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LEHRSTUHL FÜR ORGANISCHE CHEMIE I

Photochemical Reactions of Thiocarbonyl Compounds and 2-(2′-Alkenyloxy)cycloalk-2-enones

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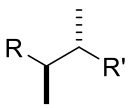
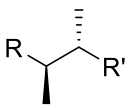
In this thesis the relative configuration of racemates is represented with straight bonds (bold or hashed). The absolute configuration of enantiomerically pure or enriched compounds is illustrated with wedged bonds (bold or hashed).

racemic		enantiomerically pure enantiomerically enriched	

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Für meine Familie

&

Alle, die mich auf dem Weg unterstützt haben

Inter- und intramolekulare [2+2]-Photocycloadditionen von cyclischen Enonen wurden in der Vergangenheit bereits ausführlich untersucht. Allerdings finden sich verhältnismäßig wenige Berichte über das photochemische Verhalten von 2-(2‘-Alkenyloxy)cyclohex-2-en-1-onen, vor allem in Bezug auf das Substitutionsmuster der beiden Doppelbindungen und des zentralen Cycloalkenonrings. Aus diesem Grund wurde in dieser Arbeit eine Vielzahl an Substraten mit unterschiedlichem Substitutionsmuster hergestellt und auf ihre Photoreaktivität untersucht. Abhängig von diesen Parametern wurden drei unterschiedliche Reaktionsverläufe beobachtet. So wurden Produkte isoliert, die entweder aus einer gekreuzten [2+2]-Photocycloaddition, einer [2+2]-Photodimerisierung oder einer Kaskade aus Cyclisierung und Wasserstoffabstraktion stammen. Dabei wurden in der Regel gute bis exzellente Ausbeuten erzielt. Des Weiteren wurden in einer umfassenden Studie verschiedene *Lewis*-Säuren auf ihre Nützlichkeit für eine enantioselektive Reaktionsführung getestet. Allerdings konnten im Allgemeinen keine reproduzierbaren Ergebnisse erzielt werden. In einem zweiten Kapitel wurden die UV/Vis Eigenschaften dreier Thiocarbonyl-Verbindungen in der Gegenwart verschiedener *Lewis*- oder *Brønsted*-Säuren ausführlich untersucht, da es wenig Literaturpräzedenz für das photochemische Verhalten dieser Substratklasse gibt. Der anschließende Versuch, einen enantioselektiven Reaktionsverlauf für die entsprechenden Photoreaktionen zu entwickeln, war nicht erfolgreich.

Inter- and intramolecular [2+2] photocycloadditions of cyclic enones have been extensively studied in the past. However, 2-(2'-alkenyloxy)cycloalk-2-en-1-ones have received considerably less attention than cycloalkenones with different substitution patterns. In this work an array of these compounds was prepared and evaluated regarding the influence of sterics at the double bonds or the cycloalkenone core and ring size on their photochemical reactivity. It was found that depending on the substitution one of three reaction pathways becomes more prominent. Hence, products originating from crossed intramolecular [2+2] photocycloaddition, [2+2] photodimerization or a cyclization/hydrogen abstraction cascade were obtained in good to excellent yields. Furthermore, an intensive screening towards an enantioselective version of these reactions was conducted with several chiral *Lewis* acids but did not give a reproducible positive result. In a second chapter, the UV/vis properties of three thiocarbonyl compounds in the presence of *Lewis* and *Brønsted* acids were intensively investigated, as literature on this chromophore class and especially its photoreactivity is scarce. Subsequent attempts towards an enantioselective reaction course were unsuccessful.

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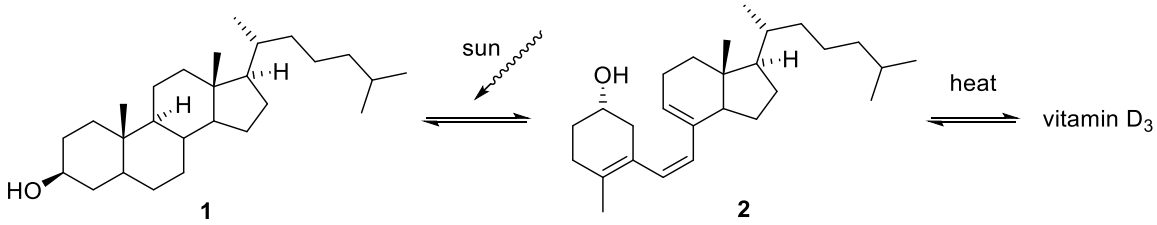
1. Introduction

"Sommer, Sonne, Sonnenbrand"

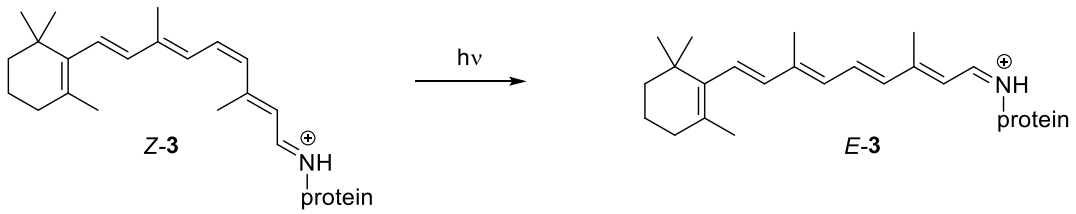
- Possenspiel, 1984 -

This fraction of song lyrics stems from the 80s and was released by a band from East Germany. It highlights the influence and impact the sun and its light can have on us. Not only do we get sunburnt, when we don't take the necessary precautions but nature has built a plethora of mechanisms that use the energy of light in a productive way.[1] Even though too much sun exposure is unhealthy for the skin, the right amount of irradiation is necessary for our bodies to produce vitamin D_3. This vitamin is important e.g. for bone mineralization or our immune system.[2] Starting from provitamin D_3 or 7-dehydrocholesterol (**1**) vitamin D_3 is produced in special skin cells (keratocytes) *via* a photochemically induced conrotatory ring opening reaction to form previtamin D_3 (**2**) (Scheme 1). A subsequent thermal antarafacial [1,7] *H*-shift then gives the final vitamin D_3.[3]



Scheme 1. Vitamin D_3 synthesis starting from provitamin D_3 (**1**).[4]

As another example, light enables us to see by a photochemical *E/Z* isomerization of 11-*cis*-retinal (*Z*-**3**) (Scheme 2).[5-7] This molecule is covalently bound to the opsin receptor in our eye. *E/Z* isomerization upon absorption of a photon leads to a conformational change in the opsin molecule which then triggers a signal cascade that eventually gives us the ability of vision.[7]



Scheme 2. *E/Z* photoisomerization of 11-*cis*-retinal (*Z*-**3**) bound to the opsin receptor as an iminium salt.[6]

Besides these biochemical processes photochemistry also bears a remarkable potential in synthetic organic chemistry, since it allows for the formation of otherwise not accessible structural motifs from high energy intermediates (IM).[8]

1.1 Enantioselectivity in Photochemistry

However, due to the high energetic nature of excited intermediates a new approach to enantioselective catalysis had to be found. The general concept of a catalyzed thermal reaction is reduction of its activation barrier by addition of a catalyst. Enantioselectivity can then be achieved by employing a chiral version of the appropriate catalyst.[9] Though, upon excitation by light molecules gain adequate energy to undergo quick subsequent reactions, for which no further catalysis is required. In order to attain enantioselective catalysis in photochemistry, it is essential that the substrate is already interacting with the chiral environment prior to excitation.[9] Thus, four main concepts have been established to achieve this goal.

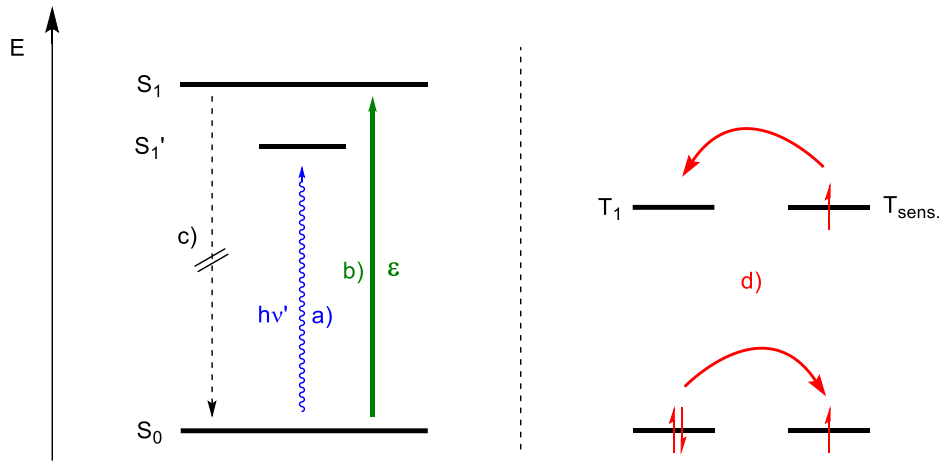


Figure 1. Strategies for chirality induction in photochemistry: a) bathochromic absorption, b) enhanced absorption, c) deactivation of decay and d) sensitization.

If substrate coordination lowers the energy of the excited level a bathochromic shift of the absorption maximum is observed and complex formation allows for selective irradiation at a higher wavelength (Figure 1, a). Even if the absorption maximum remains unchanged enantioselectivity can be induced if the substrate complex exhibits a significantly higher extinction coefficient (Figure 1, b).[9] Further, a catalyst might be able to stabilize the excited state of the substrate and therefore facilitate chirality induction by inhibition of decay pathways such as fluorescence or internal conversion (IC) (Figure 1, c). Also possible is

the shift of the reaction to another hypersurface.[9] Another very prominent strategy is the application of a sensitizer (Figure 1, d), which in total lowers the energy needed to reach the excited state. Typical triplet sensitizers undergo efficient intersystem crossing (ISC) from the singlet (S_1) to the triplet (T_1) excited state upon irradiation. They may enable reactions directly from the T_1 state of a substrate that otherwise shows insufficient ISC or decay mechanisms. Hereby, the energy of the sensitizer is used to directly excite the substrate from its ground state (S_0) into the triplet state (T_1). This transition would be forbidden under direct irradiation conditions. In case of a difference in excitation wavelength corresponding to a difference in singlet energy the sensitizer can be selectively excited and a potential racemic background reaction from the substrate's S_1 state *via* ISC can be suppressed.[9] Since the energy transfer, which stems from a mutual electron-electron exchange between substrate and sensitizer under retention of the spin multiplicity (*Dexter* mechanism),[10] is highly distance dependent and the substrate has to be in close proximity to the catalyst, asymmetric induction is possible within a chiral environment.[9] Figure 2 shows examples of the most prominent catalyst subclasses such as *Lewis* and *Brønsted* acids, hydrogen bonding catalysts as well as thioureas.

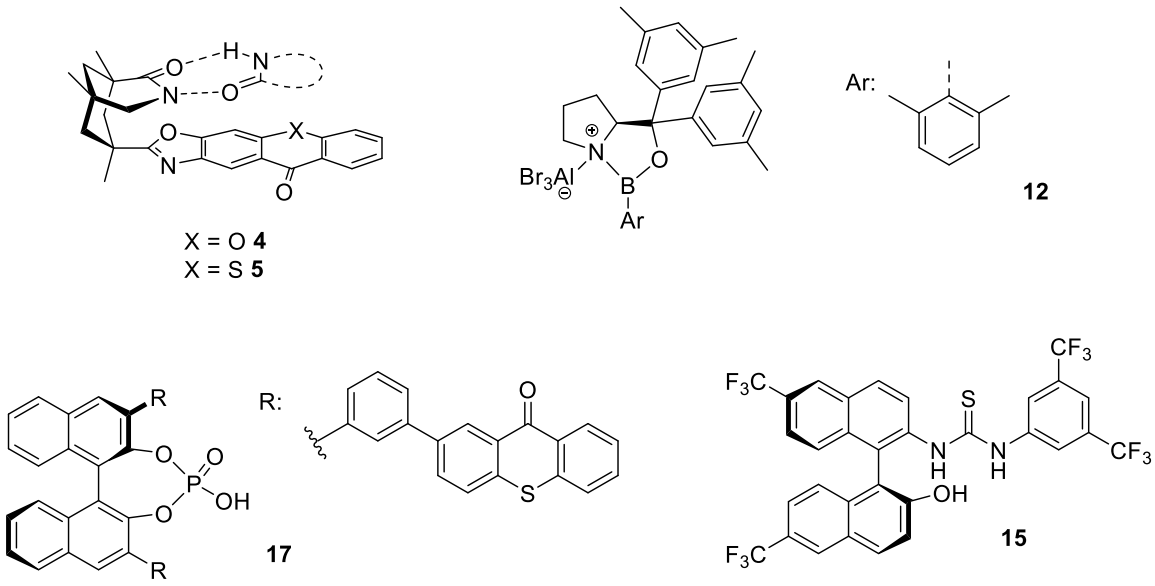
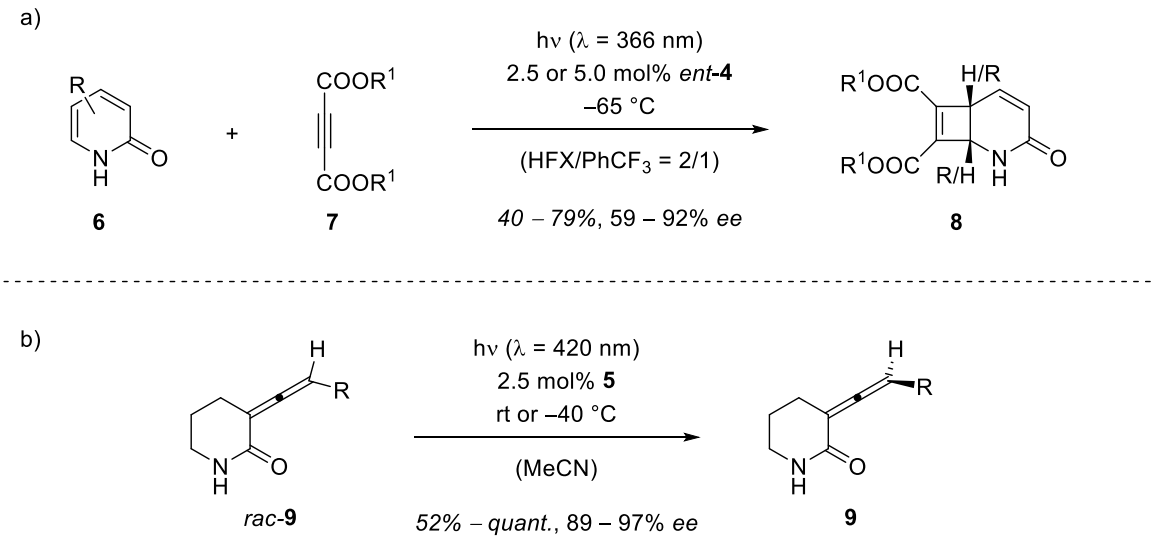


Figure 2. Examples for chiral hydrogen bonding sensitizers, *Brønsted* acids as well as oxazaborolidine-based chiral *Lewis* acids used in enantioselective photochemistry.

1.2 Hydrogen Bonding Triplet Sensiziters

One way to ensure substrate-catalyst interactions is hydrogen bonding. In this context our group has developed a variety of chiral sensitizers based on *Kemp's* triacid such as chiral xanthone **4** and thioxanthone **5**. They form a supramolecular complex with prochiral amide or lactam containing substrates in order to induce face differentiation (Figure 2).[11,12] These compounds have been used in a broad variety of sensitized reactions such as intra- and intermolecular [2+2] photocycloadditions or photochemical deracemization reactions.[11,13,14] A notable example for the versatility of these catalysts is the application of *ent*-**4** in the enantioselective conversion of different 2-pyridones **6** in an intermolecular [2+2] photocycloaddition with acetylenedicarboxylates **7** (Scheme 3, a). In this photochemical transformation yields up to 79% were achieved and the respective cyclobutenes **8** additionally showed high enantioselectivities.[15] Furthermore, thioxanthone **5** initiated the discovery and realization of a milestone in organic synthesis. When a racemic mixture of chiral allenes *rac*-**9** is bound, thioxanthone **5** enables the triplet sensitized conversion of one enantiomer into the other. A difference in energy transfer efficiencies is assumed to be the origin of this unidirectional conversion.[14] The enantiomerically enriched allenes **9** were obtained in excellent yields and enantioselectivities (Scheme 3, b).[14]

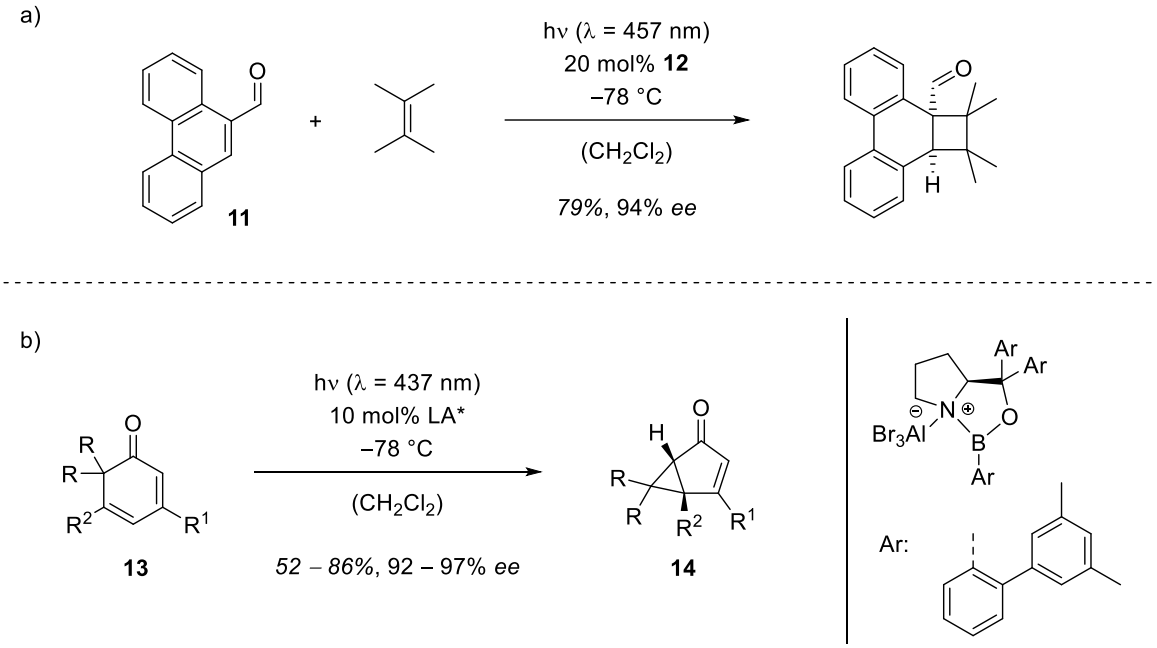


Scheme 3. a) Enantioselective intermolecular [2+2] photocycloaddition of 2-pyridones **6** with acetylenedicarboxylates **7** catalyzed by *ent*-**4**, (HFX = hexafluoro-*m*-xylene);[15] b) Deracemization of chiral allenes *rac*-**9** catalyzed by **5**.[14]

