perform the [2+2] photocycloaddition in the presence of Lewis acids **11**·$AlBr_3$, **12e**·$AlBr_3$, **12i**·$AlBr_3$, and **13**·$AlBr_3$ under standard conditions (Scheme 5). The highest enantioselectivity was recorded with the Lewis acid **11**·$AlBr_3$ if the reaction was stopped after one hour. The major diastereoisomer **15a** that was formed with a d.r. of 84:16 displayed an enantiomeric excess of 42%. The conversion was low, however, and 71% of the starting material **3** was recovered (10% *ee*).

Conclusion

In summary, this study provided new information about the mode of action of Lewis acid-mediated [2+2] photocycloaddition reactions. For the enantioselective intramolecular reaction of substrates **5**, it was found that the choice of substituents at the chiral oxazaborolidine has a large influence on the degree of enantioselecitivity. According to DFT calculations of complex **12i**·$AlBr_3$ with an enone, the lower aryl group (Ar_{down}) at the carbon atom and the aryl group at the boron atom control the accessibility to the substrate. The enone encounters a high enantioface differentiation at the β-carbon atom at which the first C–C bond formation occurs. Moreover, the aryl group at the boron atom limits the available space in *cis*-position of the terminal carbon atom in the alkenyl chain. It was found that a reversal of enantioselectivity is possible by varying the aryl groups Ar of the oxazaborolidine and a different binding mode of the enone to the Lewis acid was identified. This discovery may allow to access in the future opposite enantiomers of a given photoproduct by alteration of the substituents. Regarding the mechanism of the Lewis acid-catalyzed reaction, a reaction pathway via the π–π* triplet was substantiated. Although the higher absorbance at $\lambda = 366$ nm of the Lewis acid-enone complex vs. the free enone facilitates its preferred excitation, the faster ISC rate of the free enone compensates its lower absorbance. As a consequence, the quantum yield of the Lewis acid-mediated reaction is by a factor of 10 lower which in turn requires a high catalyst loading of 50 mol% to achieve a high degree of enantioselectivity. The effect of Lewis acids on the selectivity of photochemical reactions is not limited to aspects of enantioselectivity. We found an improved type selectivity in the intramolecular [2+2] photocycloaddition of substrate *rac*-**3**. Hydrogen abstraction products *rac*-**16** were absent if the reaction was performed in the presence of $AlBr_3$ as the Lewis acid and the facial diastereoselectivity in favor of product *rac*-**15a** increased. A concise and high-yielding synthesis of (±)-italicene (*rac*-**19a**) could thus be achieved.

Experimental Section

General information: All air and moisture sensitive reactions were carried out in heat gun-dried glassware under an argon atmosphere using standard Schlenk techniques. Room temperature refers to 22–26 °C. Temperatures of 0 °C were obtained using an ice/water bath. Temperatures of −78 °C were obtained using a dry ice/isopropanol bath. For moisture sensitive reactions, tetrahydrofuran (THF), diethyl ether (Et_2O) and dichloromethane (CH_2Cl_2) were dried using a MBSPS 800 MBraun solvent purification system. The following columns were used: Tetrahydrofuran: 2×MB-KOL-M type 2 (3 Å molecular sieve); Diethyl ether: 1×MB-KOL-A type 2 (aluminum oxide), 1×MB-KOL-M type 2 (3 Å molecular sieve); Dichloromethane: 2×MB-KOL-A type 2 (aluminum oxide). The following dry solvents are commercially available and were used without further purification: Toluene: Acros Organics, 99.8% extra dry, over molecular sieves. For photochemical reactions, dry dichloromethane was degassed by three freeze-pump-thaw cycles and stored over 4 Å molecular sieves. Technical solvents [pentane (P), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), methanol (MeOH), *n*-hexane

(nHex), ethyl acetate (EtOAc), cyclohexane (cHex)] were distilled prior to column chromatography. Commercially available chemicals were purchased from the suppliers *A*BCR, Acros, Alfa-Aesar, Sigma–Aldrich (now Merck KGaA), and TCI, and were used without further purification. For isomerizations of the photoproducts, basic alumina (Merck, aluminum oxide 90 active basic, 0.063–0.200 mm) was used.

Analytical methods and equipment: Photochemical experiments were carried out in heat gun-dried Duran tubes in a positive geometry setup (cylindrical array of 16 fluorescent tubes, 8 W nominal power) with the sample placed in the center of the illumination chamber. Fluorescent tubes of the type Hitachi UV-A (BI-B) (λ_{max} = 350 nm) and Philips Blue Light (λ_{max} = 366 nm) were employed. Enantioselective reactions were carried out at −75 °C using a *Duran* cooling finger which was attached to a high-performance cryostat (*Huber* CC80). Ozone was generated by a FisherTechnology ozone-generator Type 502. Flash column chromatography was performed with silica 60 (Merck, 230–400 mesh) as the stationary phase with the indicated eluent mixtures. Deactivation of neutral alumina (Merck, aluminum oxide 90 active neutral, 70–230 mesh) was carried out by the addition of 36 wt% water in small portions. Subsequently, the powder was spread in a petri dish and was allowed to dry on air for at least two days. Thin Layer Chromatography (TLC) was performed on silica coated glass plates (Merck, silica 60 F254) with detection by UV-light (λ = 254 nm) and/or by staining with a potassium permanganate solution [$KMnO_4$] or with a cerium ammonium molybdate solution [CAM] followed by heat treatment: $KMnO_4$-staining solution: potassium permanganate (3.00 g), potassium carbonate (20.0 g) and aqueous sodium hydroxide solution (5 wt%, 5.00 mL) in water (300 mL). CAM-staining solution: cerium sulfate tetrahydrate (1.00 g), ammonium molybdate (25.0 g) and concentrated sulfuric acid (25.0 mL) in water (250 mL). NMR spectra were recorded at room temperature either on a Bruker AVHD-300, AVHD-400, AVHD-500 or an AV-500 cryo. ^{1}H NMR spectra were referenced to the residual proton signal of chloroform-d_1 (δ = 7.26 ppm), [D$_4$]MeOH (δ = 3.31 ppm), [D$_6$]benzene (δ = 7.16 ppm) or deuterium oxide (δ = 4.79 ppm). ^{13}C NMR spectra were referenced to the ^{13}C-D triplet of $CDCl_3$ (δ = 77.16 ppm), to the ^{13}C-D septet of CD_3OD (δ = 49.00 ppm) or to the ^{13}C-D triplet of C_6D_6 (δ = 128.06 ppm). ^{19}F NMR spectra were referenced to the ^{19}F signal of CCl_3F (δ = 0 ppm). Apparent multiplets which occur as a result of coupling constant equality between magnetically non-equivalent protons are marked as virtual (virt.). The following abbreviations for single multiplicities were used: br-broad, s-singlet, d-doublet, t-triplet, q-quartet, quint-quintet, sext-sextet, sept-septet. Assignment and multiplicity of the ^{13}C NMR signals were determined by two-dimensional NMR experiments (COSY, HSQC, HMBC). Protons oriented above the molecular plane are labeled as α and those oriented below as β. Infrared spectra were recorded on a PerkinElmer Frontier IR-FTR spectrometer by ATR technique. The signal intensity is assigned using the following abbreviations: br (broad), vs. (very strong), s (strong), m (medium), w (weak). Low resolution and high resolution mass spectra were recorded on a *Thermo Scientific* LTQ-FT Ultra (ESI) or a Thermo Scientific DFS-HRMS spectrometer (EI). All melting points were determined using a Büchi M-565 melting point apparatus, with a range quoted to the nearest integer. UV/Vis spectra were measured on a PerkinElmer Lambda 35 UV/Vis spectrometer. Spectra were recorded using a Hellma precision cell made of quartz SUPRASIL® with a pathway of 1 mm or 1 cm. Solvents and concentrations are given for each spectrum. GC analysis was performed on an Agilent 7890 B gas chromatograph using an Agilent HP-5 column (30 m × 0.32 mm × 0.25 μm, SN: 19091J-413) with a flame ionization detector. The temperature method is given for the corresponding compounds. Chiral GC analysis was performed on an Agilent 7890 B gas chromatograph using an Agilent Cyclosil-B column (30 m × 0.25 mm × 0.25 μm, SN: USF620714H) or a Macherey–Nagel Lipodex E column (25 m × 0.25 mm, SN: 23393-92) with a flame ionization detector. The temperature method is given for the corresponding compounds. Chiral HPLC was performed on a Thermo-Fisher HPLC system comprising a SR3000 solvent rack, a LPG3400 SD pump, a WPS-3000 SL autosampler, a TCC-3000 SD column compartment and a DAD-3000 UV/Vis detector fitted with the appropriate Daicel column as chiral stationary phase (flow rate: 1.0 mL min^{-1}, Daicel column, time and eluent are given for the corresponding compounds). Optical rotations were recorded on a Bellingham + Stanley ADP440 + polarimeter using a cuvette with a path length of 0.05 dm. All measurements were performed using the sodium D line (λ = 589 nm) at room temperature. The specific rotation is reported as follows: $[\alpha]_D^T = 100 \times \alpha/(l \times c)$ [10^{-1} grad cm^2 g^{-1}] (α: optical rotation [deg], l: path length [dm], c: concentration of sample [g 100 cm^{-3}]).