1.3 *Lewis* and *Brønsted* Acids

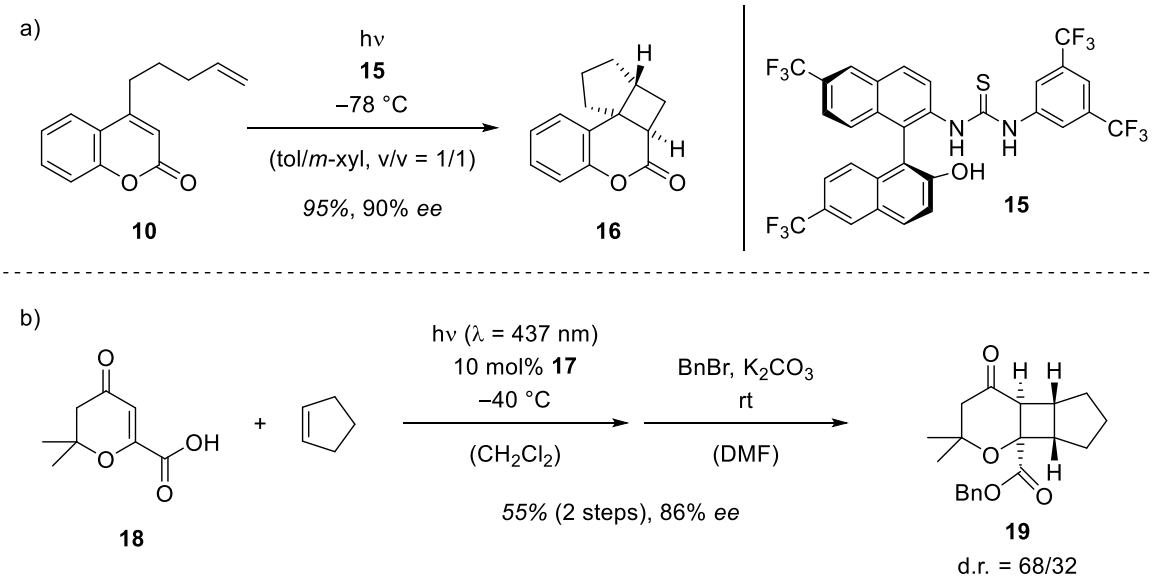
Another commonly applied method is the coordination of a *Lewis* or *Brønsted* acid to the irradiation precursor. This option was already reported by *Lewis* and *Barancyk* in 1989, as their work showed an altered photoreactivity of coumarins upon complexation with BF_3 or $EtAlCl_2$.[16] In the presence of a *Lewis* acid the normally very short lived excited state was stabilized,[17] which allowed for dimerization as well as intermolecular [2+2] photocycloaddition with alkenes.[16] Coordination to the carbonyl lone pair also resulted in a significant bathochromic shift of the $\pi\pi^*$ absorption band,[16] allowing for selective excitation of a substrate *Lewis* acid complex. Based on this observation a suitable chiral *Lewis* acid was developed in our group by activation of an oxazaborolidine with $AlBr_3$ and application in an enantioselective intramolecular [2+2] photocycloaddition of coumarins (analogues of **10**, *vide infra*) with high yields and enantiomeric excesses (*ee*s) of up to 82%.[18] Since this catalyst can be modified at the aryl substituents it can be tailored to the needs of a particular substrate.[19]

Another class of irradiation precursors, that showed improved reactivity upon addition of a *Lewis* acid, are phenanthrene-9-carboxaldehydes. Direct irradiation of the respective aldehydes resulted in a mixture of oxetane and cyclobutane products.[20] However, in combination with a *Lewis* acid no *Paternó-Büchi* reaction was observed and the substrates rather performed an *ortho*-photocycloaddition. This was achieved enantioselectively by *Stegbauer et al.* in 79% yield and 94% *ee* using the respective aldehyde **11**, 2,3-dimethyl-2-butene and only 20 mol% of the oxazaborlidine catalyst **12** (Scheme 4, a).[20] This method is not limited to [2+2] photocycloadditions of enones[21,22,23] as it was recently demonstrated by *Leverenz et al.* in an enantioselective photochemical rearrangement of 2,4-cyclohexadienones **13**. The bicyclic products **14** were obtained in high yields and excellent enantioselectivities (Scheme 4, b).[24]



Scheme 4. a) Enantioselective *Lewis* acid catalyzed *ortho*-photocycloadddition of phenanthrene-9-carboxaldehyde **11**;[20] b) Enantioselective *Lewis* acid catalyzed rearrangement of 2,4-cyclohexadienones **13**.[24]

As published by *Sivaguru* and co-workers *Brønsted* acids bear a similar potential for substrate coordination and activation. Thus, enantioface differentiation was possible in the above mentioned [2+2] photocycloaddition of coumarin **10**.[25,26] Under optimized conditions they employed chiral thiourea **15** and were able to obtain product **16** in 95% yield and 90% *ee* (Scheme 5, a).[25] It became apparent that the hydroxyl group in the naphthalene framework of **15** is vital for the course of the reaction, since it forms a hydrogen bond to the lactone oxygen atom of the coumarin.[25,26]



Scheme 5. a) Intramolecular [2+2] photocycloaddition of coumarin **10** catalyzed by thiourea **15** (tol = toluene, *m*-xyl = *m*-xylene);[25] b) Enantioselective intermolecular [2+2] photocycloaddition sensitized by chiral phosphoric acid **17**.[27]

Another more recent example of a *Brønsted* acid applied in photochemistry is depicted in Scheme 5, b).[27] This phosphoric acid **17** (Figure 2) with a 2,2'-binaphthol backbone and two thioxanthone moieties was developed in our group and represents a bifunctional photocatalyst. Spectroscopic data and density functional theory (DFT) calculations suggested a binding of the carboxylic acid **18** substrate to the catalyst *via* two hydrogen bonds. This appeared to lower its triplet energy and therefore allowed for asymmetric induction.[27] Under optimized conditions cyclobutane compound **19** was obtained with only 10 mol% catalyst loading in 55% yield over two steps and 86% *ee*.[27]

1.4 Coordinating Metal Complexes

Chiral metal complexes such as Cu(I) *bis*oxazoline (BOX) complex **20** (Figure 3) represent another class of frequently employed photocatalysts, as their steric and electronic properties can be tuned by ligand design and therefore adjusted to the irradiation precursor.[28]

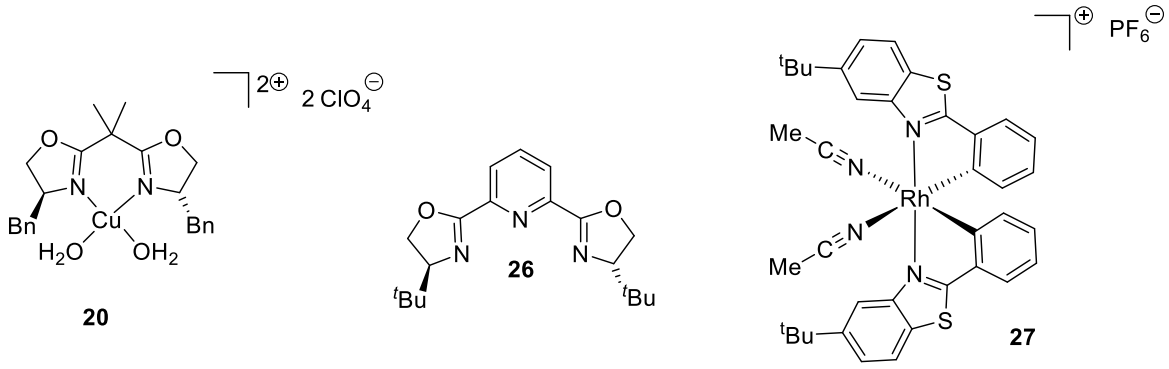
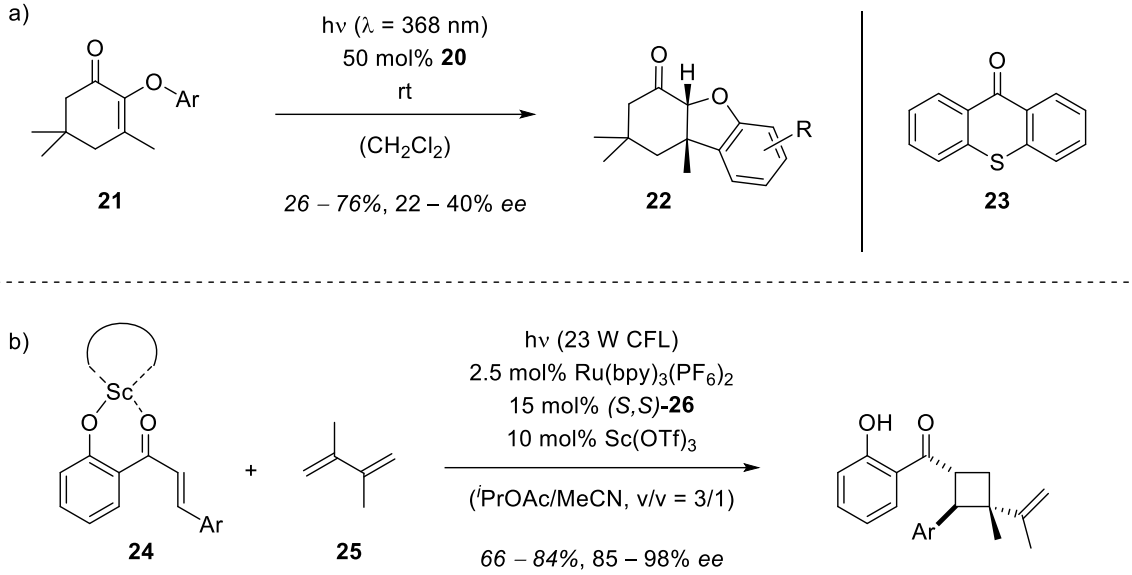


Figure 3. Examples for chiral chelating metal complexes used in enantioselective photochemistry and a commonly employed PyBOX ligand **26**.

The chelating metal complex **20** (50 mol%) in particular was reported to catalyze the [6π] cyclization of 2-aryloxycyclohex-2-enones **21** enantioselectively.[29] Direct irradiation of the substrate-catalyst complex did not result in exclusive excitation of the complexed enone but a background reaction was observed simultaneously. Thus, tetrahydrofurans **22** were obtained in moderate yields and enantioselectivities (Scheme 6, a) only. Yet, the enantioselectivity could be improved for electron-rich compounds by use of 50 mol% thioxanthone (txt) (**23**) as triplet sensitizer. In this dual catalytic approach **23** appeared to have a suitable triplet energy to sensitize bidentatedly coordinated electron-rich substrates. However, the triplet energy of the respective complex with electron-poor compounds seemed to be significantly higher, since full conversion was not achieved.[29]

Furthermore, *Yoon* and co-workers published the intermolecular [2+2] photocycloaddition of 2-hydroxychalcones **24** with diene **25** in 2016 (Scheme 6, b).[30] As in the previously mentioned example a dual catalysis strategy was applied. In contrast, the group employed the Ru-based sensitizer $Ru(bpy)_3(PF_6)_2$ paired with $Sc(OTf)_3$ and the chiral pyridine-*bis*(oxazoline) (PyBOX) ligand **26** (Figure 3). Upon coordination of the chalcone substrate to the C_2-symmetric Sc(III) complex the triplet energy of the substrate was significantly lowered and bidentate coordination ensured a rigid configuration in which on side was effectively shielded. Hence, $Ru(bpy)_3(PF_6)_2$ was able to sensitize precoordinated molecules only due to its triplet energy and a racemic background reaction was suppressed. Additionally, the diene **25** was only able to attack from one side. Therefore, high yields and excellent enantioselectivities were achieved under optimized conditions with only 2.5 mol% $Ru(bpy)_3(PF_6)_2$ and 10 mol% *Lewis* acid.[30]

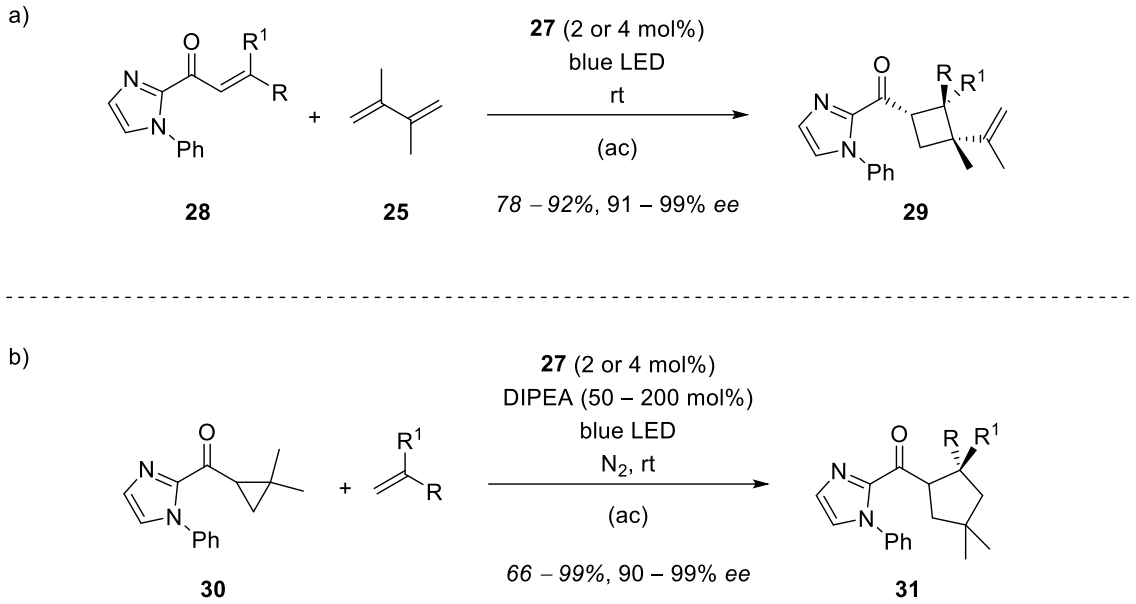


Scheme 6. a) Asymmetric [6π] cyclization catalyzed by Cu(I)-BOX complex **20**;[29] b) Enantioselective [2+2] photocycloaddition achieved by dual catalysis.[30]

In recent years the group of *Meggers* has developed an array of chiral-at-metal catalysts such as Rh complex **27** (Figure 3).[31] This catalyst as well as its Ir analogue have been used in various thermal as well as photochemical reactions such as radical and *Friedel-Crafts* alkylations,[32,33] a transfer hydrogenation,[34] [3+2] and [2+2] photocycloadditions[35,36] as well as a photochemical dearomatization.[37] The unique feature of these catalysts is their achiral ligands. The chirality of the complex solely stems from the coordination of the ligands to the metal. This is possible in two different fashions and results in a Δ– and a Λ-enantiomer, which can be obtained in equal parts from the racemic complex by application of a chiral auxiliary.[38] These bifunctional catalysts are able to induce asymmetry, while concurrently acting as a sensitizer. Thus, separate triplet sensitization is not necessary anymore.[35]

In this context, *Huang et al.* reported the visible light-mediated [2+2] photocycloaddition of various α,β-unsaturated imidazoles **28** (Scheme 7, a) catalyzed by Δ-RhS (**27**) at room temperature (rt).[35] The application of only 2 – 4 mol% of *Lewis* acid was sufficient to achieve good to very good yields and excellent enantioselectivities of up to 99% *ee* for cyclobutane products **29**. High enantioselectivities were possible due to significantly higher extinction coefficients of the Rh substrate complex compared to the substrate itself. Hence,

light was exclusively absorbed by the complex and a background reaction was efficiently suppressed.[35]



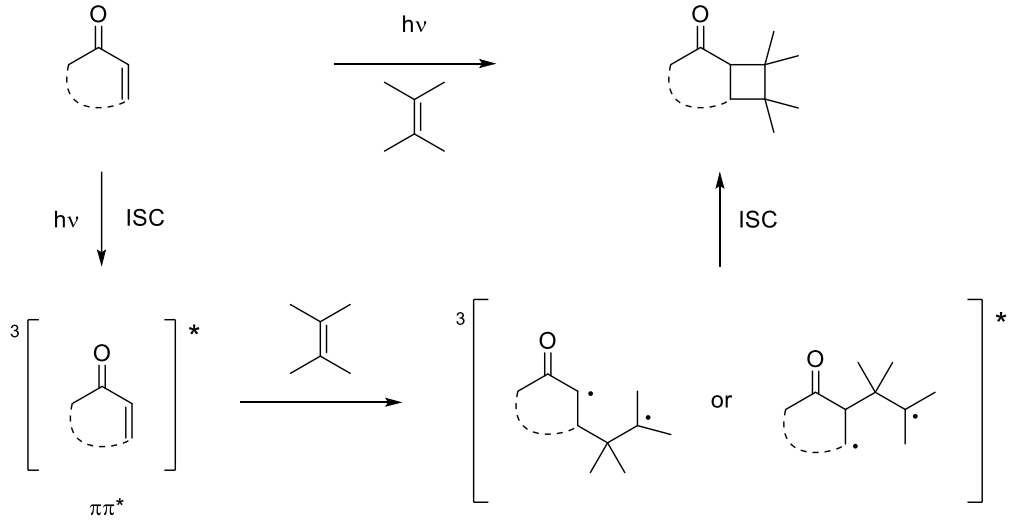
Scheme 7. a) Asymmetric intermolecular [2+2] photocycloaddition initiated by chiral-at-metal catalyst **27**;[35] Enantioselective [3+2] photocycloaddition of Rh-bound cyclopropanes **30**.[36]

The same group also presented a photochemical [3+2] cycloaddition of cyclopropanes **30** (Scheme 7, b).[36] In this case the chiral-at-metal *Lewis* acid not only enabled direct excitation of the substrate and asymmetric induction, but also lowered the reduction potential of the substrate upon coordination. Thus, the transformation could be initiated by a mild single-electron-transfer (SET) reduction of the respective cyclopropane. The chiral cyclopentanes **31** were obtained in high yields and *ee*s of 90 – 99%.[36] Both examples beared one limitation. The imidazole moiety was essential for the reaction outcome and could only be replaced by other coordinating groups such as pyridine or pyrazole, since the substrate was coordinated *via* a *N*,*O*-chelate.[31]

2. Photochemical Reactions of 2-(2′-Alkenyloxy)cycloalk-2-enones

2.1 Background and Previous Work

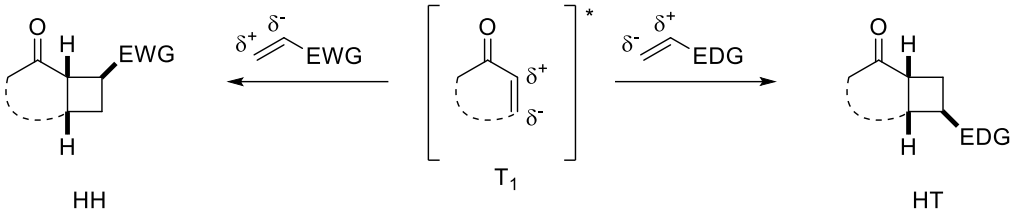
α,β-Unsaturated ketones (enones) represent a class of extensively studied compounds in photochemistry.[39,40] This class of substrates can be directly excited by light with a wavelength above 300 nm and also exhibits photophysical properties that are favorable for reactions with high yield.[39] The course of the reaction itself can be complex, however, in general it commences with the excitation of a substrate molecule from its S_0 ground state to the first singlet excited state S_1 ($n\pi^*$).[41]



Scheme 8. Mechanism of the [2+2] photocycloaddition of α,β-unsaturated carbonyl compounds with an representative alkene.