Preparation of starting materials, calculations, and mechanistic studies: The synthesis of the photocycloaddition precursors and of the proline-derived amino alcohols **9** is described in the Supporting Information, which also contains details on the preparation of the oxazaborolidines and other amino alcohol derivatives, on the preparation of the activated oxazaborolidines, on the DFT calculations, and on the mechanistic studies.

Racemic intramolecular [2+2] photocycloaddition (General Procedure 1): A solution of the respective irradiation precursor (1.00 equiv) in dichloromethane (1–3 mL) was transferred to a Duran phototube. Dichloromethane was added until a concentration of 20 mM was reached. The solution was irradiated at λ = 366 nm for the respective amount of time. After complete conversion, the solvent was removed in vacuo. The residue was purified by column chromatography with the given eluent mixture. The obtained *cis*/*trans* mixture was equilibrated over basic alumina in a small amount of dichloromethane overnight. The suspension was filtered, washed with small portions of diethyl ether, and the filtrate was concentrated.

Enantioselective intramolecular [2+2] photocycloaddition (General Procedure 2): A solution of the respective irradiation precursor (1.00 equiv) in dichloromethane (1–3 mL) was transferred to a heat-gun dried Duran phototube and the vessel was washed twice with small portions of dichloromethane. Then, a solution of activated oxazaborolidine catalyst **13**·$AlBr_3$ (50.0 mol%) in dichloromethane (1–3 mL) was transferred to the reaction mixture and the vessel was washed with small portions of dichloromethane. Dichloromethane was added until a concentration of 20 mM was reached. The solution was cooled to −75 °C within 30 min and was subsequently irradiated at λ = 366 nm for 24 h. The reaction mixture was poured into suspended silica in dichloromethane and the solvent was removed in vacuo. The dry-loaded product was purified by column chromatography with a given eluent mixture. The obtained *cis*/*trans* mixture was equilibrated over basic alumina in a small amount of dichloromethane overnight. The suspension was filtered, washed with small portions of diethyl ether, and the filtrate was concentrated.

Photocycloaddition product 6a: *Racemic*: Following GP1, enone **5a** (131 mg, 800 μmol, 1.00 equiv) was irradiated in dichloromethane (40 mL) for 8 h. After purification by column chromatography (silica, P/Et_2O = 4:1), ketone *rac*-**6a** (119 mg, 725 μmol, 91%) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone **5a** (16.4 mg, 100 μmol, 1.00 equiv) was irradiated in dichloromethane (5 mL). After purification by column chromatogra-

phy (silica, P/Et_2O = 4:1), ketone **6a** (13.2 mg, 80.4 μmol, 80%, 83% *ee*) was obtained as a colorless oil. R_f = 0.42 (pentane/Et_2O 6:4) [$KMnO_4$]; $[\alpha]_D^{25} = +156$ (c = 1.0 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.34 (virt. td, $^2J \approx {}^3J_1$ = 12.6 Hz, $^3J_2$ = 6.8 Hz, 1H, *H*H-1), 1.50–1.58 (m, 2H, H-8), 1.58–1.64 (m, 3H, H*H*-1, H-3), 1.77–1.93 (m, 3H, H-2, *H*H-4), 1.93–2.04 (m, 2H, H-7), 2.07 (ddd, ^2J = 13.1 Hz, $^3J_1$ = 9.7 Hz, $^3J_2$ = 7.0 Hz, 1H, H*H*-4), 2.17 (dddd, ^2J = 18.0 Hz, $^3J_1$ = 11.4 Hz, $^3J_2$ = 6.9 Hz, ^4J = 1.1 Hz, 1H, *H*H-6), 2.37–2.43 (m, 1H, H-3a), 2.48 (virt. ddq, $^3J_1$ = 11.4 Hz, $^3J_2$ = 7.0 Hz, $^4J_1 \approx {}^4J_2$ = 1.2 Hz, 1H, H-4a), 2.57 ppm (virt. dddt, ^2J = 18.0 Hz, $^3J_1$ = 4.7 Hz, $^3J_2$ = 3.4 Hz, $^4J_1 \approx {}^4J_2$ = 1.2 Hz, 1H, H*H*-6); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 21.2 (t, C-7), 25.1 (t, C-2), 26.9 (t, C-4), 32.9 (t, C-8), 33.1 (t, C-3), 39.6 (d, C-3a), 39.6 (t, C-6), 40.4 (t, C-1), 47.3 (d, C-4a), 50.0 (s, C-8a), 215.7 ppm (s, C-5); Chiral GC: τ_R (major) = 157.2 min, τ_R (minor) = 161.8 min, [60 °C (1 min), 100 °C (30 °C min^{-1}), 100 °C (157 min), 135 °C (3 °C min^{-1}), 200 °C (20 °C min^{-1}), 200 °C (3 min)], Cyclosil-B. The analytical data obtained matched those reported in the literature.[47]

Photocycloaddition product 6b: *Racemic*: Following GP1, enone **5b** (38.5 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) for 3 h. After purification by column chromatography (silica, P/Et_2O = 4:1), ketone *rac*-**6b** (33.5 mg, 174 μmol, 87%) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone **5b** (38.5 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (silica, P/Et_2O = 6:1), ketone **6b** (33.0 mg, 172 μmol, 86%, 86% *ee*) was obtained as a colorless oil. R_f = 0.51 (pentane/Et_2O 1:1) [$KMnO_4$]; $[\alpha]_D^{25} = +97.7$ (c = 1.5 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.94 (s, 3H, Me-2), 1.17 (s, 3H, Me-2), 1.49 (dd, ^2J = 13.4 Hz, ^4J = 1.7 Hz, 1H, *H*H-1), 1.51 (dd, ^2J = 13.1 Hz, ^3J = 6.2 Hz, 1H, *H*H-3), 1.57 (ddd, ^2J = 14.0 Hz, $^3J_1$ = 11.1 Hz, $^3J_2$ = 3.3 Hz, 1H, *H*H-8), 1.70 (d, ^2J = 13.4 Hz, 1H, H*H*-1), 1.75 (dddd, ^2J = 14.0 Hz, $^3J_1$ = 6.4 Hz, $^3J_2$ = 3.0 Hz, ^4J = 1.1 Hz, 1H, H*H*-8), 1.81–1.91 (m, 2H, H*H*-3, *H*H-7), 1.94–2.07 (m, 2H, *H*H-4, H*H*-7), 2.12–2.18 (m, 1H, H*H*-4), 2.18–2.25 (m, 1H, *H*H-6), 2.44–2.49 (m, 1H, H-3a), 2.49–2.56 (m, 1H, H*H*-6), 2.77–2.82 ppm (m, 1H, H-4a); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 20.7 (t, C-7), 27.9 (t, C-4), 29.6 (q, Me-2), 30.0 (q, Me-2), 35.0 (t, C-8), 38.9 (t, C-6), 41.8 (d, C-3a), 43.2 (s, C-2)*, 49.4 (t, C-3), 50.9 (d, C-4a), 51.3 (s, C-8a)*, 56.6 (t, C-1), 216.7 ppm (s, C-5) [*Assignment of signals is interconvertible.]; IR (ATR): $\tilde{\nu}$ = 2927 (s, sp^3-CH), 2863 (m, sp^3-CH), 1696 (vs., C=O), 1462 (m, sp^3-CH), 907 cm^{-1} (w); MS (EI, 70 eV): *m/z* (%): 192 (33) $[M]^+$, 177 (23) $[M-CH_3]^+$, 164 (17) $[M-CO]^+$, 159 (11), 136 (15), 122 (30) $[C_8H_{10}O]^+$, 110 (100) $[M-C_6H_{10}]^+$, 107 (58), 93 (20), 83 (23) $[C_6H_{11}]^+$, 67 (24), 55 (51) $[C_4H_7]^+$, 41 (20); HRMS (EI, 70 eV): calcd for $C_{13}H_{20}O$ $[M]^+$: 192.1509; found: 192.1504; calcd for $C_{12}{}^{13}CH_{20}O$ $[M]^+$: 193.1542; found: 193.1541; Chiral GC: τ_R (major) = 173.4 min, τ_R (minor) = 174.0 min, [60 °C (1 min), 100 °C (30 °C min^{-1}), 100 °C (157 min), 135 °C (3 °C min^{-1}), 200 °C (20 °C min^{-1}), 200 °C (3 min)], Cyclosil-B.

Photocycloaddition product 6c: *Racemic*: Following GP1, enone **5c** (16.6 mg, 100 μmol, 1.00 equiv) was irradiated in dichloromethane (5 mL) for 5 h. After purification by column chromatography (silica, P/EtOAc = 1:1), ketone *rac*-**6c** (14.4 mg, 86.6 μmol, 87%) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone **5c** (33.2 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (silica, P/EtOAc = 1:1), ketone **6c** (22.6 mg, 136 μmol, 68%, 82% *ee*) was obtained as a colorless oil. R_f = 0.31 (pentane/Et_2O 1:1) [$KMnO_4$]; $[\alpha]_D^{26} = +138$ (c = 1.4 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.52 (ddd, ^2J = 13.9 Hz, $^3J_1$ = 11.9 Hz, $^3J_2$ = 4.3 Hz, 1H, *H*H-8), 1.70 (dddd, ^2J = 13.9 Hz, $^3J_1$ = 4.5 Hz, $^3J_2$ = 3.2 Hz, ^4J = 1.5 Hz, 1H, H*H*-8), 1.94–2.13 (m, 4H, H-4, H-7), 2.18 (dddd, ^2J = 17.4 Hz, $^3J_1$ = 12.3 Hz, $^3J_2$ = 6.0 Hz, ^4J = 1.1 Hz, 1H, *H*H-6), 2.54–2.61 (m, 2H, H-3a, H*H*-6), 2.71 (dd, $^3J_1$ = 10.7 Hz, $^3J_2$ = 7.2 Hz, 1H, H-4a), 3.28 (d, ^2J = 9.3 Hz, 1H, *H*H-1), 3.61 (dd, ^2J = 9.3 Hz, ^3J = 5.2 Hz, 1H, *H*H-3), 3.86 (d, ^2J = 9.3 Hz, 1H, H*H*-1), 3.86 ppm (d, ^2J = 9.3 Hz, 1H, H*H*-3); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 21.3 (t, C-7), 26.8 (t, C-4), 28.6 (t, C-8), 39.9 (t, C-6), 40.9 (d, C-3a), 46.6 (d, C-4a), 51.1 (s, C-8a), 74.4 (t, C-3), 78.9 (t, C-1), 214.1 ppm (s, C-5); IR (ATR): $\tilde{\nu}$ = 2938 (m, sp^3-CH), 2843 (m, sp^3-CH), 1697 (vs., C=O), 1107 (s, sp^3-CO), 914 cm^{-1} (vs., sp^3-CO); MS (EI, 70 eV): *m/z* (%): 166 (58) $[M]^+$, 137 (27) $[M-CO]^+$, 121 (84) $[M-C_2H_5O]^+$, 110 (100) $[M-C_3H_4O]^+$, 96 (82) $[M-C_4H_6O]^+$, 82 (78) $[C_5H_6O]^+$, 79 (90), 67 (66), 55 (58) $[C_4H_7]^+$, 41 (61) $[C_3H_5]^+$; HRMS (EI, 70 eV): calcd for $C_{10}H_{14}O_2$ $[M]^+$: 166.0988; found: 166.0985; calcd for $C_9{}^{13}CH_{14}O_2$ $[M]^+$: 167.1022; found: 167.1022; Chiral GC: τ_R (minor) = 37.5 min, τ_R (major) = 37.7 min, [60 °C (0 min), 245 °C (3 °C min^{-1}), 245 °C (3 min)], Cyclosil-B.

Photocycloaddition product 6d: *Racemic*: Following GP1, enone **5d** (38.5 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) for 5 h. After purification by column chromatography (silica, P/Et_2O = 6:1), ketone *rac*-**6d** (30.4 mg, 158 μmol, 79%) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone **5d** (38.5 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (silica, P/Et_2O = 6:1), ketone **6d** (32.6 mg, 170 μmol, 85%, 89% *ee*) was obtained as a colorless oil. R_f = 0.63 (pentane/Et_2O 1:1) [$KMnO_4$]; $[\alpha]_D^{25} = +156$ (c = 1.3 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.98 (s, 3H, Me-7), 1.06 (s, 3H, Me-7), 1.36 (virt. td, $^2J \approx {}^3J_1$ = 12.3 Hz, $^3J_2$ = 7.2 Hz, 1H, *H*H-1), 1.52 (dd, ^2J = 12.6 Hz, ^3J = 6.0 Hz, 1H, *H*H-3), 1.54–1.62 (m, 2H, H*H*-3, *H*H-8), 1.69 (d, ^2J = 14.5 Hz, 1H, H*H*-8), 1.72–1.78 (m, 1H, H*H*-1), 1.78–1.89 (m, 3H, H-2, *H*H-4), 2.15 (d, ^2J = 14.8 Hz, 1H, *H*H-6), 2.19 (ddd, ^2J = 13.0 Hz, $^3J_1$ = 9.5 Hz, $^3J_2$ = 6.6 Hz, 1H, H*H*-4), 2.25 (d, ^2J = 14.8 Hz, 1H, H*H*-6), 2.36 (dd, $^3J_1$ = 11.6 Hz, $^3J_2$ = 6.6 Hz, 1H, H-4a), 2.38–2.43 ppm (m, 1H, H-3a); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 24.8 (t, C-2), 27.3 (t, C-4), 28.5 (q, Me-7), 31.0 (q, Me-7), 33.0 (t, C-3), 34.6 (s, C-7), 42.7 (d, C-3a), 43.1 (t, C-1), 46.0 (d, C-4a), 47.7 (t, C-8), 49.6 (s, C-8a), 53.8 (t, C-6), 216.7 ppm (s, C-5); IR (ATR): $\tilde{\nu}$ = 2941 (s, sp^3-CH), 2895 (m, sp^3-CH), 2868 (m, sp^3-CH), 1700 (vs., C=O), 1467 cm^{-1} (m, sp^3-CH); MS (EI, 70 eV): *m/z* (%): 192 (40) $[M]^+$, 177 (18) $[M-CH_3]^+$, 149 (41) $[M-C_3H_7]^+$, 136 (81) $[M-C_4H_8]^+$, 125 (35) $[C_8H_{13}O]^+$, 108 (56) $[C_7H_8O]^+$, 93 (44), 82 (100) $[C_6H_{10}]^+$, 54 (30), 41 (18); HRMS (EI, 70 eV): calcd for $C_{13}H_{20}O$ $[M]^+$: 192.1509; found: 192.1513; Chiral GC: τ_R (minor) = 169.7 min, τ_R (major) = 170.3 min, [60 °C (1 min), 100 °C (30 °C min^{-1}), 100 °C (157 min), 135 °C (3 °C min^{-1}), 200 °C (20 °C min^{-1}), 200 °C (3 min)], Cyclosil-B.

Photocycloaddition product 6e: *Racemic*: Following GP1, enone **5e** (30.0 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) for 47 h. After purification by column chromatography (silica, P/Et_2O = 5:1), ketone *rac*-**6e** (16.6 mg, 111 μmol, 56%) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone **5e** (30.0 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (silica, P/Et_2O = 5:1), ketone **6e** (16.2 mg, 108 μmol, 54%, 80% *ee*) was obtained as a colorless oil. R_f = 0.26 (pentane/Et_2O 5:1) [$KMnO_4$]; $[\alpha]_D^{25} = +292$ (c = 1.1 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.42 (ddd, ^2J = 13.0 Hz, $^3J_1$ = 10.7 Hz, $^3J_2$ = 9.1 Hz, 1H, *H*H-7), 1.54–1.59 (m, 1H, *H*H-5), 1.59–1.67 (m, 1H, H*H*-5), 1.68–1.74 (m, 1H, H*H*-7), 1.76–1.83 (m, 1H, *H*H-4), 1.83–1.91 (m, 4H, *H*H-6, H*H*-4, H-1), 1.92 (virt. dq, ^2J = 4.8 Hz, $^3J_1 \approx {}^3J_2 \approx {}^3J_3$ = 2.2 Hz, 1H, H*H*-6), 2.22 (ddd, $^3J_1$ = 10.7 Hz, $^3J_2$ = 4.4 Hz, ^4J = 2.0 Hz, 1H, H-3a), 2.35 (virt. ddt, ^2J = 17.9 Hz, $^3J_1$ = 7.8 Hz, $^3J_2 \approx {}^4J$ = 2.0 Hz, 1H, *H*H-2), 2.49–2.56 (m, 1H, H-4a), 2.78 ppm (virt. dddt, ^2J = 17.9 Hz, $^3J_1$ = 12.5 Hz, $^3J_2$ = 9.6 Hz, $^4J_1 \approx {}^4J_2$ = 0.8 Hz, 1H, H*H*-2); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 25.8 (t, C-4), 26.0 (t, C-6), 32.1 (t, C-1), 33.4 (t, C-5), 37.4 (t, C-7), 38.2 (t, C-2), 40.6 (d, C-4a),