From this electronically excited state the molecule can either relax back to the ground state *via* fluorescence or a non-radiative process such as IC, perform a photochemical reaction, or undergo ISC to the first excited triplet state T_1, which is usually of $\pi\pi^*$ character.[41,42] ISC is very efficient in enones and their T_1 state is relatively long lived. Thus, photoreactions commonly occur from the T_1 state. This triplet state can be quenched by olefins to form a 1,4-diradical which remains on the triplet hypersurface. After a second ISC the singlet 1,4-diradical can either show cyclization to the cyclobutane product or fragmentation back to the starting materials (Scheme 8). Also the T_1 state is directly accessible by application of a sensitizer (*vide supra*).[41,43]

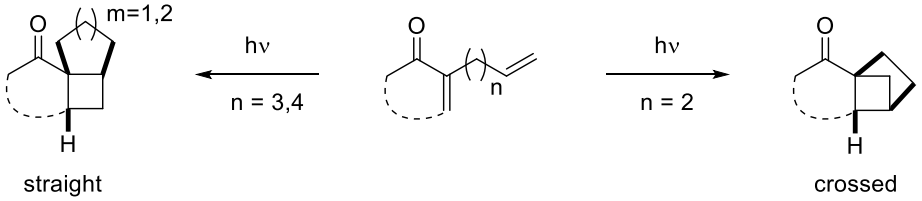
The regioselectivity of the reaction is determined by an umpolung of the enone upon excitation. In consequence the α-position becomes electrophilic and the β-carbon atom turns into a nucleophilic center. In case of a radical addition of the triplet state substrate to an electron-deficient olefin the head-to-head (HH) product is formed (Scheme 9, left). In contrast, use of an electron-rich olefin yields the head-to-tail (HT) product (Scheme 9, right).[39,41]



Scheme 9. Regioselectivity in the intermolecular [2+2] photocycloaddition of enones with electron rich or electron deficient olefins.

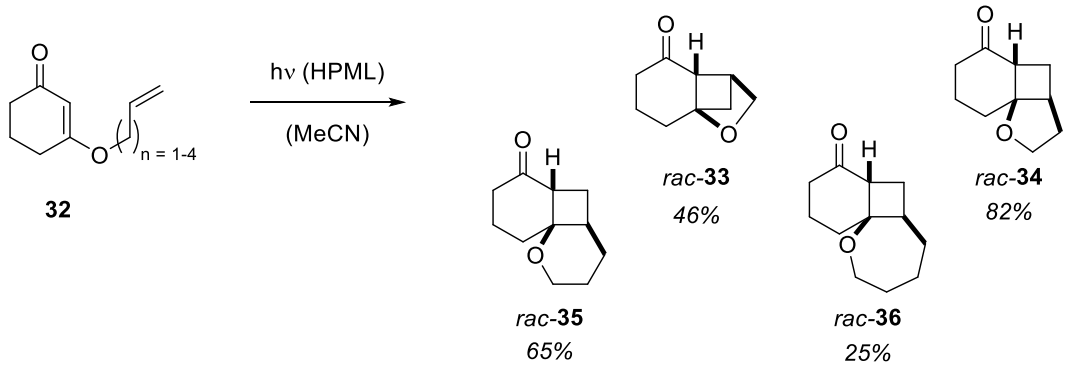
Intramolecular [2+2] photocycloaddition reactions benefit from an improved regioselectivity[44,45] and cyclic enones represent the most frequently used class of substrates.[39,46,47] For these chromophores the favored position for attachment of a tether is the α- or β-position.[48] However, the electronic structure of the enone is irrelevant to the regioselectivity in this case.

In the intramolecular photoreaction the length of the tether is vital for the irradiation outcome.[49] If two olefinic moieties are linked by three or four atoms, a parallel approach of the olefin to the α,β-unsaturated ketone is preferred, which results in formation of straight products (Scheme 10, left).[42] This demonstrates the influence of the *rule of five* which suggests that due to entropy and strain factors formation of a five-membered ring in the first cyclization step is favored.[50] For a shorter tether (n = 2) the olefin has to approach in a crossed fashion in order to allow for a five-membered ring to be formed first and therefore, mainly the crossed products are attained (Scheme 10, right).[42]



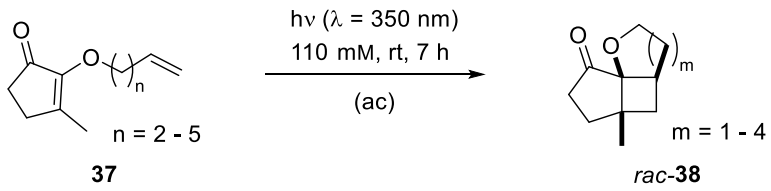
Scheme 10. Regioselectivity of the intramolecular [2+2] photocycloaddition of α-substituted enones.

This general concept of intramolecular regioselectivity is for example in accordance with experimental results from *Mattay* and co-workers. In their studies they investigated the photochemical behavior of a set of 3-(alkenyloxy)-2-cyclohexenones **32**.[51,52] For a short tether consisting of two atoms the crossed [2+2] photocycloaddition product *rac*-**33** was obtained in 46% yield. Longer side chains gave the straight photoproducts *rac*-**34** – *rac*-**36** in 25 – 82% yield (Scheme 11). Irradiation in the presence of NEt_3 led to a photochemically induced reductive ring opening of the cyclobutanes to produce spirocyclic compounds.[52] Similar results upon UV irradiation of 3-(alkenyloxy)cycloalk-2-enones were published by the groups of *Matlin*[53] and *Ikeda*.[54]



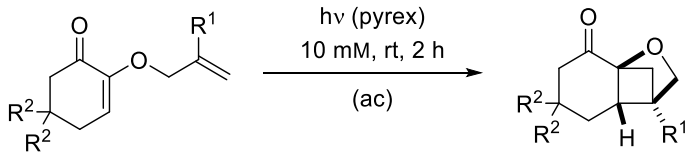
Scheme 11. Cyclization of 3-(Alkenyloxy)-2-cyclohex-1-enones with different side chain length by use of a high pressure mercury lamp (HPML).[51,52]

Furthermore, the intramolecular [2+2] photocycloaddition of 2-(alkenyloxy)cyclopent-2-enones **37** was reported by *Pirrung et al.* in 1989. The group obtained the straight pro-ducts *rac*-**38** in moderate to excellent yields (Scheme 12).[55] The regioselectivity is in agreement with the results mentioned above. It represents a good example for the use of C-2 alkenyloxy substituted cycloalkenones in intramolecular photochemistry.



Scheme 12. Intramolecular [2+2] photocycloaddition of 2-(alkenyloxy)-2-cyclopentenones **37** with different tether length.[55]

In contrast, to their in α-position substituted analogues, 2-(2'-alkenyloxy)cycloalk-2-enones represent a compound class that has received little attention in [2+2] photocycloaddition chemistry so far. Under thermal conditions this class of substrates has been employed by *Ponaras et al.* in a variation of *Claisen* rearrangements.[56-58] To our knowledge *Ikeda et al.* were the first to explore these compounds photochemically.[59,60] Employing a high-pressure mercury lamp as light source, equipped with a pyrex filter, irradiation of three exemplary 2-allyloxycyclohex-2-enones **39** – **41** in acetone (ac) as the solvent was performed and the expected crossed products *rac*-**42** – *rac*-**44** were obtained in 53 – 63% yield (Scheme 13). Here, the solvent acts as a sensitizer and, as further studies showed, the reaction can also be performed in benzene in the presence of acetophenone (sensitizer). The transformation proceeded in benzene even without the presence of acetophenone but the reaction rate dropped considerably.[59,60] The structure of the attained molecules was assumed from spectroscopic data and subsequently confirmed by X-ray structure analysis. Beside the [2+2] photocycloadditions the group intensively studied subsequent reactions including the rearrangements of the respective reduced mesylated species.[60]



39 – 41 *rac*-**42** – *rac*-**44**

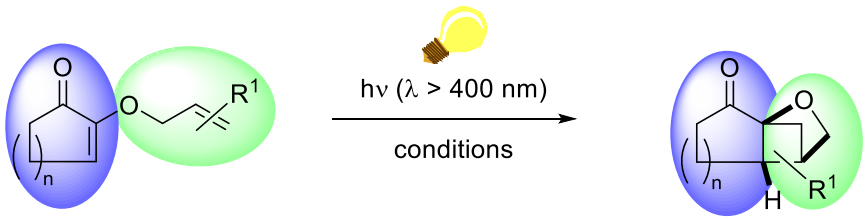
39, *rac*-**42** R^1 = R^2 = H *57%*
40, *rac*-**43** R^1 = Me, R^2 = H *63%*
41, *rac*-**44** R^1 = H, R^2 = Me *53%*

Scheme 13. Intramolecular [2+2] photocycloaddition of 2-(alkenyloxy)cyclohex-2-enones **39 – 41**.[60]

2.2 Project Aims

Our initial interest in the intramolecular [2+2] photocycloaddition of 2-(2'-alkenyloxy)cyclohex-2-enones was sparked by the intriguing first reports on the subject described above. It seemed feasible to accomplish these photochemical reactions under visible light irradiation instead of UV light with the aid of a suitable sensitizer. So first it was thought to optimize this reaction type for visible light catalysis and investigate the photophysical properties of the parent substrate **39**.

Furthermore, we aspired to broaden the substrate scope, since other reaction pathways were anticipated depending on the ring size of the cyclic enone, its substitution pattern as well as the substitution of the olefinic side chain. Our goal was to develop a general protocol for substrate synthesis and the intramolecular [2+2] photocycloaddition of various compounds alike (Scheme 14).



Scheme 14. Visible light-mediated inramolecular [2+2] photocycloaddition of 2-(2'-alkenyloxy)cyclohex-2-enones.

Additionally, this project was driven by the ambition to develop a method for the enantioselective intramolecular [2+2] photocycloaddition of this substrate class. To this end, we thought to employ a chelating *Lewis* acid or a metal complex that would allow for a bidentate coordination of the substrate at the carbonyl and ether oxygen atoms to form a stable five membered ring conformation. Upon irradiation this was expected to induce proper enantioface differentiation (Figure 4).

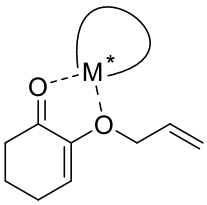
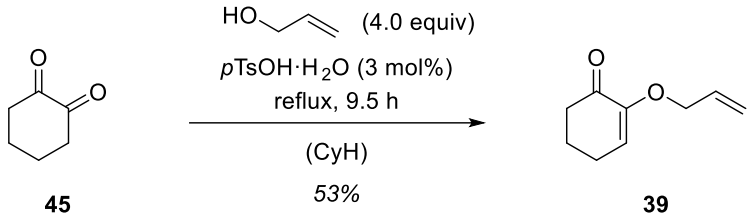


Figure 4. Bidentate coordination of **39** to a chiral *Lewis* acid or metal complex.

2.3 Substrate Synthesis and Reaction Optimization

2.3.1 Synthesis of a Model Substrate

For initial studies and the determination of photophysical properties substrate **39** was chosen as a model substrate. It had previously been synthesized by *Ikeda et al.* in 74% yield from diketone **45** and allylic alcohol in the presence of a catalytic amount of *p*-toluenesulfonic acid (*p*TsOH) in a *Dean-Stark* apparatus.[60] It has been shown that a substitution of benzene with tol in this case is not feasible due to the low boiling point of the allylic alcohol.[61] However, cyclohexane (CyH) was found to be suitable for azeotropic removal of water[62] and due to its lower boiling point beared the necessary properties for a replacement of benzene. Hence, according to this modified procedure allyloxyclyclohexenone **39** was obtained from **45** in a *Dean-Stark* apparatus in 53% yield (Scheme 15).



Scheme 15. Synthesis of the model substrate **39**.

2.3.2 Investigation of Photophysical Properties

Next, the photophysical properties of **39** were investigated (Figure 5). UV/vis experiments in CH_2Cl_2 revealed two absorption maxima at λ = 259 nm and λ = 305 nm with extinction coefficients of ε = 3736 $cm^{-1}M^{-1}$ and ε = 99 $cm^{-1}M^{-1}$, respectively. The first maximum can be assigned to the symmetry-allowed $\pi\pi^*$ transition and is already visible at a concentration of 0.5 mM. In order to observe the symmetry-forbidden $n\pi^*$ transition the concentration had to be increased to 50 mM at which concentration the second maximum was detected as a shoulder of the $\pi\pi^*$ transition.[63]

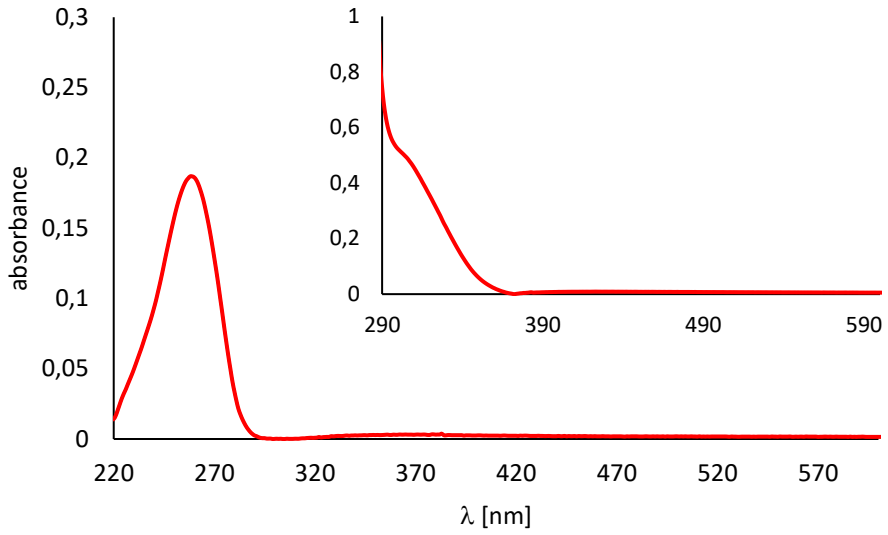


Figure 5. UV/vis spectrum of compound **39** (0.5 mM, CH_2Cl_2; 50 mM, CH_2Cl_2).

Further luminescence spectroscopy was conducted in CH_2Cl_2 at rt at 0.1 mM concentration under steady state conditions. The resulting luminescence and a UV/vis spectrum at the same concentration, both normalized to the maximum intensity, are shown in Figure 6. An excitation scan was performed and confirmed that the fluorescence stems from the relaxation of compound **39** from its S_1 state.[63]

Frozen into a glass matrix at 77K, under pulsed conditions, the substrate also showed phosphorescence (Figure 7). The 0,0-transition located at λ = 505 – 510 nm corresponds to a triplet energy of E_T (T_1) = 235 $\pm$ 2 kJmol^{-1} (Figure 7). Since fluorescence as well as phosphorescence were observed, it can be assumed that 2-(allyloxy)cyclohex-2-enone (**39**) is excited into the S_1 ($\pi\pi^*$) singlet state and subsequently undergoes ISC to the first triplet state T_1 ($n\pi^*$) as was expected for an enone chromophore (*vide supra*). For our purpose of visible light irradiation, a sensitizer with a triplet energy of $E_T \geq 240$ nm had to be chosen in order for the reaction to proceed.[63]

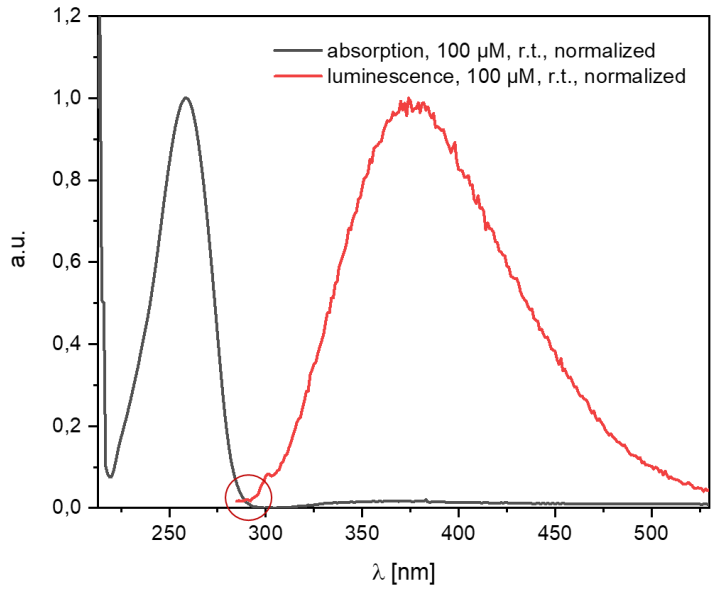


Figure 6. Recorded UV/vis spectrum of **39** in CH_2Cl_2 (c = 100 µM), normalized to $A_{259\ nm}$ (black) and recorded luminescence (UV280 filter glass applied) of **39** in CH_2Cl_2 (c = 100 µM) at ambient conditions, normalized to $I_{374\ nm}$ (red).[63]

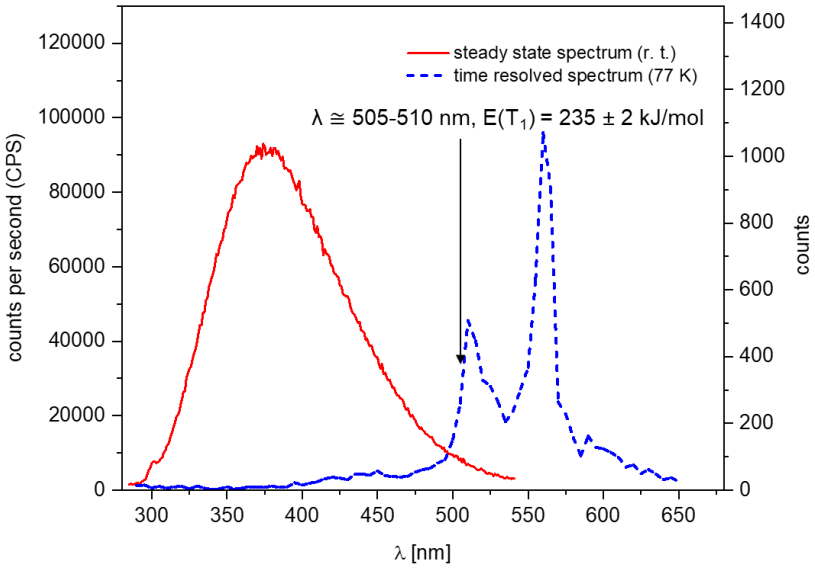
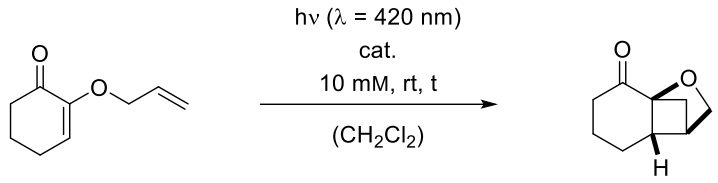


Figure 7. Steady state spectrum of **39** in CH_2Cl_2 (c = 100 µM) at ambient conditions (UV280 filter glass applied) given in counts per second (red, solid line) and time resolved spectrum (WG300 filter glass applied) of **39** in CH_2Cl_2 (c = 100 µM) after 50 µs delay at 77 K in counts (blue, dashed line).[63]

2.3.3 Choice of a Triplet Sensitizer

In this regard, txt (**23**) with a triplet energy of E_T = 268 kJmol^{-1}[64] represented a good starting point. Nevertheless, a variety of triplet sensitizers was tested in a series of preliminary studies (Table 1). First of all, a 10 mM solution of substrate **39** in CH_2Cl_2 was subjected to direct irradiation at λ = 350 nm, which gave the product *rac*-**42** after 2.5 h in a relatively low yield (Y) of 35% (Entry 1). This low yield was attributed to potential decomposition due to the harsher UV light. Yet, addition of 10 mol% of benzophenone at the same wavelength improved the yield significantly to 61% (Entry 2), which is in accordance with the originally published reaction by *Ikeda et al.*[60] (*vide supra*). A switch of the sensitizer to txt (**23**) made visible light irradiation at λ = 420 nm possible and product *rac*-**42** was obtained in 73% yield after 2.5 h (Entry 3). Recent work in our group on deracemization by a chiral sensitizer showed a potential to reduce the catalyst loading of a thioxanthone sensitizer down to 1 mol%.[65] Further experiments revealed that in our case the catalyst loading could also be reduced to 2.5 mol% without affecting yield or reaction time (Entries 3 – 5). The Ir-based complexes ^{F}Irpic, Ir(*p*Fppy)$_3$ and Ir(ppy)$_3$ catalyzed the [2+2] photocycloaddition in a similar manner to txt (**23**) (Entries 6 – 8). However, the reaction time was influenced by the catalyst's triplet energy. Overall, sensitizers with a triplet energy of E_T > 250 kJmol^{-1} led to complete conversion within 2.5 h and yields between 61% and 81%. A further decrease in triplet energy resulted in an increase in reaction time (Entries 7 – 8). For example, the reaction with Ir(*p*Fppy)$_3$ (E_T = 245 nm)[66] required 3 h until all starting material was consumed (Entry 7). In the case of Ir(ppy)$_3$ the reaction time was doubled compared to the experiments performed with **23** (Entry 8). However, in both cases the yield did not suffer under the prolonged irradiation (Entry 7 – 8). Due to its low triplet energy of E_T = 193 kJmol^{-1}[67] Ru(bpy)$_3$(PF$_6$)$_2$ did not initiate the photoreaction even after an extended period of irradiation (Entry 9) but the starting material was recovered quantitatively. No photoreaction was observed at λ = 420 nm for the selected reaction time in the absence of a photosensitizer (Entry 10). For any further reaction optimization and extension of the substrate scope 10 mol% **23** were chosen to ensure better reproducibility of the catalyst weigh-in on small scale.[63]

Table 1. Variation of the triplet sensitizer employed in the [2+2] photocycloaddition of **39**.[63]



39 *rac*-**42**

#	cat.	[mol%]	E_T [kJ/mol]	T [h]	Y [%]
1	-[a]	-	-	2.5	35
2	benzophenone[a]	10	290[68]	2.0	61
3	txt	10	265[64]	2.5	73
4	txt	5.0	265	2.5	72
5	txt	2.5	265	2.5	70
6	^{F}Irpic	2.5	256[69]	2.5	81
7	Ir(*p*Fppy)$_3$	2.5	245[66]	3.0	69
8	Ir(ppy)$_3$	2.5	231[66]	5.0	85
9	Ru(bpy)$_3$(PF$_6$)$_2$	2.5	193[67]	27	(rsm)
10	-	-	-	3.0	-

[a] irradiation at λ = 350 nm

2.4 Substrate Scope

2.4.1 Synthesis of Irradiation Precursors

Generally, the 2-(2'-alkenyloxy)cycloalk-2-enones that were used as substrates in the intramolecular [2+2] photocycloaddition were synthesized in one simple step from the commercially available diketones **45**, **46**, **47**, or **48** (Figure 8) and either the respective allylic alcohols in a condensation reaction (method **A**) or the respective allyl bromides in a nucleophilic substitution (method **B**) (Scheme 16).[63]

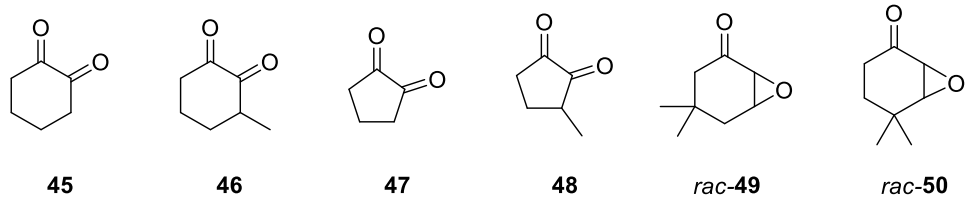
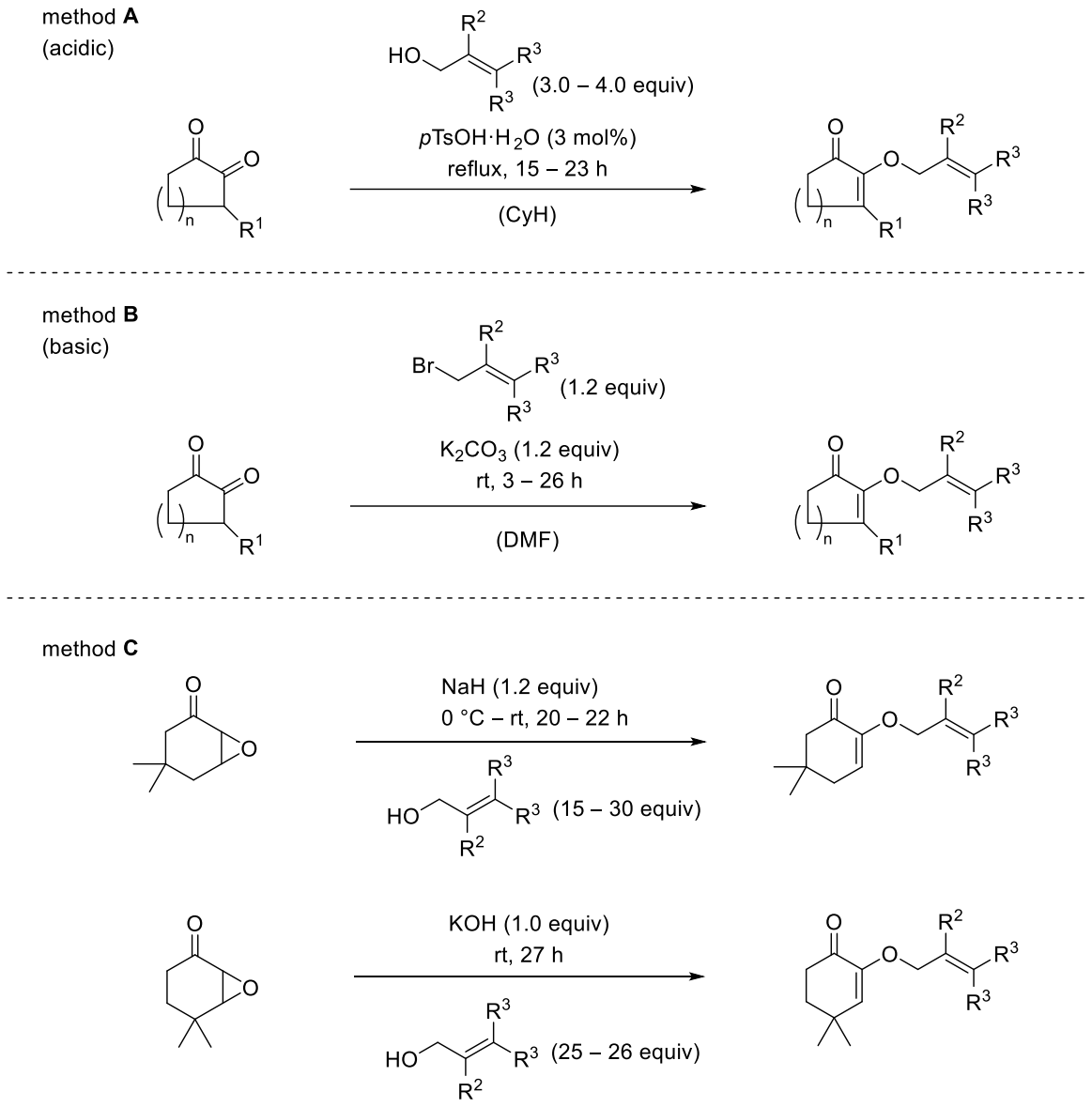


Figure 8. Structures of the starting materials for the synthesis of 2-(2'-alkenyloxy)cyclohex-2-enones.

Depending on the combination of starting materials, the reaction conditions were alternated between these two main methods **A** and **B**. For substrates that are substituted at a sp^3-carbon atom in the core cyclohexenone ring, a third method **C** was developed (Scheme 16), which employed epoxides *rac*-**49** and *rac*-**50** as intermediary compounds (Figure 8). Method **A** is derived from the procedure published by *Ikeda et al*.[59,60] and a publication by *Rodriguez et al*.[70] In analogy to the initial synthesis of model substrate **39**, *p*TsOH was used and the reactants were refluxed in CyH in a *Dean-Stark* apparatus for 15 – 23 hours (h). For those cases, when the reaction failed completely or yields were very low under acidic conditions, alternative method **B**, which employed K_2CO_3 at rt in DMF was chosen. It was modified form literature known procedures.[71] The respective diketones of *rac*-**49** and *rac*-**50** were not commercially available, so a route *via* an epoxide (method **C**) was pursued. The epoxides *rac*-**49** and *rac*-**50** underwent nucleophilic substitution when treated with an excess of allylic alcohol in the presence of a strong base (NaH or KOH).[29,56,72] The yields for all obtained irradiation precursors (compounds **39** – **42**, **51** – **68**) ranged from low to good (6 – 84%) (Figure 9). Since the amount of each obtained substrate was sufficient for photochemical evaluation, no attempt was made to improve the reaction conditions further.[63]



Scheme 16. Synthetic methods for substrate synthesis.[63]

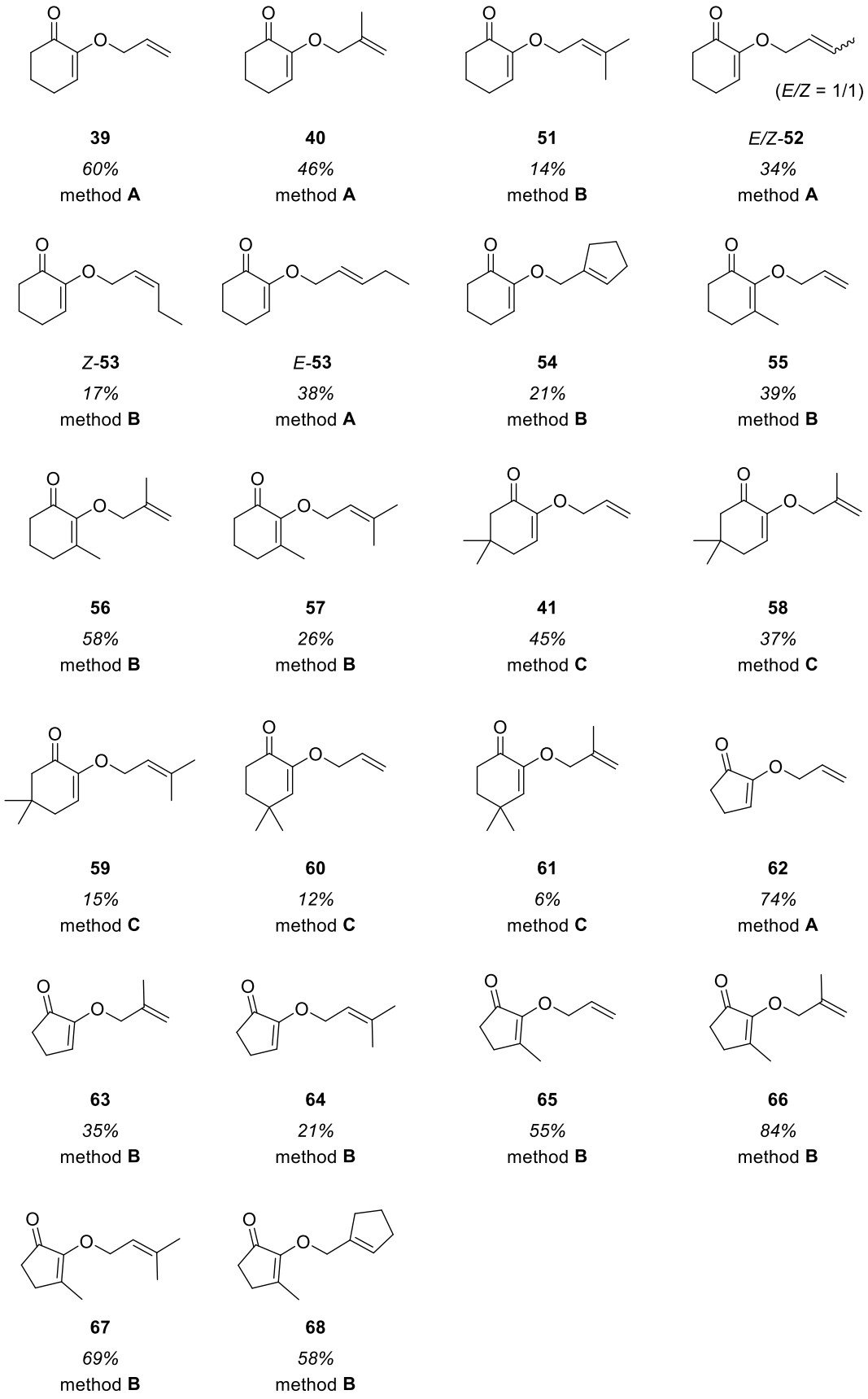
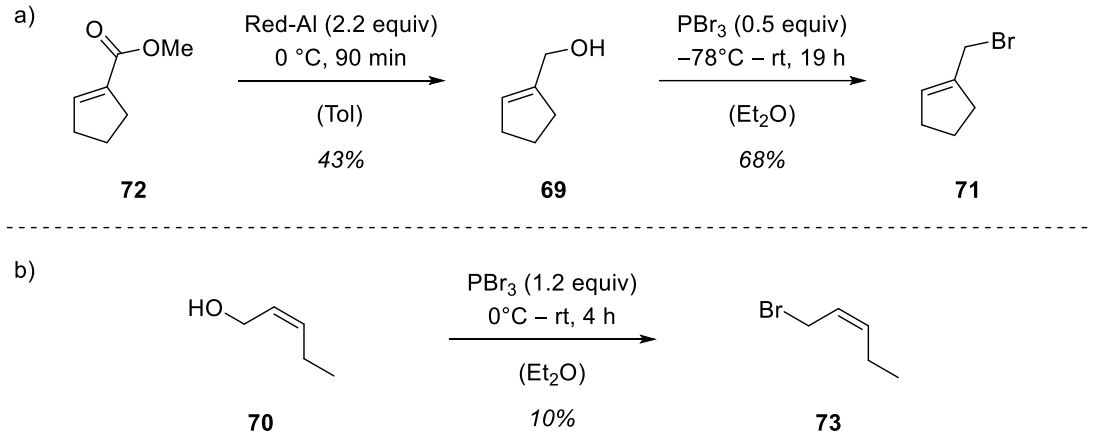


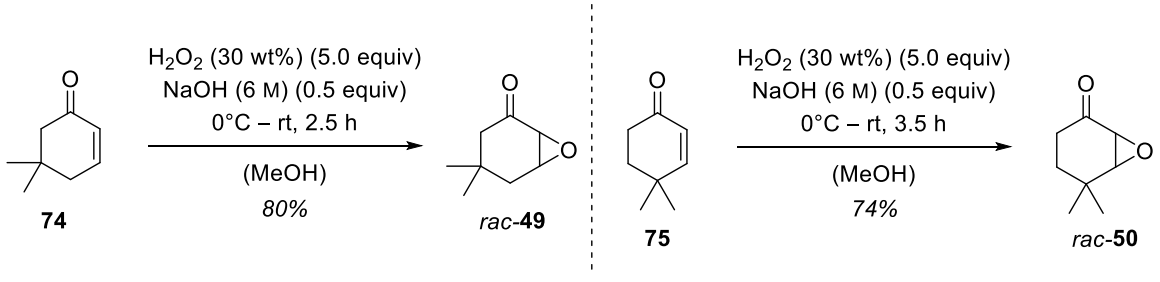
Figure 9. Structure, yield and method of synthesis of the irradiation precursors investigated in this work.[63]

Not commercially available allyl bromides were prepared from the corresponding alcohols **69** and **70**. Hence, cyclic allyl bromide **71** was obtained in a two-step procedure[73,74] starting from methyl cyclopent-1-ene-1-carboxylate (**72**) in 29% overall yield (Scheme 17, a). Treatment of **70** with PBr_3[75] gave (*Z*)-1-bromopent-2-ene (**73**) in 10% yield (Scheme 17, b).[63] The yield was assumed to be low due to the volatility of product **73**.