47.1 (d, C-3a), 53.0 (s, C-7a), 222.8 ppm (s, C-3); Chiral GC: τ_R (minor) = 82.4 min, τ_R (major) = 90.8 min, [60 °C (1 min), 100 °C (30 °C min^{-1}), 100 °C (157 min), 135 °C (3 °C min^{-1}), 200 °C (20 °C min^{-1}), 200 °C (3 min)], Cyclosil-B. The analytical data obtained matched those reported in the literature.[48]

Photocycloaddition product 6f: *Racemic*: Following GP1, enone **5f** (35.7 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) for 5 h. After purification by column chromatography (silica, P/Et_2O = 5:1), ketone *rac*-**6f** (24.2 mg, 136 μmol, 68%) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone **5f** (35.7 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (silica, P/Et_2O = 5:1), ketone **6f** (29.5 mg, 165 μmol, 83%, 86% *ee*) was obtained as a colorless oil. R_f = 0.58 (pentane/Et_2O 1:1) [$KMnO_4$]; $[\alpha]_D^{25} = +155$ (c = 1.1 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.06 (s, 3H, Me-3a), 1.29–1.36 (m, 1H, *H*H-3), 1.36–1.42 (m, 1H, *H*H-1), 1.45 (ddd, ^2J = 13.7 Hz, $^3J_1$ = 9.1 Hz, $^3J_2$ = 4.2 Hz, 1H, *H*H-8), 1.57–1.63 (m, 1H, H*H*-3), 1.71–1.83 (m, 4H, H*H*-1, H-2, H*H*-8), 1.86 (ddd, ^2J = 12.7 Hz, ^3J = 7.2 Hz, ^4J = 1.4 Hz, 1H, *H*H-4), 1.88–1.98 (m, 2H, H-7), 2.01 (dd, ^2J = 12.7 Hz, ^3J = 11.0 Hz, 1H, H*H*-4), 2.21–2.28 (m, 1H, *H*H-6), 2.37–2.44 ppm (m, 2H, H-4a, H*H*-6); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 22.0 (t, C-7), 22.9 (q, Me-3a), 23.9 (t, C-2), 29.5 (t, C-8), 35.1 (t, C-4), 40.0 (t, C-6), 41.7 (t, C-1), 42.0 (t, C-3), 44.6 (s, C-3a), 45.3 (d, C-4a), 51.3 (s, C-8a), 216.5 ppm (s, C-5); Chiral GC: τ_R (minor) = 131.9 min, τ_R (major) = 136.7 min, [60 °C (1 min), 100 °C (30 °C min^{-1}), 100 °C (157 min), 135 °C (3 °C min^{-1}), 200 °C (20 °C min^{-1}), 200 °C (3 min)], Cyclosil-B. The analytical data obtained matched those reported in the literature.[49]

Photocycloaddition product 6g: *Racemic*: Following GP1, enone **5g** (38.5 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) for 5.5 h. After purification by column chromatography (silica, P/Et_2O = 6:1), a product mixture was obtained, which contains inseparable impurities. To facilitate purification, the mixture was submitted to ozonolysis which was conducted at −78 °C in dichloromethane (3 mL). Completion of the reaction was indicated by blue coloration during ozone introduction. The blue color was removed by an argon gas flow and dimethyl sulfide (1 mL) was added. Subsequently, the mixture was warmed to room temperature and the solvent was removed in vacuo. The residue was purified by column chromatography (silica, P/Et_2O = 6:1). After the work-up process, ketone **6g** (19.7 mg, 102 μmol, 51%) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone **5g** (38.5 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (silica, P/Et_2O = 6:1), a product mixture was obtained, which contains inseparable impurities. To facilitate purification, the mixture was submitted to ozonolysis which was conducted at −78 °C in dichloromethane (3 mL). Completion of the reaction was indicated by blue coloration during ozone introduction. The blue color was removed by an argon gasflow and dimethyl sulfide (1 mL) was added. Subsequently, the mixture was warmed to room temperature and the solvent was removed in vacuo. The residue was purified by column chromatography (silica, P/Et_2O = 6:1). After the work-up process, ketone **6g** (6.20 mg, 32.2 μmol, 16%, 55% *ee*) was obtained as a colorless oil. R_f = 0.66 (pentane/Et_2O 1:1) [$KMnO_4$]; $[\alpha]_D^{25} = +140$ (c = 1.1 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.03 (s, 3H, Me-4), 1.05 (s, 3H, Me-4), 1.21–1.30 (m, 1H, *H*H-1), 1.50–1.62 (m, 1H, *H*H-3), 1.68–1.78 (m, 5H, H*H*-1, *H*H-2, H*H*-3, *H*H-7, *H*H-8), 1.80–1.91 (m, 2H, H*H*-2, H*H*-8), 1.91–1.98 (m, 1H, H*H*-7), 1.98–2.00 (m, 1H, H-3a), 2.17 (s, 1H, H-4a), 2.18–2.33 ppm (m, 2H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 21.4 (t, C-7), 25.1 (q, Me-4), 26.9 (t, C-2), 27.6 (q, Me-4), 28.2 (t, C-3), 34.5 (t, C-8), 36.9 (s, C-4), 40.4 (t, C-1), 41.1 (t, C-6), 45.1 (s, C-8a), 52.0 (d, C-3a), 57.4 (d, C-4a), 214.3 ppm (s, C-5); Chiral GC: τ_R (minor) = 157.6 min, τ_R (major) = 161.9 min, [60 °C (1 min), 100 °C (30 °C min^{-1}), 100 °C (157 min), 135 °C (3 °C min^{-1}), 200 °C (20 °C min^{-1}), 200 °C (3 min)], Cyclosil-B. The analytical data obtained matched those reported in the literature.[42]

Photocycloaddition product 6h: *Racemic*: Following GP1, enone **5h** (18.0 mg, 100 μmol, 1.00 equiv) was irradiated in dichloromethane (5 mL) for 8 h. After purification by column chromatography (silica, P/EtOAc = 2:1), ketone *rac*-**6h** (14.4 mg, 79.9 μmol, 80%) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone **5h** (36.1 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (silica, P/EtOAc = 2:1), ketone **6h** (25.8 mg, 143 μmol, 72%, 84% *ee*) was obtained as a colorless oil. R_f = 0.37 (pentane/Et_2O 1:1) [$KMnO_4$]; $[\alpha]_D^{26} = +142$ (c = 1.5 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.08 (s, 3H, Me-3a), 1.45 (ddd, ^2J = 14.4 Hz, $^3J_1$ = 8.6 Hz, $^3J_2$ = 5.9 Hz, 1H, *H*H-8), 1.77 (virt. dt, ^2J = 14.4 Hz, $^3J_1 \approx {}^3J_2$ = 5.0 Hz, 1H, H*H*-8), 1.87–2.02 (m, 3H, *H*H-4, H-7), 2.20–2.31 (m, 2H, H*H*-4, *H*H-6), 2.46 (virt. dt, ^2J = 16.6 Hz, $^3J_1 \approx {}^3J_2$ = 5.2 Hz, 1H, H*H*-6), 2.68 (dd, $^3J_1$ = 11.0 Hz, $^3J_2$ = 7.0 Hz, 1H, H-4a), 3.26 (d, ^2J = 9.1 Hz, 1H, *H*H-3), 3.30 (d, ^2J = 9.2 Hz, 1H, *H*H-1), 3.83 (d, ^2J = 9.1 Hz, 1H, H*H*-3), 3.95 ppm (d, ^2J = 9.2 Hz, 1H, H*H*-1); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 18.1 (q, Me-3a), 21.9 (t, C-7), 24.9 (t, C-8), 34.8 (t, C-4), 40.2 (t, C-6), 45.0 (d, C-4a), 45.5 (s, C-3a), 51.7 (s, C-8a), 80.0 (t, C-1), 81.1 (t, C-3), 214.6 ppm (s, C-5); IR (ATR): $\tilde{\nu}$ = 2935 (m, sp^3-CH), 2838 (m, sp^3-CH), 1699 (vs., C=O), 1054 (s, sp^3-CO), 932 cm^{-1} (s, sp^3-CO); MS (EI, 70 eV): *m/z* (%): 180 (15) $[M]^+$, 135 (55) $[C_9H_{11}O]^+$, 122 (31), 109 (100) $[C_7H_9O]^+$, 95 (46), 79 (61), 67 (51), 55 (97) $[C_4H_7]^+$, 41 (45) $[C_3H_5]^+$; HRMS (EI, 70 eV): calcd for $C_{11}H_{16}O_2$ $[M]^+$: 180.1145; found: 180.1143; calcd for $C_{10}{}^{13}CH_{16}O_2$ $[M]^+$: 181.1178; found: 181.1183; Chiral GC: τ_R (minor) = 42.7 min, τ_R (major) = 43.3 min, [60 °C (0 min), 130 °C (30 °C min^{-1}), 130 °C (38 min), 160 °C (5 °C min^{-1}), 240 °C (15 °C min^{-1}), 240 °C (2 min)], Cyclosil-B.