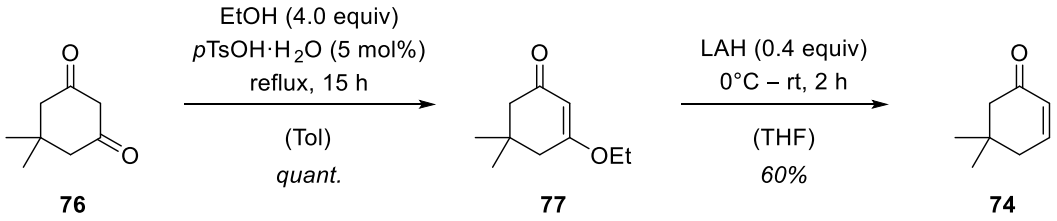
Scheme 17. a) Synthesis of cyclic allyl bromide **71** from methyl cyclopent-1-ene-1-carboxylate (**72**); b) Synthesis of (*Z*)-1-bromopent-2-ene (**73**) from the respective alcohol **70**.[63]

Epoxides *rac*-**49** and *rac*-**50** that were used to access substrates **41**, and **58** – **61** (method **C**) were synthesized by epoxidation of the respective dimethylcyclohex-2-enones **74** and **75** with H_2O_2 under basic conditions.[76] The products *rac*-**49** and *rac*-**50** were isolated in 80% and 74% yield, respectively (Scheme 18) and subsequently treated with an allylic alcohol to afford irradiation precursors **41**, and **58** – **61**.[63]



Scheme 18. Epoxidation of cyclohexenones **74** and **75** with H_2O_2.[63]

In contrast to **75**, 5,5-dimethylcyclohex-2-enone (**74**) is not commercially available and was therefore prepared according to a literature-known procedure[22] starting from dimedone (**76**) *via* vinyl ether **77** in two steps and was afforded in a total yield of 60% (Scheme 19).[63]



Scheme 19. Synthesis of cyclohexenone **74** starting from dimedone (**76**).[63]

Yields for the synthesis of irradiation precursors **60** and **61** were low (12% and 6%) (Figure 9), which resulted in a limited supply of starting material for photochemical reactions. Difficulties in removal of the excess allylic alcohol as well as the formation of side product *rac*-**78** were reasons for the inefficiency of this transformation. Compound *rac*-**78** was obtained irrespective of the allylic alcohol employed in the nucleophilic substitution. The compound was UV-inactive, highly polar and showed twice the mass of epoxide *rac*-**50** on GC-MS. Subsequently, single crystals were grown from a saturated solution of *rac*-**78** in CH_2Cl_2 and X-ray structure analysis revealed the dimeric structure of *rac*-**78** (relative configuration only) (Figure 10).[63]

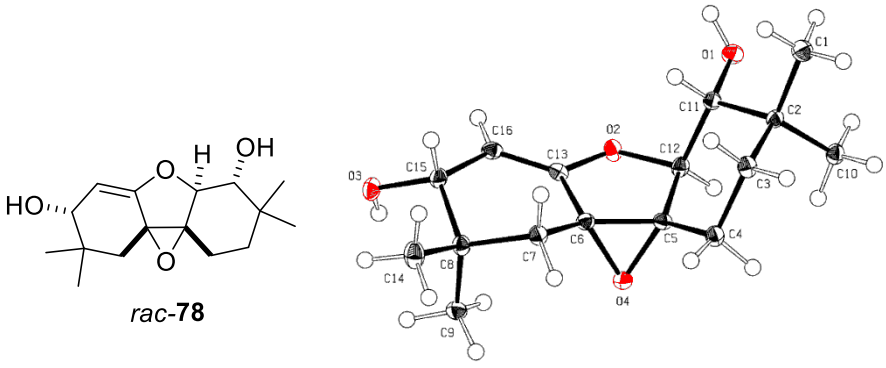
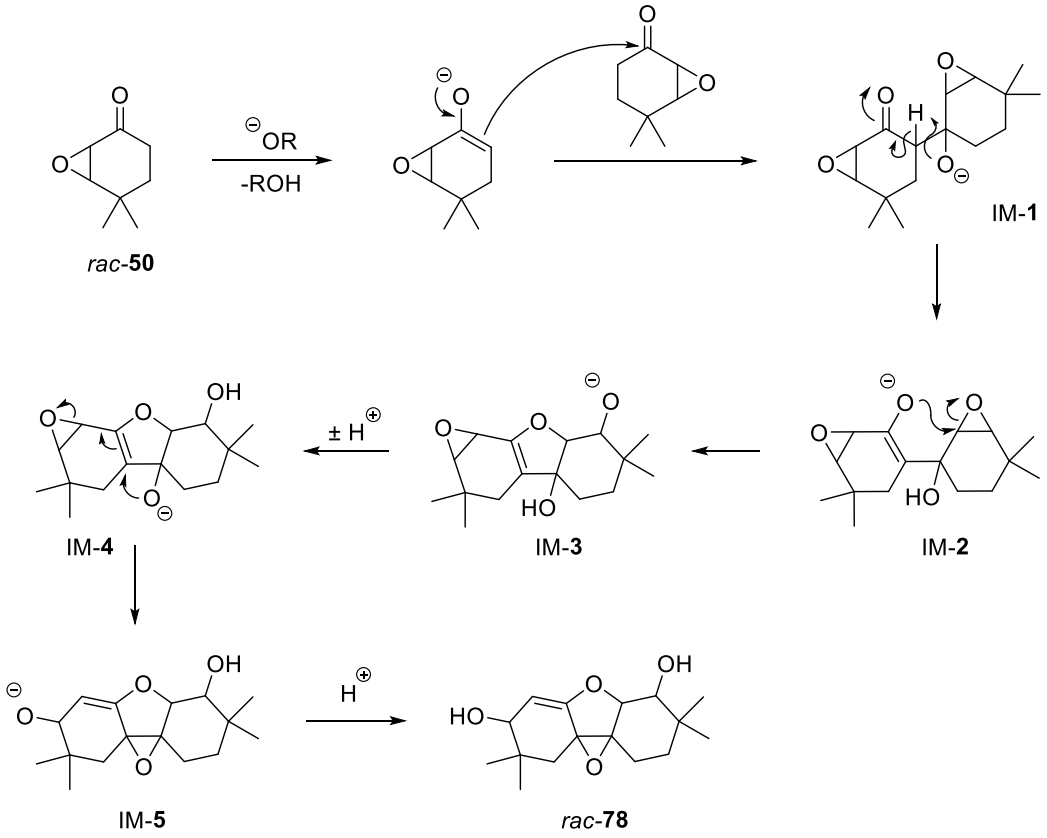


Figure 10. Structure of side product *rac*-**78** obtained by dimerization of epoxide *rac*-**50**. Ellipsoids in the ORTEP structure are displayed at the 50% probability level.[63]

A mechanistic proposal for the formation of *rac*-**78** is depicted in Scheme 20. As a first step an aldol reaction between two epoxide molecules catalyzed by base could be envi-

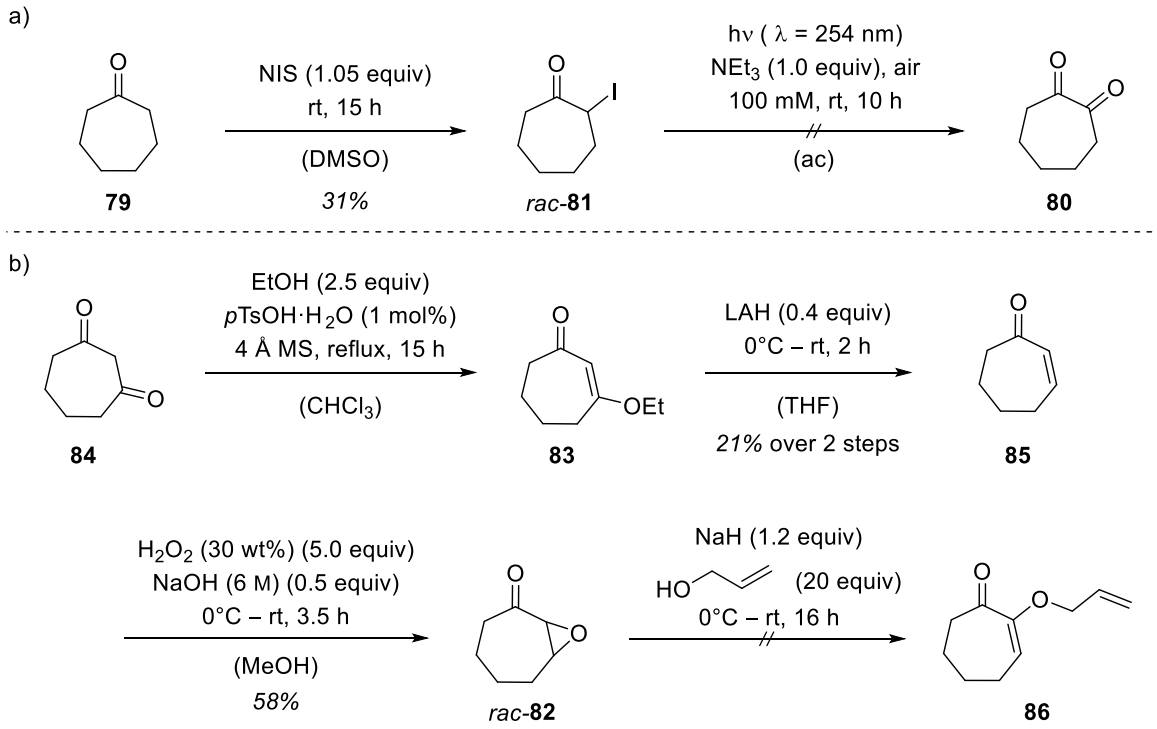
sioned and would result in anion IM-**1**. Intramolecular proton exchange would subsequently form the enolate nucleophile IM-**2**, which may attack one of the oxirane moieties. This would simultaneously allow the formation of a dihydrofuran ring (intermediate IM-**3**), which renders this assumption plausible. A second tautomerization would then yield species IM-**4**. In an intramolecular S_N2'-type reaction the new epoxide moiety, which is present in the final side product, could be formed. Final protonation of IM-**5** would then give the observed side product *rac*-**78**.[63]



Scheme 20. Mechanistic proposal for the formation of *rac*-**78**.[63]

Prior to any irradiation experiments, UV/vis spectra of all substrates were recorded. The absorption maxima ranged from λ = 247 nm to λ = 263 nm, whereby compounds that were methylated at the chromophore (C-3 position) showed slightly lower absorption maxima than the non-substituted compounds. Extinction coefficients reached values between approximately ε = 3700 $cm^{-1}M^{-1}$ and ε = 10100 $cm^{-1}M^{-1}$, which is in agreement with the data obtained for model substrate **39**.[63]

In an attempt to extend the substrate scope to cycloheptenone compounds, a synthetic two-step procedure[77-79] from cycloheptanone (**79**) to 1,2-cycloheptanedione (**80**) was attempted. The α-iodinated compound *rac*-**81** was obtained in 31% yield. However, the second step, a photochemical oxidation using NEt_3 and air,[79] could not be reproduced with our set up (Scheme 21, a). Secondly, the established route *via* an epoxide species *rac*-**82** and subsequent nucleophilic epoxide opening (method **C**) was tested. Formation of the enol ether **83**[80] from 1,3-diketone **84** directly followed by reduction with lithium aluminum hydride (LAH) afforded the cycloheptenone **85** in 21% over two steps. Subsequent epoxidation was achieved in 58% yield (Scheme 21, b). However, the final nucleophilic substitution of the allylic alcohol was not successful and cycloheptenone substrates were not pursued further.

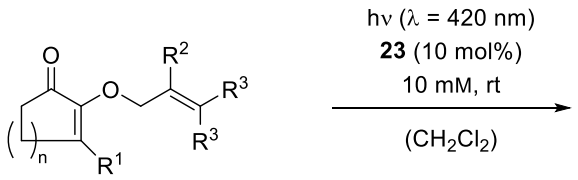


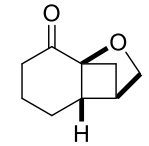
Scheme 21. a) Failed synthetic route towards 1,2-cycloheptanedione (**80**) (NIS = *N*- iodosuccinimide); b) Failed synthetic route towards 2-(allyloxy)cyclohept-2-enone (**86**).

2.4.2 Irradiation Experiments

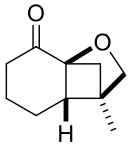
The prepared array of cyclohexenone substrates was tested under the irradiation conditions optimized for enone **39** (*vide supra*). The photoreactions were performed on small scale with 50 – 200 μmol of the respective substrate in a 10 mM CH_2Cl_2 solution. Irradiation was conducted at λ = 420 nm with a txt (**23**) loading of 10 mol% until full conversion was reached according to thin layer chromatography (TLC) (1.5 – 19 h).[63]

Allyloxy- and methallyloxy-substituted cycloalk-2-enones **40**, **41**, **55**, **56**, **58**, **60** and **63** performed similar to **39** and the corresponding crossed [2+2] photocycloaddition products *rac*-**43**, *rac*-**44** and *rac*-**87** – *rac*-**91** were obtained in mostly good to excellent yields (73% – quant.) (Scheme 22). Exceptions were the dimethylated compound *rac*-**90** (38%) and the cyclopentanone *rac*-**91** (34%). In both cases full conversion was observed but difficulties arose during purification. Both products were hard to detect on TLC. Additionally, the amount of irradiation precursor **61** was limited and the reaction was therefore performed on a small scale. This modification possibly accounts for the low yield of *rac*-**90** due to product loss during chromatographic purification. A selection of irradiation experiments (*rac*-**42**, *rac*-**88** and *rac*-**89**) was repeated at a larger scale of 1 mmol. Herein, the concentration was increased to 25 mM and the catalyst loading could be reduced to 2.5 mol%. Even though prolonged reaction times were necessary to achieve full conversion, the chemoselectivity remained unchanged and yields were as good as or higher than on small scale (Scheme 22). This result demonstrates the potential of this protocol for an application in preparative organic synthesis.[63]

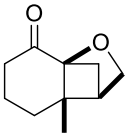




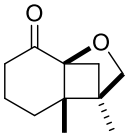
rac-**42**
73% (91%)[a]



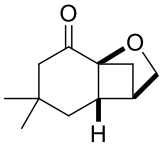
rac-**43**
91%



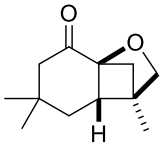
rac-**87**
91%



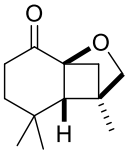
rac-**88**
88% (94%)[a]



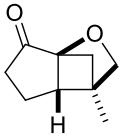
rac-**44**
quant.



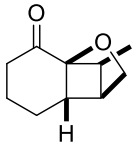
rac-**89**
90% (92%)[a]



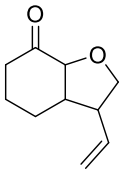
rac-**90**
38%



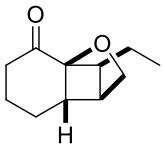
rac-**91**
34%



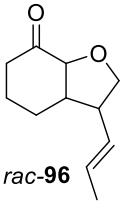
rac-**92**
78%



rac-**93**

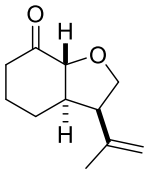


rac-**95**

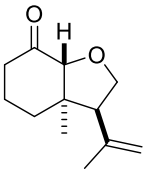


rac-**96**

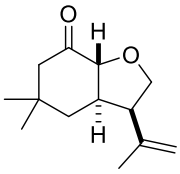
quant. (from *E*-**53**) *rac*-**95**/*rac*-**96** = 82/18
90% (from *Z*-**53**) *rac*-**95**/*rac*-**96** = 83/17



rac-**97**
65%
d.r. > 95/5



rac-**98**
79%
d.r. > 95/5



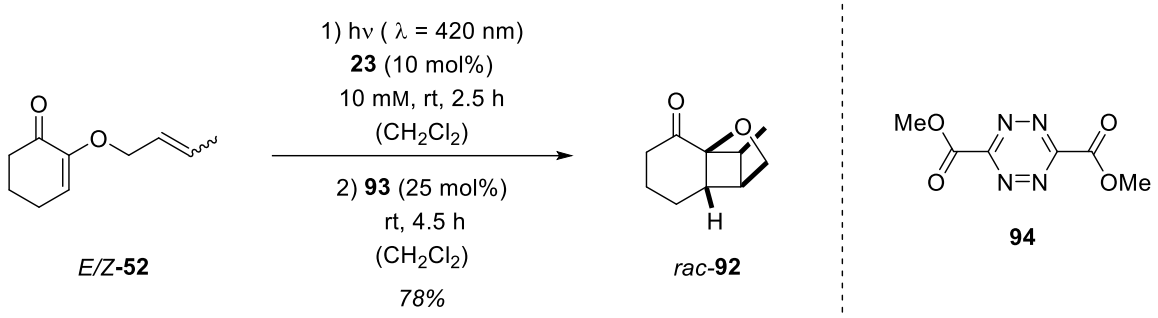
rac-**99**
86%
d.r. > 95/5

[a] reaction was performed on a 1 mmol scale with 2.5 mol% catalyst and *c* = 25 mM

Scheme 22. Visible light-mediated intramolecular [2+2] photocycloaddition and hydrogen abstraction reaction of various 2-(2'-alkenyloxy)cycloalkenones.[63]

As discussed in chapter 2.1 'Background and Previous Work', the crossed cyclobutane products are suspected to be formed *via* a 1,4-diradical intermediate. Due to free rotation

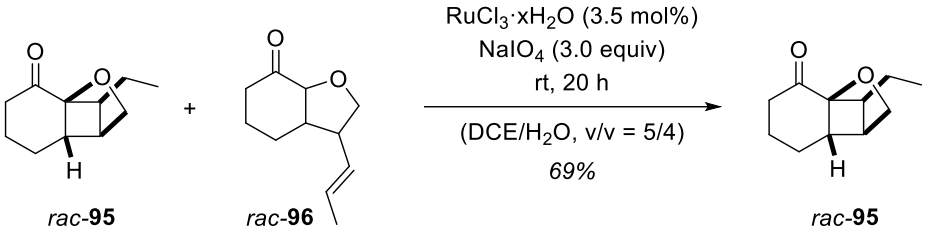
around the inherent single bond of this intermediate, we anticipated the thermodynamically more stable product to be formed. For substrates that contain a 1,2-disubstituted olefinic side chain, this implies the possibility of stereoconvergence in the [2+2] photocycloaddition.[21,81] For this reason *E/Z*-**52** was prepared from a 1/1 mixture of crotyl alcohol (*vide supra*). Irradiation under standard conditions gave *rac*-**92** as a single diastereoisomer (Scheme 22) with a small amount of olefinic impurity *rac*-**93** (80% yield, *rac*-**92**/*rac*-**93** = 93/7).[63]