Photocycloaddition product 6i: *Racemic*: Following GP1, enone **5i** (41.3 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) for 5 h. After purification by column chromatography (silica, P/Et_2O = 6:1), ketone *rac*-**6i** (36.4 mg, 176 μmol, 88%) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone **5i** (41.3 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (silica, P/Et_2O = 6:1), ketone **6i** (34.7 mg, 168 μmol, 84%, 96% *ee*) was obtained as a colorless oil. R_f = 0.62 (pentane/Et_2O 1:1) [$KMnO_4$]; $[\alpha]_D^{25} = +228$ (c = 1.3 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.90 (s, 3H, Me-7), 1.01 (s, 3H, Me-3a), 1.04 (s, 3H, Me-7), 1.23–1.34 (m, 2H, *H*H-3, *H*H-8), 1.39 (virt. td, $^2J \approx {}^3J_1$ = 12.2 Hz, $^3J_2$ = 7.0 Hz, 1H, *H*H-1), 1.62 (virt. ddt, ^2J = 12.7 Hz, ^3J = 6.2 Hz, $^4J_1 \approx {}^4J_2$ = 1.5 Hz, 1H, H*H*-3), 1.69–1.84 (m, 3H, H-2, *H*H-4), 1.91 (d, ^2J = 14.2 Hz, 1H, H*H*-8), 1.93–1.99 (m, 1H, H*H*-1), 2.02 (dd, ^2J = 12.5 Hz, ^3J = 11.2 Hz, 1H, H*H*-4), 2.12 (ddd, ^2J = 16.1 Hz, $^4J_1$ = 2.5 Hz, $^4J_2$ = 1.3 Hz, 1H, *H*H-6), 2.21 (dd, ^2J = 16.1 Hz, ^4J = 0.8 Hz, 1H, H*H*-6), 2.36 ppm (ddd, $^3J_1$ = 11.2 Hz, $^3J_2$ = 7.7 Hz, ^4J = 1.3 Hz, 1H, H-4a); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 24.3 (q, Me-3a), 24.3 (t, C-2), 28.0 (q, Me-7), 31.8 (q, Me-7), 33.9 (s, C-7), 34.8 (t, C-4), 40.8 (t, C-3), 42.8 (t, C-8), 43.7 (d, C-4a), 44.0 (t, C-1), 45.4 (s, C-3a), 50.0 (s, C-8a), 52.7 (t, C-6), 216.2 ppm (s, C-5); Chiral GC: τ_R (major) = 94.3 min, τ_R (minor) = 95.0 min, [60 °C (0.5 min), 70 °C (10 °C min^{-1}), 114 °C (0.4 °C min^{-1}), 200 °C (10 °C min^{-1}), 200 °C (3 min)], Lipodex E. The analytical data obtained matched those reported in the literature.[49]

Photocycloaddition product 6j: *Racemic*: Following GP1, enone **5j** (32.9 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) for 8 h at λ = 350 nm. After purification by column

chromatography (silica, P/Et_2O = 5:1), ketone *rac*-**6j** (20.6 mg, 125 μmol, 63%) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone **5j** (32.9 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (silica, P/Et_2O = 5:1), ketone **6j** (20.2 mg, 123 μmol, 61%, 76% *ee*) was obtained as a colorless oil. R_f = 0.60 (pentane/Et_2O 1:1) [$KMnO_4$]; $[\alpha]_D^{25} = +222$ (c = 1.1 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.14 (s, 3H, Me-4a), 1.30–1.38 (m, 1H, *H*H-5), 1.44–1.52 (m, 1H, *H*H-7), 1.59–1.70 (m, 3H, *H*H-4, H*H*-5, H*H*-7), 1.70–1.84 (m, 3H, *H*H-1, H-6), 2.01–2.09 (m, 2H, H*H*-1, H*H*-4), 2.20 (ddd, $^3J_1$ = 11.0 Hz, $^3J_2$ = 4.7 Hz, ^4J = 2.0 Hz, 1H, H-3a), 2.34 (virt. ddt, ^2J = 18.8 Hz, $^3J_1$ = 9.8 Hz, $^3J_2 \approx {}^4J$ = 2.0 Hz, 1H, *H*H-2), 2.62–2.71 ppm (m, 1H, H*H*-2); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 23.2 (q, Me-4a), 25.1 (t, C-6), 27.1 (t, C-1), 34.5 (t, C-4), 38.5 (t, C-7), 38.8 (t, C-2), 42.3 (t, C-5), 43.8 (s, C-4a), 45.6 (d, C-3a), 53.6 (s, C-7a), 223.4 ppm (s, C-3); Chiral GC: τ_R (minor) = 14.8 min, τ_R (major) = 14.9 min, [60 °C (0 min), 120 °C (30 °C min^{-1}), 120 °C (10 min), 240 °C (30 °C min^{-1}), 240 °C (2 min)], Cyclosil-B. The analytical data obtained matched those reported in the literature.[48]

Photocycloaddition products *trans*-6k and *cis*-6k: *Racemic*: Following GP1, enone *cis*-**5k** (35.7 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) for 8 h at a wavelength of λ = 366 nm. After purification by column chromatography (P/Et_2O = 4:1), a mixture of ketones *rac-trans*-**6k** and *rac-cis*-**6k** (32.7 mg, 183 μmol, 92%, d.r. = 50:50) was obtained as a colorless oil. Following GP1, enone *trans*-**5k** (35.7 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) for 8 h at a wavelength of λ = 366 nm. After purification by column chromatography (P/Et_2O = 4:1), a mixture of ketones *rac-trans*-**6k** and *rac-cis*-**6k** (33.0 mg, 185 μmol, 93%, d.r. = 50:50) was obtained as a colorless oil. *Enantioselective*: Following GP2, enone *cis*-**5k** (35.7 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (P/Et_2O = 5:1), a mixture of ketones *trans*-**6k** (79% *ee*) and *cis*-**6k** (55% *ee*) (13.5 mg, 75.7 μmol, 38%, d.r. = 83:17) was obtained as a colorless oil. Following GP2, enone *trans*-**5k** (35.7 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL). After purification by column chromatography (P/Et_2O = 5:1), a mixture of ketones *trans*-**6k** (86% *ee*) and *cis*-**6k** (74% *ee*) (15.7 mg, 88.1 μmol, 44%, d.r. = 86:14) was obtained as a colorless oil. *trans*-**6k**: R_f = 0.58 (pentane/Et_2O 1:1) [$KMnO_4$]; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.94 (d, ^3J = 7.5 Hz, 3H, Me-4), 1.29–1.39 (m, 1H, *H*H-3), 1.49–1.63 (m, 5H, H-1, H*H*-3, H-8), 1.75–1.84 (m, 2H, H-2), 1.89–1.98 (m, 2H, H-7), 1.98–2.04 (m, 1H, H-3a), 2.04–2.14 (m, 2H, H-4, *H*H-6), 2.40 (virt. dt, ^2J = 18.4 Hz, $^3J_1 \approx {}^3J_2$ = 3.6 Hz, 1H, H*H*-6), 2.52 ppm (d, ^3J = 11.2 Hz, 1H, H-4a); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 17.3 (q, Me-4), 21.3 (t, C-7), 25.2 (t, C-2), 32.5 (t, C-8)*, 33.0 (t, C-1)*, 33.3 (d, C-4), 40.6 (t, C-3), 41.1 (t, C-6), 45.8 (s, C-8a), 47.9 (d, C-3a), 51.3 (s, C-4a), 214.9 ppm (s, C-5) [*Assignment of signals is interconvertible.]; Chiral GC: τ_R (major) = 55.4 min, τ_R (minor) = 58.1 min, [60 °C (0 min), 115 °C (15 °C min^{-1}), 115 °C (50 min), 160 °C (5 °C min^{-1}), 220 °C (30 °C min^{-1}), 220 °C (2 min)], Cyclosil-B. *cis*-**6k**: R_f = 0.58 (pentane/Et_2O 1:1) [$KMnO_4$]; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.98 (d, ^3J = 6.8 Hz, 3H, Me-4), 1.24–1.38 (m, 1H), 1.47–1.63 (m, 3H), 1.56–1.75 (m, 1H), 1.68–1.74 (m, 1H), 1.75–1.86 (m, 2H), 1.89–1.98 (m, 1H), 2.03–2.21 (m, 3H, H-4a), 2.33–2.46 (m, 2H, H-3a, H-4), 2.57 ppm (virt. dt, ^2J = 17.8 Hz, $^3J_1 \approx {}^3J_2$ = 3.9 Hz, 1H, H*H*-6); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 14.7 (q, Me-4), 20.9 (t), 26.7 (t), 26.9 (t), 31.3 (d, C-4), 32.5 (t), 39.0 (t), 39.6 (t), 43.3 (d, C-3a), 47.4 (s, C-8a), 56.0 (d, C-4a), 214.0 ppm (s, C-5); Chiral GC: τ_R (minor) = 56.8 min, τ_R (major) = 57.6 min, [60 °C (0 min), 115 °C (15 °C min^{-1}), 115 °C (50 min), 160 °C (5 °C min^{-1}), 220 °C (30 °C min^{-1}), 220 °C (2 min)], Cyclosil-B. The analytical data obtained matched those reported in the literature.[47]