Scheme 23. Intramolecular [2+2] photocycloaddition of *E/Z*-**52** and subsequent removal of the olefinic side product.[63]

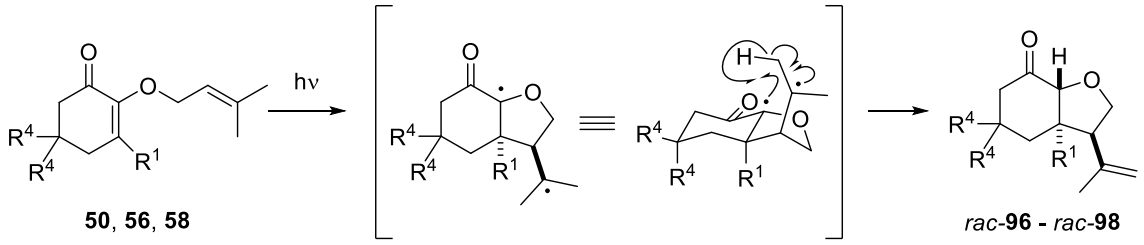
The olefinic side product *rac*-**93** was removed by treatment of the crude product mixture with 25 mol% 3,6-bis(methoxycarbonyl)-1,2,4,5-tetrazine (**94**) at rt (Scheme 23). This method had been used before to remove olefinic impurities after [2+2] photocycloadditions by *Poplata et al.*[22] and gave the clean product *rac*-**92** in a good yield of 78%. Its relative configuration was assigned based on NOESY spectra. Additionally, substrates *E*-**53** and *Z*-**53** were synthesized and subjected to the standard irradiation conditions individually. Both compounds gave the same photoproduct *rac*-**95** accompanied by a more relevant amount of side product *rac*-**96** in similar yields and chemoselectivities (from *E*-**53**: quant., *rac*-**95**/*rac*-**96** = 82/18; from *Z*-**53**: 90%, *rac*-**95**/*rac*-**96** = 83/17) (Scheme 22). However, in this case removal of the olefinic impurity by inverse electronic demand *Diels-Alder* reaction with tetrazine **94** was not successful and only improved the product ratio slightly (79%, *rac*-**95**/*rac*-**96** = 88/12). Fortunately, removal of *rac*-**96** was achieved by oxidation with $RuCl_3$ and $NaIO_4$ in a mixture of dichloroethane (DCE) and water.[24] After purification, the pure product *rac*-**95** was obtained in 69% yield (Scheme 24). As for *rac*-**92,** the relative configuration was deduced from NOESY spectra and the configuration of the double bond

in *rac*-**96** was determined to be *E* based on the coupling constant between the two olefinic protons (^3J = 15.3 Hz).[63]



Scheme 24. Removal of side product *rac*-**96** by oxidation with $RuCl_3$ and $NaIO_4$.[63]

The side products *rac*-**93** and *rac*-**96** are likely to originate from the intermediary 1,4-diradical that undergoes intramolecular hydrogen abstraction to form the exocyclic double bond (*vide infra*). This reaction course had been observed previously in the literature[82] and was therefore not completely unexpected. The observed stereoconvergence and side product formation support the hypothesis made for the course of the reaction and also highly suggest that the reaction takes place on the triplet hypersurface. Our research also showed an increased amount of olefinic side product with the better stabilization of the secondary radical resulting from *E*-**53** and *Z*-**53**.[63]

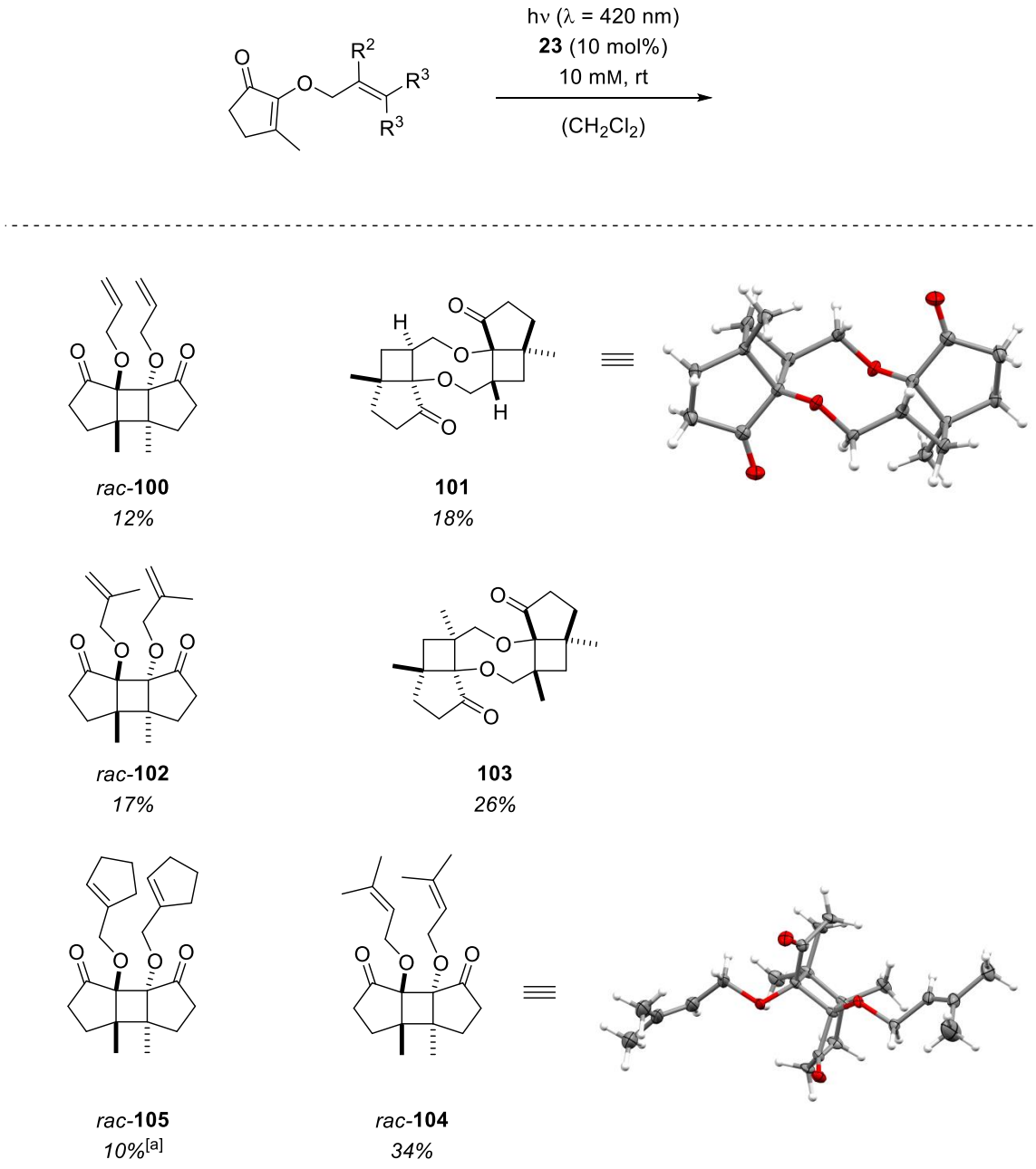


Scheme 25. Proposed formation of hydrogen abstraction products *rac*-**97** – *rac*-**99** *via* a 1,4-diradical.[63]

For substrates **51**, **57** and **59**, which exhibit a trisubstituted olefinic tether, this hydrogen abstraction becomes the dominant reaction pathway upon sensitized irradiation and no [2+2] cycloaddition products were identified in these experiments. The resulting tetrahydrofuran compounds *rac*-**97** – *rac*-**99** were obtained in good yields (65 – 86%) with excellent diastereoselectivity (d.r. > 95/5) (Scheme 22). Hence, this reaction poses synthetic potential, since it allows for three contiguous stereogenic centers to be built up in one step. The relative configuration of products *rac*-**97** – *rac*-**99** was assigned by ^{1}H NMR coupling constants and NOESY spectroscopic data. Concerning the mechanism (Scheme 25), the

first step in this transformation presumably occurs in analogy to the C-C bond formation mentioned previously (Scheme 10). The triplet excited state of the respective cyclohex-enone undergoes intramolecular addition to the olefinic side chain. This cyclization to a five-membered ring generally occurs in a *cis* and *trans* fashion, respectively. However, due to the steric hindrance between R^1 and the $C(Me)_2$ moiety in this 1,4-diradical, cyclobutane formation is unfavored and the *trans* intermediate undergoes an intramolecular hydrogen abstraction to form the observed products, whereas the *cis* intermediate undergoes C-C bond cleavage to the starting material.[63]

Cyclopentenones **65** – **68** with an additional methyl group in the β-position exhibited a different reactivity when compared to their six-membered cyclic analogues **55** – **57**. For this substrate class the [2+2] photodimerization became the preferred reaction pathway (Scheme 26), which has been observed as an alternative reaction outcome in the past.[83,84] Because two double bonds are available in each component, **65** gave a set of dimeric products once subjected to standard irradiation conditions. Two of these products *rac*-**100** and **101** could be isolated in 12% and 18%, respectively, and were characterized. Product *rac*-**100** arose from the intermolecular [2+2] photocycloaddition of the cyclic enone double bonds in the thermodynamically favored *cis*-*anti*-*cis* configuration.[39,44,46] The *cis* fusion between the five-membered ring and the cyclobutane was expected due to the rigidity of the skeleton. The *anti* configuration of the cyclopentanones assures a minimum of steric repulsion.[63]



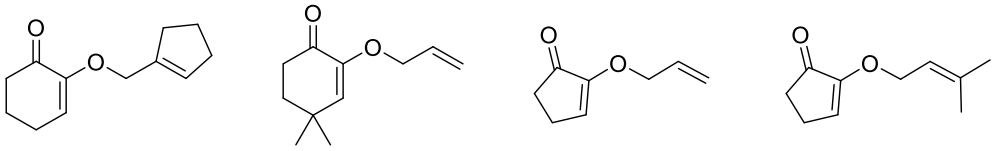
[a] performed with $^{F}Ir_{pic}$ (2.5 mol%) as catalyst

Scheme 26. [2+2] Photodimerization of 3-methyl-2-(allyloxy)cyclopentenones **65**, **66**, **67**, and **68**, including ORTEP structures of products **101** and *rac*-**103**. Ellipsoids in the ORTEP structure are displayed at the 50% probability level.[63]

The second dimerization product **101** also displayed symmetry according to ^{1}H NMR data. Crystals of the compound were grown from a saturated solution of **101** in CH_2Cl_2 and single-crystal X-ray analysis confirmed the molecular structure, which displays an inversion center and therefore S_2 symmetry.[85] The ORTEP model is depicted in Scheme 26. The

compound possesses a bicyclo[3.2.0]heptane core that is *cis* fused and all substituents within the cyclobutane are oriented in a *cis* fashion. The two identical fragments are characterized by an inverted absolute configuration. Photodimerization in a HH manner similar to *rac*-**100** is common for cyclopentenones,[83,84,86] whereas the intermolecular HH [2+2] photocycloaddition between cyclopentenones and monosubstituted olefins is less precedented. Herein a HT preference is usually expected, even though selectivities are not significant.[84,87] Thus, we were delighted to observe the formation of **101**. The low combined yields of *rac*-**100** and **101** suggested that other dimeric compounds were formed but could not be isolated in a pure form. The overall yield for the photochemical transformation of **66** was slightly better (43%) and yet again the two regioisomers *rac*-**102** and **103** were prepared (Scheme 26). The structure assignment of **103** was based on the previously obtained crystal structure of **101**. For the sterically more demanding substrates **67** and **68** only a single product was isolated. In contrast to prenyloxy substituted enone **57**, no intramolecular cyclization/hydrogen abstraction sequence was observed for these irradiation precursors. The product *rac*-**104** obtained from 3-methyl-2-[(3-methylbut-2-en-1-yl)oxy]cyclopent-2-en-1-one (**67**) (34%) presented the same C_2-symmetric relative configuration as compounds *rac*-**100** and *rac*-**102**, which was confirmed in this case by single crystal structure analysis (Scheme 26). Conversion of the cyclopentenyl containing cyclopentenone **68** could only be achieved by the use of 2.5 mol% $^{F}Ir_{pic}$ instead of txt (**23**), but even with this adaptation, the yield of *rac*-**105** remained very low (10%). The difference in the photochemical reactivity between the investigated cyclohexenone and cyclopentenone examples is astonishing. Only a single example was observed (compound *rac*-**91**), in which the corresponding cyclopentenone behaved in a similar way to the cyclohexenone.[63]

No product formation was achieved for the cyclohexenones **54** and **60** as well as cyclopentenones **62** and **64** (Figure 11). Under standard conditions, no conversion was detected by TLC for six-membered ring compounds **54** and **60**, even after prolonged irradiation (18 – 28 h). When **62** and **64** were subjected to the reaction conditions, the starting material was consumed completely, but full decomposition was observed. Direct irradiation of compounds **54**, **62**, and **64** at λ = 350 or 366 nm also resulted in decomposition at full conversion.[63]



54 60 62 64

Figure 11. Cycloalkenones unsuitable for visible light-mediated [2+2] photocycloadditions.

In summary, a broad selection of structurally diverse products was prepared by visible light-mediated irradiation of 2-(2'-alkenyloxy)cycloalk-2-enones in the presence of txt (**23**) as sensitizer. The cyclohexenones either underwent [2+2] photocycloaddition or a cyclization/hydrogen abstraction cascade in moderate to excellent yields with a high degree of diastereoselectivty. In these photochemical reactions, up to four stereogenic centers can be generated in one step, which classifies the obtained products as promising scaffolds for further functionalization. In contrast, the cyclopentenones preferentially underwent intermolecular [2+2] photodimerization.

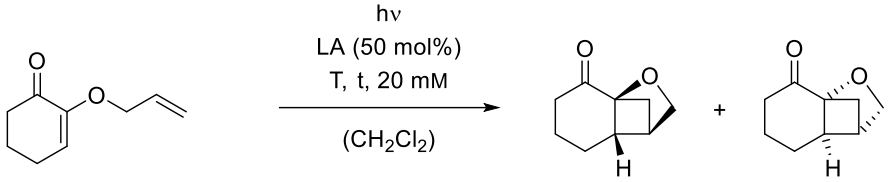
2.5 Studies towards Enantioselectivity

2.5.1 Previous Work

As previously mentioned, apart from expanding the substrate scope of the crossed intramolecular [2+2] photocycloaddition we also envisioned to establish a protocol for the enantioselective version of this reaction. Preliminary experiments had been undertaken in our group by *Verena Edtmüller*.[61] UV/vis experiments conducted with model substrate **39** revealed a significant bathochromic shift (∼ 50 nm) of the absorption maximum of **39** upon addition of the *Lewis* acid $EtAlCl_2$. This favorable result prompted investigations into the crossed [2+2] photocycloaddition in the presence of a chiral, chelating *Lewis* acid metal complex. Photochemical reactions were performed at λ = 366 nm and the most important results are listed in Table 2. First, $TiCl_4$ was tested in a racemic reaction, however, no product was isolated. Further experiments with a Ti-(*R*)-binol complex at –25 °C and –75 °C afforded the product **42** in a maximum yield of 11% and with 6% *ee*. Application of the Yb-(*R*)-binol or Cu(I) complex **20** could neither increase the enantioselectivity nor the yield and both values remained low. Hence, it was concluded that this type of complexes are not

suitable for the use in an enantioselective [2+2] photocycloaddition of this particular substrate.[61] In a last attempt chiral-at-metal Rh complex *ent*-**27** was tested regarding its capability to induce enantioface differentiation. For this experiment, the wavelength (λ = 420 nm) and reaction time were increased, and the concentration of the reaction solution was lowered to 10 mM. To our delight, cyclobutane *ent*-**42** was isolated in 47% yield and 59% *ee*.[88] As this catalyst showed promising results concerning yield and more importantly enantioselectivity without prior optimization, we were prompted to explore this substrate-catalyst combination further.

Table 2. Variation of the reaction conditions of the [2+2] photocycloaddition of **39** in the presence of chiral *Lewis* acids.[61]



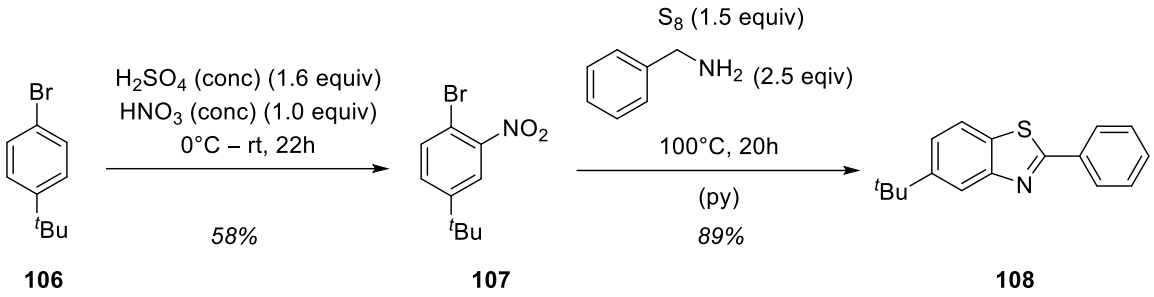
39 **42** *ent*-**42**

#	LA	λ [nm]	T [°C]	t [h]	Y [%]	*ee* [%]
1	$TiCl_4$	366	rt	10	-	-
2	Ti-[(*R*)-binol]Cl_2	300	–75	12	11	6
3	Ti-[(*R*)-binol]Cl_2	366	–25	40	8	4
4	Yb-[(*R*)-binol](OTf)$_3$	366	rt	20	5	2
5	**20**	366	–25	20	11	2
6[a]	Λ-RhS (*ent*-**27**)	420	rt	48	47	59

[a] *c* = 10 mM, T = temperature, unpublished results by Verena Edtmüller[88]

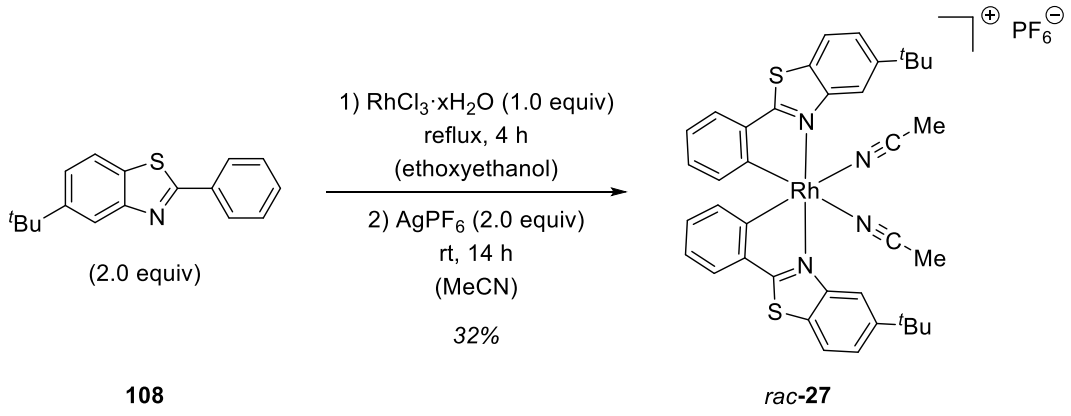
2.5.2 Catalyst Synthesis

Chiral-at-metal complex **27** (previously described in chapter 1) is not commercially available and was therefore prepared starting from $RhCl_3 \cdot xH_2O$ according to a procedure developed by the *Meggers* group.[38] The reaction sequence consisted of the synthesis of the racemic RhS complex (*rac*-**27**), an auxiliary-induced separation of diasteroisomers, followed by acid catalyzed removal of the auxiliary.