Photocycloaddition products 15a and 15b: *Racemic*: Following GP1, enone *rac*-**3** (273 mg, 1.32 mmol, 1.00 equiv) was irradiated in dichloromethane (66 mL) for 14 h. Different from GP1, the reaction mixture was treated with triethylamine (1 mL) instead of basic alumina and the solvent was removed in vacuo. The residue was purified by column chromatography (silica, P/Et_2O = 5:1). Starting material *rac*-**3** as well as the product mixture, which was submitted to ozonolysis, were isolated. The ozonolysis was conducted at −78 °C in dichloromethane (3 mL). Completion of the reaction was indicated by blue coloration during ozone introduction. The blue color was removed by an argon gasflow and dimethyl sulfide (1 mL) was added. Subsequently, the mixture was warmed to room temperature, the solvent was removed in vacuo and the residue was purified by column chromatography (silica, P/Et_2O = 5:1). After the work-up process, ketones *rac*-**15a** and *rac*-**15b** (211 mg, 1.02 mmol, 77%, d.r. = 67:33, *rac*-**15a**/*rac*-**15b**) were obtained as a colorless oil and starting material *rac*-**3** (17.7 mg, 85.8 μmol, 6%) was recovered. *Racemic in the presence of aluminum bromide*: In analogy to GP2, enone *rac*-**3** (41.3 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) using aluminum bromide as catalyst for 24 h. After purification by column chromatography (silica, P/Et_2O = 6:1), ketones *rac*-**15a** and *rac*-**15b** (25.5 mg, 124 μmol, 62%, d.r. = 82:18, *rac*-**15a**/*rac*-**15b**) were obtained as a colorless oil. *Enantioselective*: Following GP2, enone *rac*-**3** (41.3 mg, 200 μmol, 1.00 equiv) was irradiated in dichloromethane (10 mL) using activated catalyst **11**·$AlBr_3$ for 1 h. After purification by column chromatography (silica, P/Et_2O = 6:1), ketones **15a** and **15b** [5.30 mg, 25.7 μmol, 13%, d.r. = 84:16, **15a** (43% *ee*)/**15b** (21% *ee*)] were obtained as a colorless oil and starting material *ent*-**3** (29.1 mg, 141 μmol, 71%, 10% *ee*) was recovered. *Separation of diastereoisomers*: A mixture of diastereomers *rac*-**15a** and *rac*-**15b** (500 mg) was separated by column chromatography (silica, P/Et_2O = 30:1) with a conventional column (36 mm diameter, 300 mm length). The collected fractions were analyzed by gas chromatography and were combined to six fractions [(content of *rac*-**15b**)]: [F1 ($\geq$ 99.5%)], [F2 (90 < 99.5%)], [F3 (10 < 90%)]; [(content of *rac*-**15a**)]: [F4 (90 < 99%)], [F5 (99 < 99.5)], [F6 ($\geq$ 99.5%)]. The fractions F3, F4 and F5 were purified under the same conditions iteratively (subsequently from F3 to F5) until F3 contained less than 15 mg of the product mixture. Finally, F2, F3, F4, F5 were purified subsequently. **15a**: R_f = 0.66 (pentane/Et_2O 1:1) [CAM, $KMnO_4$]; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.84 (d, ^3J = 7.2 Hz, 3H, Me-1), 1.03 (s, 3H, Me-4β), 1.07 (s, 3H, Me-4α), 1.48–1.55 (m, 1H, *H*H-2), 1.59–1.76 (m, 4H, H-3, *H*H-7, *H*H-8), 1.84–2.07 (m, 5H, H-1, H*H*-2, H-3a, H*H*-7, H*H*-8), 2.15–2.25 (m, 2H, H-4a, *H*H-6), 2.28–2.36 ppm (m, 1H, H*H*-6); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 16.7 (q, Me-1), 20.5 (t, C-7), 25.1 (t, C-3), 25.7 (q, Me-4β), 27.6 (q, Me-4α), 29.0 (t, C-8), 34.7 (t, C-2), 37.0 (s, C-4), 40.9 (t, C-6), 41.0 (d, C-1), 47.8 (s, C-8a), 51.6 (d, C-3a), 58.4 (d, C-4a), 214.7 ppm (s, C-5); Chiral GC: τ_R (minor) = 25.3 min, τ_R (major) = 25.9 min, [60 °C (0.5 min), 200 °C (4 °C min^{-1}), 200 °C (5 min)], Lipodex E. **15b**: R_f = 0.66 (pentane/Et_2O 1:1) [CAM, $KMnO_4$]; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.89 (d, ^3J = 6.7 Hz, 3H, Me-1), 1.03 (s, 3H, Me-4β), 1.06 (s, 3H, Me-4α), 1.42 (virt. qd, $^2J \approx {}^3J_1 \approx {}^3J_2$ = 12.3 Hz, $^3J_3$ = 6.6 Hz, 1H, *H*H-2), 1.48–1.73 (m, 4H, H-1, H-3, *H*H-8), 1.73–1.91 (m, 3H, H*H*-2, *H*H-7, H*H*-8), 1.94–2.04 (m, 1H, H*H*-7), 2.06 (d, ^3J = 8.0 Hz, 1H, H-3a), 2.11–2.21 (m, 1H, *H*H-6), 2.25–2.35 ppm (m, 2H, H-4a, H*H*-6); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 12.8 (q, Me-1), 21.5 (t, C-7), 24.9 (q, Me-4β), 26.6 (t, C-3), 27.3 (q, Me-4α), 33.0 (t, C-8), 35.4 (t, C-2), 36.3 (s, C-4), 41.1 (t, C-6), 44.7 (d, C-1), 46.5 (s, C-8a), 52.2 (d, C-4a), 53.1 (d, C-3a), 214.1 ppm (s, C-5); Chiral GC: τ_R (major) = 24.3 min,

τ_R (minor) = 24.6 min, [60 °C (0.5 min), 200 °C (4 °C min^{-1}), 200 °C (5 min)], Lipodex E. The analytical data obtained matched those reported in the literature.[42]

Ketone *rac*-17a: A solution of *n*-butyllithium (2.50 M in hexane, 3.54 mL, 8.85 mmol, 6.00 equiv) was added to a solution of diisopropylamine (955 mg, 1.33 mL, 9.44 mmol, 6.40 equiv) in tetrahydrofuran (15 mL, 630 mM) at −78 °C. The resulting mixture was stirred for 1 h at −78 °C. A solution of ketone *rac*-**15a** (304 mg, 1.47 mmol, 1.00 equiv) in tetrahydrofuran (15 mL, 100 mM) was added dropwise to the freshly prepared lithium diisopropylamide solution at −78 °C. After 6 h, DMPU (2.27 g, 2.14 mL, 17.7 mmol, 12.0 equiv) and iodomethane (1.67 g, 735 μL, 11.8 mmol, 8.00 equiv) were added in sequence, during which a colorless precipitate was formed. The suspension was allowed to slowly warm to room temperature over the course of 15 h. The brown reaction mixture was transferred to a silica-packed column, the reaction vessel was rinsed with dichloromethane and the reaction mixture was filtered with a solvent mixture (P/Et_2O = 5:1). The product containing fractions were combined and after removal of the solvent in vacuo, the residue was purified by column chromatography (silica, P/Et_2O = 10:1). Ketone *rac*-**17a** (305 mg, 1.38 mmol, 94%, d.r. = 90:10) was obtained as a colorless oil. R_f = 0.77 (pentane/Et_2O 1:1) [CAM, $KMnO_4$]; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.82 (d, ^3J = 7.2 Hz, 3H, Me-1), 1.01 (s, 3H, Me-4β), 1.09 (s, 3H, Me-4α), 1.09 (d, ^3J = 7.1 Hz, 3H, Me-6), 1.33 (virt. tdd, $^2J \approx {}^3J_1$ = 13.5 Hz, $^3J_2$ = 11.9 Hz, $^3J_3$ = 2.3 Hz, 1H, *H*H-7), 1.49–1.56 (m, 1H, *H*H-2), 1.56–1.64 (m, 1H, *H*H-3), 1.70 (virt. tt, $^2J \approx {}^3J_1$ = 13.0 Hz, $^3J_2 \approx {}^3J_3$ = 7.6 Hz, 1H, H*H*-3), 1.76–1.83 (m, 1H, *H*H-8), 1.84–1.92 (m, 2H, H-1, H*H*-7), 1.94 (d, ^3J = 8.2 Hz, 1H, H-3a), 2.01 (virt. tt, $^2J \approx {}^3J_1$ = 13.1 Hz, $^3J_2 \approx {}^3J_3$ = 6.9 Hz, 1H, H*H*-2), 2.07–2.15 (m, 2H, H-6, H*H*-8), 2.19 ppm (s, 1H, H-4a); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 16.5 (q, Me-6), 16.9 (q, Me-1), 24.9 (t, C-3), 25.5 (q, Me-4β), 27.9 (q, Me-4α), 29.0 (t, C-8), 29.3 (t, C-7), 34.6 (t, C-2), 37.2 (s, C-4), 39.9 (d, C-1), 45.8 (d, C-6), 48.7 (s, C-8a), 51.9 (d, C-3a), 57.9 (d, C-4a), 216.5 ppm (s, C-5); The analytical data obtained matched those reported in the literature.[42]

Ketone *rac*-17b: A solution of *n*-butyllithium (2.50 M in hexane, 1.51 mL, 3.76 mmol, 6.00 equiv) was added to a solution of diisopropylamine (406 mg, 566 μL, 4.01 mmol, 6.40 equiv) in tetrahydrofuran (6.27 mL, 640 mM) at −78 °C. The resulting mixture was stirred for 1 h at −78 °C. A solution of ketone *rac*-**15b** (129 mg, 627 μmol, 1.00 equiv) in tetrahydrofuran (6.27 mL, 100 mM) was added dropwise to the freshly prepared lithium diisopropylamide solution at −78 °C. After 6 h, DMPU (965 mg, 910 μL, 7.53 mmol, 12.0 equiv) and iodomethane (712 mg, 312 μL, 5.02 mmol, 8.00 equiv) were added in sequence, during which a colorless precipitate was formed. The suspension was allowed to slowly warm to room temperature over the course of 15 h. The brown reaction mixture was transferred to a silica-packed column, the reaction vessel was rinsed with dichloromethane and the reaction mixture was filtered with a solvent mixture (P/Et_2O = 5:1). The product containing fractions were combined and after removal of the solvent in vacuo, the residue was purified by column chromatography (silica, P/Et_2O = 10:1). Ketone *rac*-**17b** (119 mg, 540 μmol, 86%) was obtained as a colorless oil. R_f = 0.77 (pentane/Et_2O 1:1) [CAM, $KMnO_4$]; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.90 (d, ^3J = 6.7 Hz, 3H, Me-1), 1.00 (s, 3H, Me-4β), 1.07 (d, ^3J = 7.0 Hz, 3H, Me-6), 1.09 (s, 3H, Me-4α), 1.41 (virt. qd, $^2J \approx {}^3J_1 \approx {}^3J_2$ = 12.3 Hz, $^3J_3$ = 7.0 Hz, 1H, *H*H-2), 1.49–1.67 (m, 4H, H-1, H-3, *H*H-7), 1.75 (virt. dt, ^2J = 12.4 Hz, $^3J_1 \approx {}^3J_2$ = 6.2 Hz, 1H, H*H*-2), 1.89 (ddd, ^2J = 13.7 Hz, $^3J_1$ = 5.6 Hz, $^3J_2$ = 3.5 Hz, 1H, *H*H-8), 1.94–2.07 (m, 3H, H-3a, H*H*-7, H*H*-8), 2.16–2.26 (m, 1H, H-6), 2.31 ppm (s, 1H, H-4a); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 13.2 (q, Me-1), 15.8 (q, Me-6), 24.9 (q, Me-4β), 26.3 (t, C-3), 27.8 (q, Me-4α), 30.4 (t, C-7), 33.7 (t, C-8), 35.7 (t, C-2), 36.7 (s, C-4), 45.1 (d, C-6), 45.9 (d, C-1), 47.0 (s, C-8a), 51.8 (d, C-4a), 54.2 (d, C-3a), 215.6 ppm (s, C-5); The analytical data obtained matched those reported in the literature.[42]

Triflate *rac*-18a: A solution of *n*-butyllithium (2.50 M in hexane, 363 μL, 908 μmol, 4.00 equiv) was added to a solution of diisopropylamine (96.4 mg, 135 μL, 953 μmol, 4.20 equiv) in tetrahydrofuran (2.27 mL, 420 mM) at −78 °C. The resulting mixture was stirred for 30 min. A solution of ketone *rac*-**17a** (50.0 mg, 227 μmol, 1.00 equiv) in tetrahydrofuran (2.27 mL, 100 mM) was added dropwise to the freshly prepared lithium diisopropylamide solution at −78 °C. After 7.5 h, a solution of Comins reagent (401 mg, 1.02 mmol, 4.50 equiv) in tetrahydrofuran (1.02 mL, 1.00 M) was added dropwise to the enolate solution, during which the solution turned deep brown. After 5 min, the reaction mixture was allowed to warm to room temperature in the course of 30 min. The brown reaction mixture was transferred to a column packed with deactivated, neutral alumina*, the reaction vessel was rinsed with dichloromethane and the reaction mixture was filtered with a solvent mixture (P/CH_2Cl_2 = 15:1). The product containing fractions were combined and after removal of the solvent in vacuo, the residue was purified by column chromatography (deactivated neutral alumina, P/CH_2Cl_2 = 15:1) three consecutive times in order to remove residual Comins reagent. Triflate *rac*-**18a** (59.8 mg, 170 μmol, 75%) was obtained as a colorless oil. [*Deactivation is described in the general information.] R_f = 0.47 (pentane) [CAM, $KMnO_4$]; ^{1}H NMR (500 MHz, C_6D_6, 25 °C, TMS): δ = 0.58 (d, ^3J = 7.2 Hz, 3H, Me-1), 1.00 (s, 3H, Me-4β), 1.04 (s, 3H, Me-4α), 1.24–1.39 (m, 2H, *H*H-2, *H*H-8), 1.41–1.51 (m, 3H, H-3, H*H*-8), 1.51–1.74 (m, 7H, H-1, H-3a, Me-6, H-7), 1.85 (virt. dtd, ^2J = 13.3 Hz, $^3J_1 \approx {}^3J_2$ = 9.5 Hz, $^3J_3$ = 6.7 Hz, 1H, H*H*-2), 2.39 ppm (br s, 1H, H-4a); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 15.9 (q, Me-1), 17.3 (q, Me-6), 24.8 (t, C-3), 24.9 (q, Me-4β), 26.8 (q, Me-4α), 26.8 (t, C-8), 29.5 (t, C-7), 34.9 (t, C-2), 35.6 (s, C-4), 40.6 (d, C-1), 48.7 (s, C-8a), 49.4 (d, C-4a), 51.1 (d, C-3a), 119.1 (qs, $^1J_{CF}$ = 320 Hz, CF_3), 128.5 (s, C-6)*, 145.2 ppm (s, C-5) [*The ^{13}C signal of C-6 overlaps with the solvent signal of C_6D_6. However, the signal can be located with the help of a HMBC crosspeak with the proton signal of Me-6 to assign the ^{13}C signal of C-6.]; ^{19}F NMR (376 MHz, C_6D_6, 25 °C, TMS): δ = −75.4 (s, 3F, CF_3); IR (ATR): $\tilde{\nu}$ = 2953 (m, sp^3-CH), 2870 (m, sp^3-CH), 1410 (s, SO), 1201 (vs., sp^3-CF), 1141 (vs., sp^3-CF), 898 cm^{-1} (vs., SO); MS (EI, 70 eV): *m/z* (%): 352 (51) $[M]^+$, 308 (14), 281 (74), 266 (100), 252 (14), 220 (17), 205 (68), 187 (64), 159 (56), 145 (73), 109 (39), 82 (55), 55 (42) $[C_4H_7]^+$; HRMS (EI, 70 eV): calcd for $C_{16}H_{23}O_3F_3{}^{32}S$ $[M]^+$: 352.1315; found: 352.1310; calcd for $C_{15}{}^{13}CH_{23}O_3F_3{}^{32}S$ $[M]^+$: 353.1348; found: 353.1344.