Scheme 27. Synthesis of thiazole ligand **108** in a two-step procedure starting from 1-bromo-4-*tert*-butylbenzene (**106**).

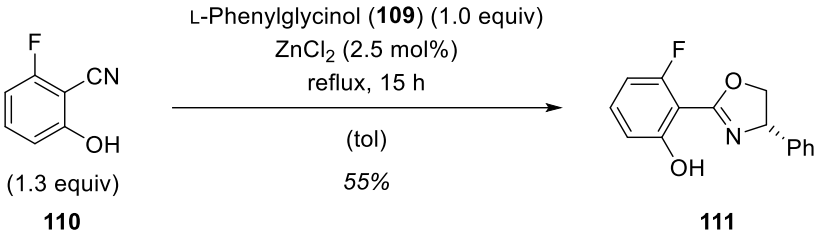
In the first step the achiral ligand was obtained in a two-step procedure (Scheme 27). Nitration of 1-bromo-4-*tert*-butylbenzene (**106**) afforded nitro compound **107** in 58%. Subsequent treatment with benzyl amine and elementary sulfur gave the thiazole ligand **108** in 52% overall yield.



Scheme 28. Synthesis of the racemic RhS complex (*rac*-**27**).

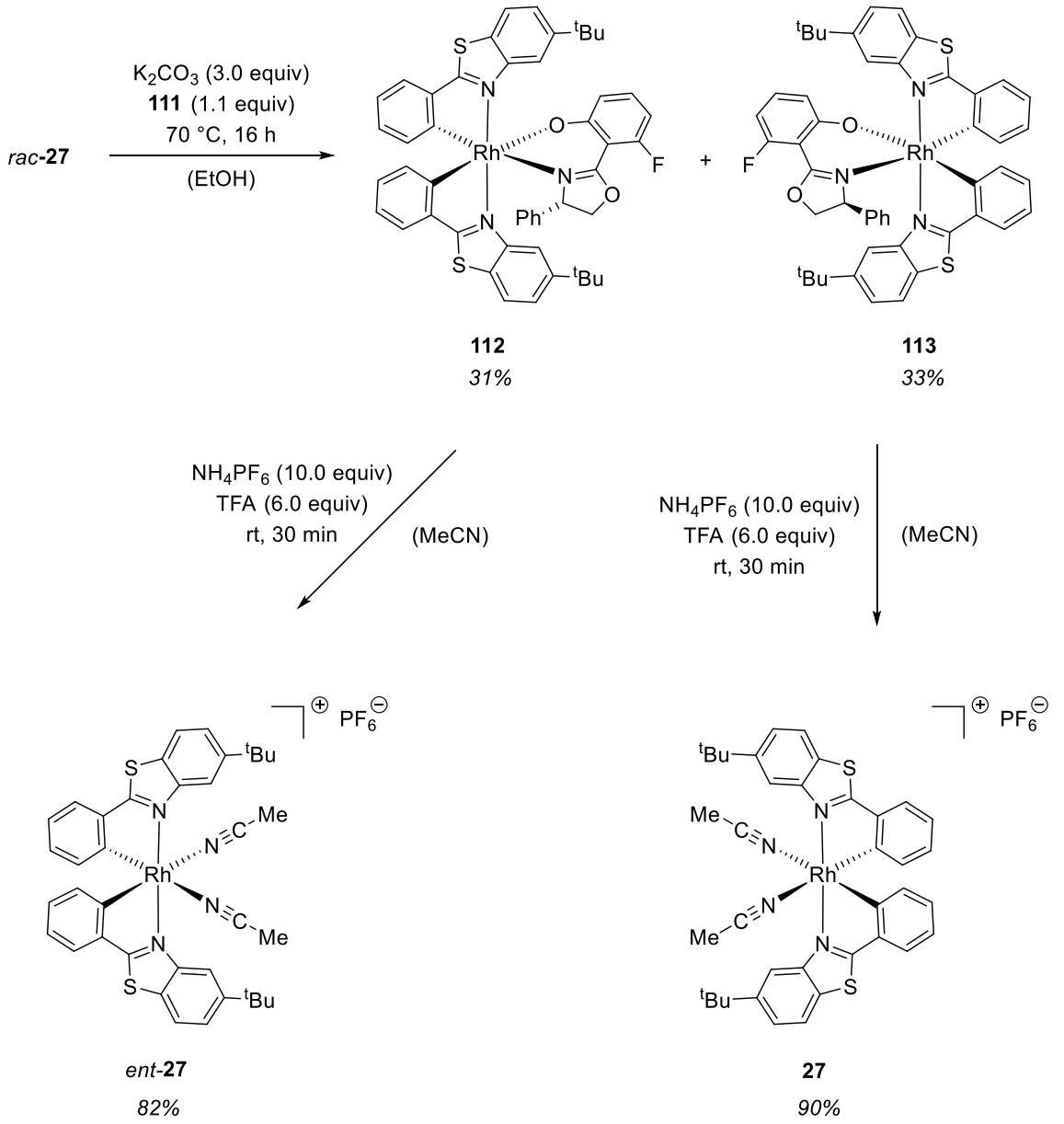
Next, the racemic rhodium complex *rac*-**27** was synthesized. For this purpose $RhCl_3 \cdot xH_2O$ was refluxed with two equivalents of ligand **108** in a mixture of ethoxyethanol and H_2O for

4 h in which time the respective chlorido-Rh complex was formed. The chloride was removed from the metal by precipitation of AgCl after addition of $AgPF_6$ in MeCN. The vacant coordination sites were then occupied by two MeCN molecules and *rac*-**27** was obtained in 32% yield (Scheme 28). The chiral auxiliary employed in this reaction sequence was derived from the chiral pool. Hence, L-phenylglycinol (**109**) was treated with 2-cyano-3-fluorophenol (**110**) in the presence of $ZnCl_2$ to yield the chiral oxazoline **111** in 55% (Scheme 29).



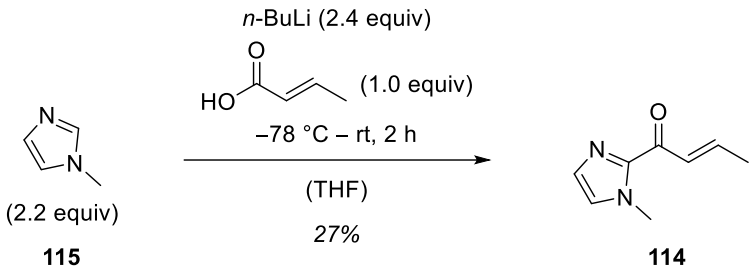
Scheme 29. Synthesis of chiral auxiliary **111**.

Subsequent reaction of **111** with *rac*-RhS (*rac*-**27**) under basic conditions afforded the two diastereoisomers **112** and **113** in 31% and 33% yield, respectively (Scheme 30). The decreased yield compared to the literature (**112**: 44%, **113**: 46%)[38] was attributed to difficulties in the separation of diastereoisomers. An attempt of a selective precipitation of **112** in EtOH did not give either of the diastereoisomers in pure form. However, a change to flash column chromatography (P/Et_2O) made proper separation possible. Finally, the chiral auxiliary was removed under acidic conditions by addition of trifluoroacetic acid (TFA) to a solution of the respective diastereoisomers **112** or **113** in MeCN. This was done in the presence of NH_4PF_6 to assure the right counter ion as this potentially has an effect on the performance of the catalyst. **27** and its enantiomer *ent*-**27** were obtained in good yields after purification (90% and 82%) (Scheme 30).



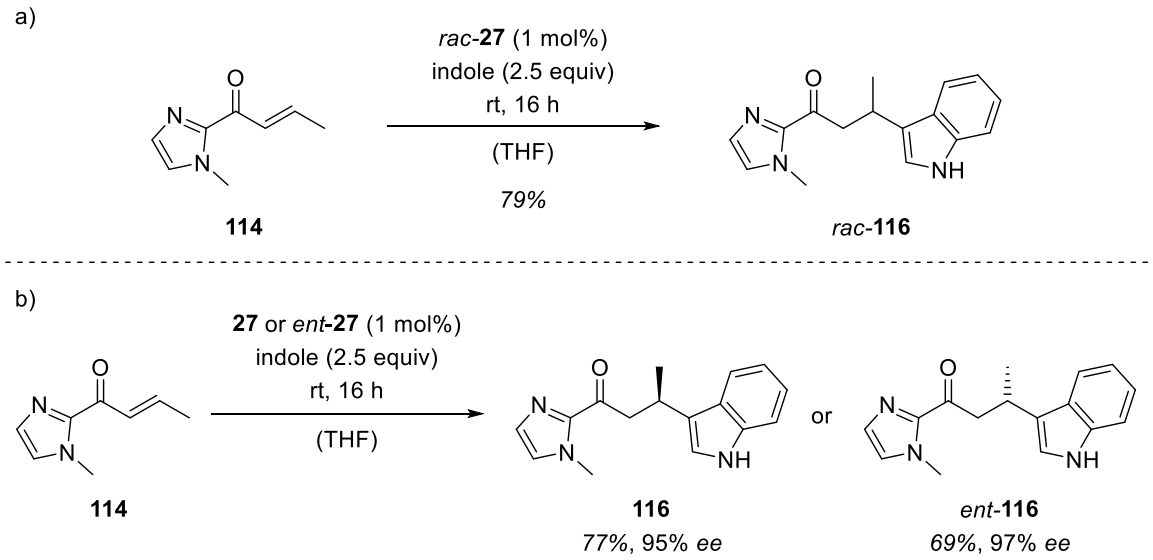
Scheme 30. Enantiomer resolution of *rac*-**27** assisted by chiral auxiliary **111**.

Before any photoreaction was performed, verification of a successful synthesis of the chiral catalysts **27** and *ent*-**27** was desired. For this purpose, a literature-known transformation was chosen. The *Friedel-Crafts* alkylation of 1*H*-indole was originally catalyzed by the Ir analogue of *ent*-**27**,[33] however, this alkylation had been proven to be adequate for catalyst verification of *ent*-**27** by *Verena Edtmüller*.[61] Substrate **114** was prepared from 1-methylimidazole (**115**) and crotonic acid in 27% yield (Scheme 31). The relatively low yield is in accordance with the literature[33] and therefore no optimization of the reaction conditions was attempted.



Scheme 31. Substrate synthesis for the enantioselective *Friedel-Crafts* alkylation.

The *Friedel-Crafts* alkylation was first performed with 1 mol% of *rac*-**27** and the alkylated product *rac*-**116** was isolated in 79% yield (Scheme 32, a). Afterwards, the Δ- and Λ-enatiomers of RhS were applied under the same reaction conditions with equal catalyst loading (Scheme 32, b). Both catalysts performed excellently with enantioselectivities of 95% or above and yields of 77% and 69% for **116** and *ent*-**116**, respectively. In this case, **116** was obtained from Δ-RhS (**27**) and *ent*-**116** was isolated from the reaction catalyzed by *ent*-**27**. The yields are comparable to the amount of product *rac*-**116** obtained in the racemic reaction.



Scheme 32. Racemic (a) and enatioselective *Friedel-Crafts* alkylation of Indol (b) catalyzed by RhS catalysts *rac*-**27**, **27**, and *ent*-**27**.

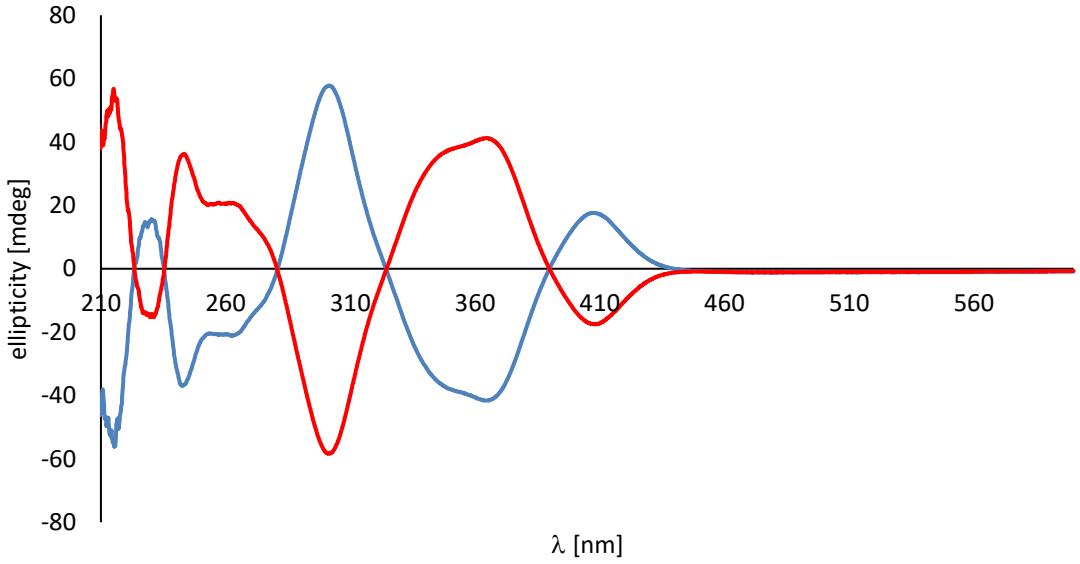


Figure 12. CD spectra of Δ-RhS (**27**) (blue) and Λ-RhS (*ent*-**27**) (red) recorded in CH_3OH (*c* = 0.2 mM).

As additional verification, circular dichroism (CD) spectra of **27** and *ent*-**27** in MeOH were recorded (Figure 12). As expected, the two compounds exhibit maxima at the same wavelength with approximately same intensity, but opposite algebraic sign. This is a good illustration for the mirrored structure of both enantiomers. Most importantly though, the recorded spectra matched the literature.[89] With the results of enantioselective test reactions and CD spectra in hand, we were satisfied, that the catalyst was of sufficient quality for an application in the envisioned enantioselective intramolecular [2+2] photocycloaddition of 2-(2'-alkenyloxy)-cyclohexenones. For the following series of experiments towards an enantioselective protocol, the Δ-enantiomer (**27**) was chosen as the employed catalyst.

2.5.3 Reaction Optimization with the Chiral-at-metal Rh Catalyst

After successful catalyst synthesis and activity verification, the photophysical behavior of enone **39** upon addition of catalyst **27** was evaluated. To this purpose UV/vis spectroscopy was performed (Figure 13) and the spectra revealed a pronounced absorption of the Rh catalyst up into the visible range. Thus, it was not possible to detect a bathochromic shift in the absorption maximum of **39** as it is most likely obscured by the catalyst's absorption bands. The spectrum recorded after addition of 1.0 equivalent of *rac*-**27** appeared to be a mere addition of the two individual spectra. However, a slightly more pronounced tailing

in the visible region above λ = 400 nm was observed. This tailing and the proof that this chiral-at-metal catalyst had already shown catalytic activity in our system convinced us to move forward with the optimization of the irradiation conditions.

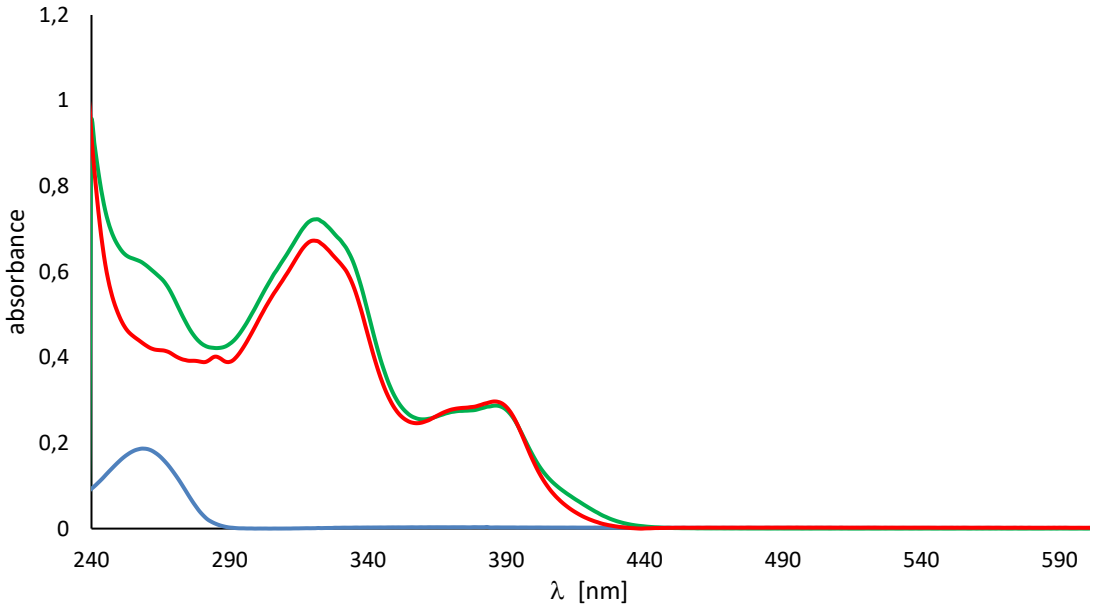
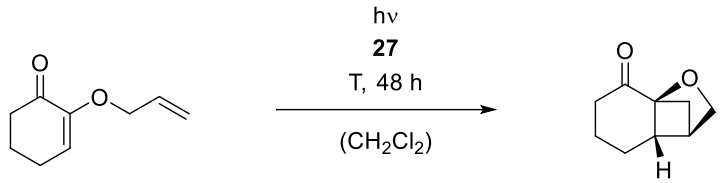


Figure 13. UV/vis spectra of **39** (0.5 mM, blue), *rac*-RhS (*rac*-**27**) (0.5 mM, red) and **39** with 1.0 equiv of *rac*-RhS (*rac*-**27**) (0.5 mM, green) in CH_2Cl_2.