Triflate *rac*-18b: A solution of *n*-butyllithium (2.50 M in hexane, 363 μL, 908 μmol, 4.00 equiv) was added to a solution of diisopropylamine (96.4 mg, 135 μL, 953 μmol, 4.20 equiv) in tetrahydrofuran (2.27 mL, 420 mM) at −78 °C. The resulting mixture was stirred for 40 min. A solution of ketone *rac*-**17b** (50.0 mg, 227 μmol, 1.00 equiv) in tetrahydrofuran (2.27 mL, 100 mM) was added dropwise to the freshly prepared lithium diisopropylamide solution at −78 °C. After 8.5 h, a solution of Comins reagent (401 mg, 1.02 mmol, 4.50 equiv) in tetrahydrofuran (1.02 mL, 1.00 M) was added dropwise to the enolate solution, during which the solution turned deep brown. After 5 min, the reaction mixture was allowed to warm to room temperature in the course of 30 min. The brown reaction mixture was transferred to a column packed with deactivated, neutral alumina*, the reaction vessel was rinsed with dichloromethane and the reaction mixture was filtered with a solvent mixture (P/CH_2Cl_2 = 15:1). The product containing fractions were combined and after removal of the solvent in vacuo, the resi-

due was purified by column chromatography (deactivated neutral alumina, P/CH_2Cl_2 = 15:1) three consecutive times in order to remove residual Comins reagent. Triflate *rac*-**18b** (63.8 mg, 181 μmol, 80%) was obtained as a colorless oil. [*Deactivation is described in the general information.] R_f = 0.47 (pentane) [CAM, $KMnO_4$]; ^{1}H NMR (500 MHz, C_6D_6, 25 °C, TMS): δ = 0.85 (d, ^3J = 5.6 Hz, 3H, Me-1), 0.95 (s, 3H, Me-4α), 0.97 (s, 3H, Me-4β), 1.26–1.36 (m, 4H, *H*H-1, *H*H-2, *H*H-3, *H*H-8), 1.40–1.52 (m, 2H, H*H*-3, H*H*-8), 1.55–1.61 (m, 2H, H*H*-2, H-3a), 1.62 (s, 3H, Me-6), 1.72 (virt. dt, ^2J = 16.7 Hz, $^3J_1 \approx {}^3J_2$ = 6.1 Hz, 1H, *H*H-7), 1.90 (virt. dt, ^2J = 16.7 Hz, $^3J_1 \approx {}^3J_2$ = 6.7 Hz, 1H, H*H*-7), 2.49 ppm (br s, 1H, H-4a); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 13.0 (q, Me-1), 17.2 (q, Me-6), 23.9 (q, Me-4β), 26.5 (t, C-3), 26.7 (q, Me-4α), 30.5 (t, C-7), 31.0 (t, C-8), 35.7 (t, C-2), 35.8 (s, C-4), 43.2 (d, C-4a), 44.6 (d, C-1), 48.1 (s, C-8a), 52.8 (d, C-3a), 119.1 (qs, $^1J_{CF}$ = 320 Hz, CF_3), 128.6 (s, C-6)*, 145.5 ppm (s, C-5) [*The ^{13}C signal of C-6 overlaps with the solvent signal of C_6D_6. However, the signal can be located with the help of a HMBC crosspeak with the proton signal of Me-6 to assign the ^{13}C signal of C-6.]; ^{19}F NMR (376 MHz, C_6D_6, 25 °C, TMS): δ = −75.4 (s, 3F, CF_3); IR (ATR): $\tilde{\nu}$ = 2953 (m, sp^3-CH), 2870 (m, sp^3-CH), 1410 (s, SO), 1201 (vs., sp^3-CF), 1141 (vs., sp^3-CF), 898 cm^{-1} (vs., SO); MS (EI, 70 eV): *m/z* (%): 352 (51) $[M]^+$, 308 (14), 281 (74), 266 (100), 252 (14), 220 (17), 205 (68), 187 (64), 159 (56), 145 (73), 109 (39), 82 (55), 55 (42) $[C_4H_7]^+$; HRMS (EI, 70 eV): calcd for $C_{16}H_{23}O_3F_3{}^{32}S$ $[M]^+$: 352.1315; found: 352.1310; calcd for $C_{15}{}^{13}CH_{23}O_3F_3{}^{32}S$ $[M]^+$: 353.1348; found: 353.1344.

Italicene (*rac*-19a): Palladium(II) acetate (3.91 mg, 17.0 μmol, 10.0 mol%) was added to a solution of triflate *rac*-**18a** (59.8 mg, 170 μmol, 1.00 equiv), triphenylphosphine (13.4 mg, 50.9 μmol, 30.0 mol%) and lithium formate monohydrate (59.4 mg, 848 μmol, 5.00 equiv) in dimethylformamide (3.39 mL, 50.0 mM). The resulting mixture was heated to 60 °C. The reaction mixture turned black in 7 min. After stirring for 20 min, the reaction mixture was allowed to cool to room temperature. The suspension was transferred to a column packed with deactivated, neutral alumina*, the reaction vessel was rinsed with dichloromethane and the reaction mixture was filtered with pentane. The product containing fractions were combined and after removal of the solvent in vacuo, the residue was purified by column chromatography (deactivated neutral alumina, pentane) three consecutive times to remove residual triphenylphosphine. In order to remove pentane completely without losing too much of the volatile product *rac*-**19a**, the vessel was evacuated at room temperature to 100 mbar and loaded with air in sequence five times. The title compound *rac*-**19a** (31.5 mg, 154 μmol, 91%) was obtained as a colorless oil. [*Deactivation is described in the general information.] R_f = 0.71 (pentane) [CAM, $KMnO_4$]; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.78 (d, ^3J = 7.2 Hz, 3H, Me-1), 0.91 (s, 3H, Me-4β), 0.96 (s, 3H, Me-4α), 1.46 (dd, ^2J = 12.4 Hz, ^3J = 6.9 Hz, 1H, *H*H-2α), 1.53–1.59 (m, 1H, *H*H-3β), 1.60–1.69 (m, 2H, H*H*-3α, *H*H-8), 1.69–1.76 (m, 5H, H-1, H-3a, Me-6), 1.76–1.81 (m, 2H, H-7), 1.84 (virt. dt, ^2J = 12.8 Hz, $^3J_1 \approx {}^3J_2$ = 3.5 Hz, 1H, H*H*-8), 1.88 (br s, 1H, H-4a), 2.02 (virt. tt, $^2J \approx {}^3J_1$ = 12.3 Hz, $^3J_2 \approx {}^3J_3$ = 7.0 Hz, 1H, H*H*-2β), 5.30–5.34 ppm (m, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 16.6 (q, Me-1), 24.5 (q, Me-6), 24.9 (t, C-3), 24.9 (q, Me-4β), 27.2 (q, Me-4α), 27.8 (t, C-7), 28.1 (t, C-8), 34.8 (s, C-4), 35.0 (t, C-2), 39.7 (d, C-1), 45.4 (s, C-8a), 48.0 (d, C-4a), 51.5 (d, C-3a), 121.1 (d, C-5), 136.2 ppm (s, C-6); The analytical data obtained matched those reported in the literature.[39]

Isoitalicene (*rac*-19b): Palladium(II) acetate (4.06 mg, 18.1 μmol, 10.0 mol%) was added to a solution of triflate *rac*-**18b** (63.8 mg, 181 μmol, 1.00 equiv), triphenylphosphine (14.3 mg, 54.3 μmol, 30.0 mol%) and lithium formate monohydrate (63.3 mg, 905 μmol, 5.00 equiv) in dimethylformamide (3.62 mL, 50.0 mM). The resulting mixture was heated to 60 °C. The reaction mixture turned black in 10 min. After stirring for 20 min, the reaction mixture was allowed to cool to room temperature. The suspension was transferred to a column packed with deactivated, neutral alumina*, the reaction vessel was rinsed with dichloromethane and the reaction mixture was filtered with pentane. The product containing fractions were combined and after removal of the solvent in vacuo, the residue was purified by column chromatography (deactivated neutral alumina, pentane) three consecutive times to remove residual triphenylphosphine. In order to remove pentane completely and avoid any loss of the volatile product *rac*-**19b**, the vessel was evacuated at room temperature to 100 mbar and loaded with air in sequence five times. The title compound *rac*-**19b** (35.8 mg, 175 μmol, 97%) was obtained as a colorless oil. [*Deactivation is described in the general information.] R_f = 0.71 (pentane) [CAM, $KMnO_4$]; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.82 (d, ^3J = 6.3 Hz, 3H, Me-1), 0.90 (s, 3H, Me-4β), 0.91 (s, 3H, Me-4α), 1.39–1.67 (m, 5H, H-1, *H*H-2, H-3, *H*H-8), 1.68–1.77 (m, 5H, H*H*-2, H-3a, Me-6), 1.82 (ddd, ^2J = 14.9 Hz, $^3J_1$ = 9.5 Hz, $^3J_2$ = 5.5 Hz, 1H, H*H*-8), 1.90 (virt. dt, ^2J = 16.5 Hz, $^3J_1 \approx {}^3J_2$ = 5.8 Hz, 1H, *H*H-7), 1.94–2.02 (m, 2H, H-4a, H*H*-7), 5.36–5.40 (m, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, 27 °C, TMS): δ = 13.5 (q, Me-1), 24.1 (q, Me-4β), 24.5 (q, Me-6), 26.5 (t, C-3), 27.2 (q, Me-4α), 28.6 (t, C-7), 33.1 (t, C-8), 35.2 (s, C-4), 36.3 (t, C-2), 41.0 (d, C-4a), 43.9 (s, C-8a), 45.0 (d, C-1), 53.6 (d, C-3a), 121.8 (d, C-5), 135.7 (s, C-6); The analytical data obtained matched those reported in the literature.[39]

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Conflict of interest

The authors declare no conflict of interest.

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