Initial screening of the reaction conditions involved the variation of catalyst loading, reaction temperature and substrate concentration (Table 3). As a starting point the previously described conditions (entry 1)[88] were applied and the reported results could be reproduced with a similar yield of 44% and a slightly increased enantioselectivity of 66% (entry 2). However, a small background reaction was observed in the absence of **27** over a reaction time of 48 h and gave 12% of the crossed product *rac*-**42** (entry 3). A decrease in T to 0 °C neither improved the yield nor the selectivity (30%, 57% *ee*; entry 4). Hence, all further optimization was performed at rt. A subsequent increase in catalyst loading to 10 mol% afforded a high *ee* of 82% but unfortunately decreased the yield significantly to 16% (entry 5). Next, the influence of higher and lower substrate concentrations on the reaction outcome was evaluated with *c* = 5 or 20 mM (entries 6-7). In both cases slightly higher enantioselectivities of 70% and 80% *ee* were obtained but at the same time less product **42** was isolated (30% and 26%). Therefore, the following solvent screening was conducted at 10 mM concentration with 2 mol% of Δ-RhS (**27**) at rt.

Table 3. Variation of catalyst loading, reaction temperature and concentration in the enantioselective [2+2] photocycloaddition of **39**.



39 **42**

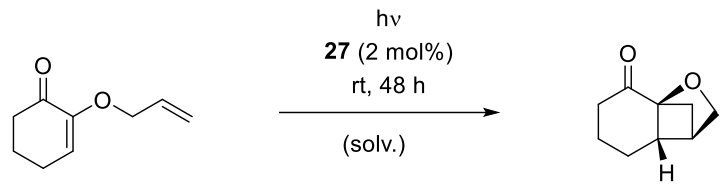
#	λ [nm]	c [mM]	cat [mol%]	T [°C]	t [h]	Y [%]	*ee* [%]
1[a]	420	10	2	rt	48	47	59
2	420	10	2	rt	48	44	66
3	420	10	-	rt	48	12[b]	-
4	420	10	2	0	48	30	57
5	420	10	10	rt	48	16	82
6	420	5	2	rt	48	30	70
7	420	20	2	rt	48	26	80

[a] unpublished work by *Verena Edtmüller*; [b] determined by ^{1}H NMR

A selection of solvents that are most commonly used in photochemistry were assessed and the results are shown in Table 4. No product was isolated from irradiation experiments performed in ac or MeCN (entries 2 – 3). Additionally, for MeCN a discoloration of the catalyst solution was observed upon solvation. This could indicate a change in the catalyst's absorption properties for this specific solvent. Thus, **27** appeared to be an unsuitable candidate for irradiation at λ = 420 nm in MeCN. The [2+2] photocycloaddition of enone **39** in DCE gave, compared to the reaction performed in CH_2Cl_2, similar results with 30% yield and 69% *ee* (entries 1 and 4). From simple observation the catalyst was insoluble in CyH. Nevertheless, the experiment was performed (entry 5). As it was to be expected in this case, product **42** was obtained in a very low yield and enantioselectivity (2%, –6% *ee*). Interestingly, the other enantiomer was formed preferentially, even if this preference was very low.

$PhCF_3$ was tested last, however, the substrate was poorly soluble. The enantioselectivity observed was within the same range as our initial results but overall less product **42** was isolated (entry 6).

Table 4. Solvent variation in the enantioselective [2+2] photocycloaddition of **39**.



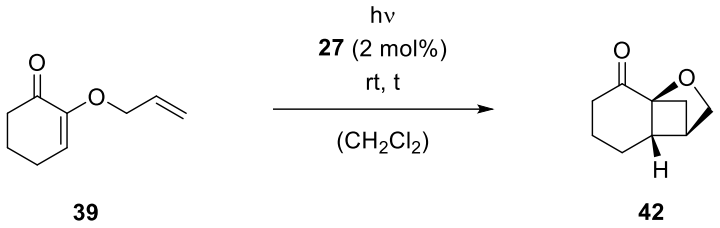
39 **42**

#	λ [nm]	c [mM]	solv.	Y [%]	*ee* [%]	note
1	420	10	CH_2Cl_2	44	66	
2	420	10	ac	-	-	
3	420	10	MeCN	-	-	cat. discoloration
4	420	10	DCE	30	69	
5	420	10	CyH	2[a]	–6	cat. insoluble
6	420	10	$PhCF_3$	11	68	sub. poorly soluble

[a] product contained a small amount of impurities

Next, an initial variation of the wavelength was conducted (Table 5). For any wavelength other than λ = 420 nm, light emitting diodes (LEDs) were used instead of the fluorescent light tubes (FLT). At λ = 405 nm full conversion was already reached after 24 h, though, the shorter wavelength also resulted in a lower yield and lower *ee* of the product **42** (entry 1). In contrast, irradiation at a longer wavelength (λ = 425 nm) resulted in the, so far, best results of 77% yield and 74% enantioselectivity (entry 3). This might also be partly due to a smaller line-width of the emitting LED compared to the broad emission band of FLTs.

Table 5. Initial variation of the wavelength in the enantioselective [2+2] photocycloaddition of **39**.

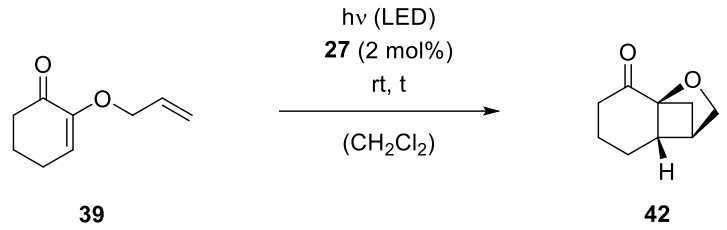


39 **42**

#	λ [nm]	c [mM]	t [h]	Y [%]	*ee* [%]
1	405	10	24	18	38
2	420	10	48	44	66
3	425	10	48	77	74

Since a background reaction had been observed without addition of the catalyst previously and substrate or product decomposition under the irradiation conditions were suspected, the reaction time was reduced to 15 h and followed by a more extensive screening of wavelength (Table 6). Full conversion was not achieved at this time and therefore the reaction outcome was evaluated based on the starting material (sm) to product (prod) ratio in addition to yield and *ee*. In general, an increase in recovered starting material (rsm) was witnessed with an increase in wavelength (entries 1, 3 and 4). Experiments performed at λ = 405 and 425 nm pose an exception to this observation, which can be explained by their higher individual photon flux and therefore higher energetic output. Low to moderate yields and *ee*s were obtained for wavelengths shorter than λ = 420 nm (entries 1 – 3). The product **42** was obtained in excellent enantioselectivities of over 90% for λ = 420 and 425 nm, yet the isolated yields remained very low (entries 4 – 5), which is in correlation with the lower conversion at this wavelength. In addition, purification was complicated by the presence of two compounds during flash column chromatography and added a possible reason for the decreased yield.

Table 6. Wavelength variation in the enantioselective [2+2] photocycloaddition of **39**.



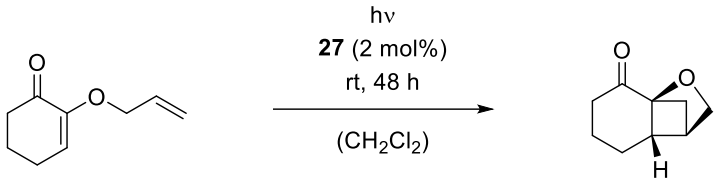
39 **42**

#	λ [nm]	c [mM]	t [h]	Y [%]	*ee* [%]	sm/prod[a]
1	398	10	15	31	37	16/84
2	405	10	15	26	19	traces of sm
3	415	10	15	37[b]	55	50/50
4	420	10	15	5	95	40/60
5	425	10	15	16	91	43/57

[a] determined by ^{1}H NMR, [b] product contained a small amount of impurities

Before further optimization was possible, a problem with different catalyst batches arose. Even though the respective batches were prepared according to the same procedure and were pure according to ^{1}H NMR spectroscopy, their performance in the photochemical reactions varied greatly (Table 7). In order to overcome this problem a new method for catalyst verification had to be found. Simple elemental analysis (EA) turned out to be the most reliable and efficient method. Batches of catalyst **27** with good results in EA also gave good results in the [2+2] photocycloaddition (entries 1 and 2). Thus, any further catalyst batch was evaluated accordingly.

Table 7. Dependency of irradiantion results on the catalyst composition.



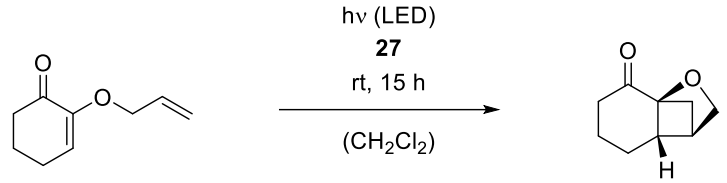
39 **42**

#	λ [nm]	c [mM]	Y [%]	*ee* [%]	EA found[a]
1	420	10	44	66	C 53.11, H 4.78, N 5.61, S 7.26
2	420	10	24	67	C 52.70, H 4.23, N 6.88, S >5.29
3	420	10	23	26	C 48.01, H 4.84, N 9.77, S 5.69

[a] EA calc. for $C_{38}H_{38}F_6N_4PRhS_2$: C 52.90, H 4.44, N 6.49, S 7.43

In an additional set of experiments at improved wavelength (λ = 425 nm) and reaction time (15 h) the catalyst loading was varied once again (Table 8). Independent of the added amount of catalyst **27** the yields remained around 20% (entries 1,3 and 4), while excellent enantioselectivities were achieved (82 – 95% *ee*). A reaction on 50 μmol instead of 100 μmol scale further revealed a dependency of this intramolecular [2+2] photocycloaddition on the reaction scale as a slightly higher yield of 33% was obtained (entry 2).

Table 8. Variation of the catalyst loading and scale dependency of the enantioselective [2+2] photocycloaddition of **39**.

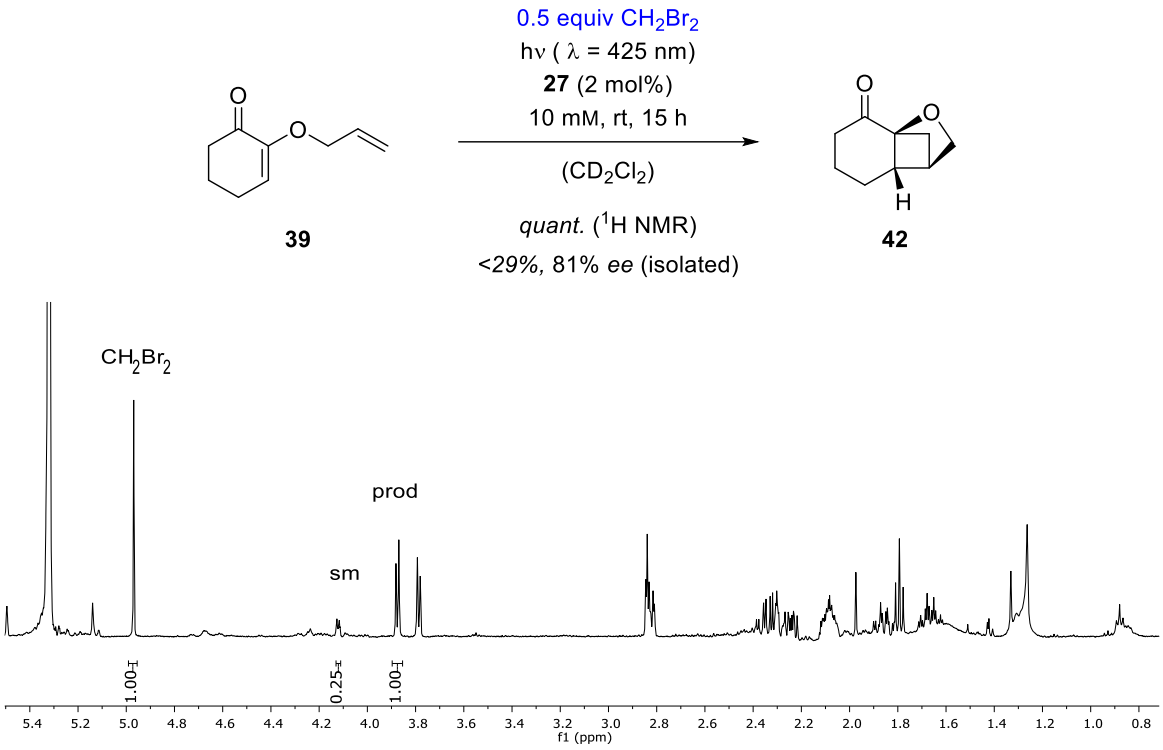


39 **42**

#	λ [nm]	c [mM]	cat [mol%]	Y [%]	*ee* [%]	sm/prod[a]
1	425	10	4	21	94	19/81
2[b]	425	10	2	33[c]	95	12/88
3	425	10	2	22[c]	92	31/69
4	425	10	1	21	82	-

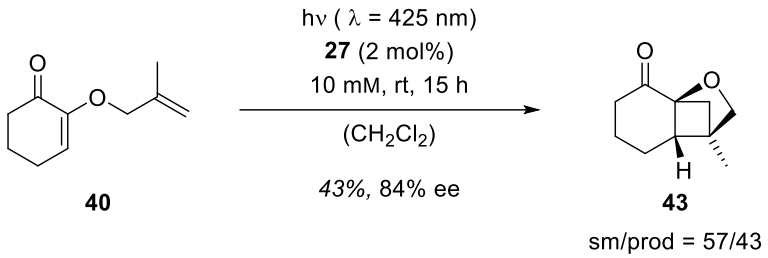
[a] determined by ^{1}H NMR, [b] 0.05 mmol instead of 0.1 mmol, [c] product contained a small amount of impurities

In a last experiment with substrate **39**, the photochemical reaction was conducted in the presence of CH_2Br_2 as internal standard in an NMR tube and the reaction was observed by ^{1}H NMR spectroscopy. Irradiation for 15 h gave quantitative yield according to the ^{1}H NMR spectrum. However, only 29% of product **42** containing a small amount of impurity were isolated. The *ee* was determined to be 82% (Scheme 33). This raised the question of potential volatility or instability of product **42** on silica (SiO_2). Both cases were investigated and neither assumption turned out to be correct. It is more likely that product loss occurred during purification due to the small reaction scale which is in accordance with the previously obtained results (*vide supra*).



Scheme 33. Enantioselective intramolecular [2+2] photocycloaddition of **39** in the presence of CH_2Br_2 as internal standard.

Finally, substrate **40** was subjected to the enatioselective reaction conditions and we were able to obtain the crossed product **43** in an excellent yield of 43% at 43% conversion with a good *ee* of 84% (Scheme 34).



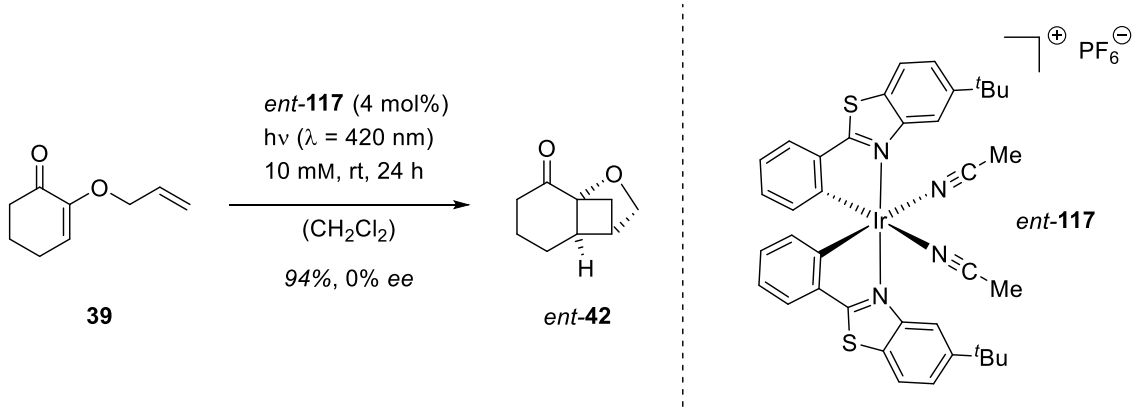
Scheme 34. Enantioselective [2+2] photocycloaddition of **40**.

In summary, reaction conditions for the enantioselective intramolecular [2+2] photocycloaddition of 2-(allyloxy)cyclohex-2-enone (**39**) were extensively screened concerning wavelength, solvent, catalyst loading, T and reaction time. The best result was obtained at λ = 425 nm, *c* = 10 mM, t = 48 h with 2 mol% **27** in CH_2Cl_2 at rt. In this case, a good yield

and enantioselectivity (77%, 74% *ee*) were achieved. However, the biggest challenge remained the reproducibility of previously obtained results. Therefore, we concluded that despite the promising results within this optimization, Rh complex **27** is not a perfectly suitable catalyst for the [2+2] photocycloaddition we envisioned with the established substrate scope.

2.5.4 Application of other *Lewis* Acids

In consequence, we began the search for a more suitable chiral *Lewis* acid. For this purpose the Ir analogue *ent*-**117** was tested. Irradiation of cyclohexenone **39** with 4 mol% *ent*-**117** over 24 h gave an excellent yield of 94%, however, the product *ent*-**42** was obtained as a racemic mixture (Scheme 35).



Scheme 35. Intramolecular [2+2] photocycloaddition of **39** in the presence of Λ-IrS (*ent*-**117**).

Since no bathochromic shift was observed for the model substrate **39** upon addition of catalyst **27** and results from photochemical reactions with this catalyst were inconsistent, our next goal was to evaluate the coordination of **39** to a *Lewis* acid as well as the background reaction further. $EtAlCl_2$ had already been reported to induce a bathochromic shift and was therefore chosen for UV/vis titration experiments (Figure 14). The UV/vis spectra of enone **39** containing different equivalents of $EtAlCl_2$ showed a red shift in the absorption maximum of up to 31 nm to λ = 289 nm, as expected. This bathochromic shift was accompanied by a decrease of the absorption intensity and additional signal broadening. Furthermore, an increased tailing in the visible region was detected. Coordination saturation appeared to be complete upon addition of 5.0 equivalents of *Lewis* acid because the absorption maximum

did not shift further. A higher amount of $EtAlCl_2$ induced a broadening of the absorption band and changed its shape slightly. This could possibly be reasoned by a second coordination to the ether oxygen atom and further explain the existence of more than one isosbestic point.

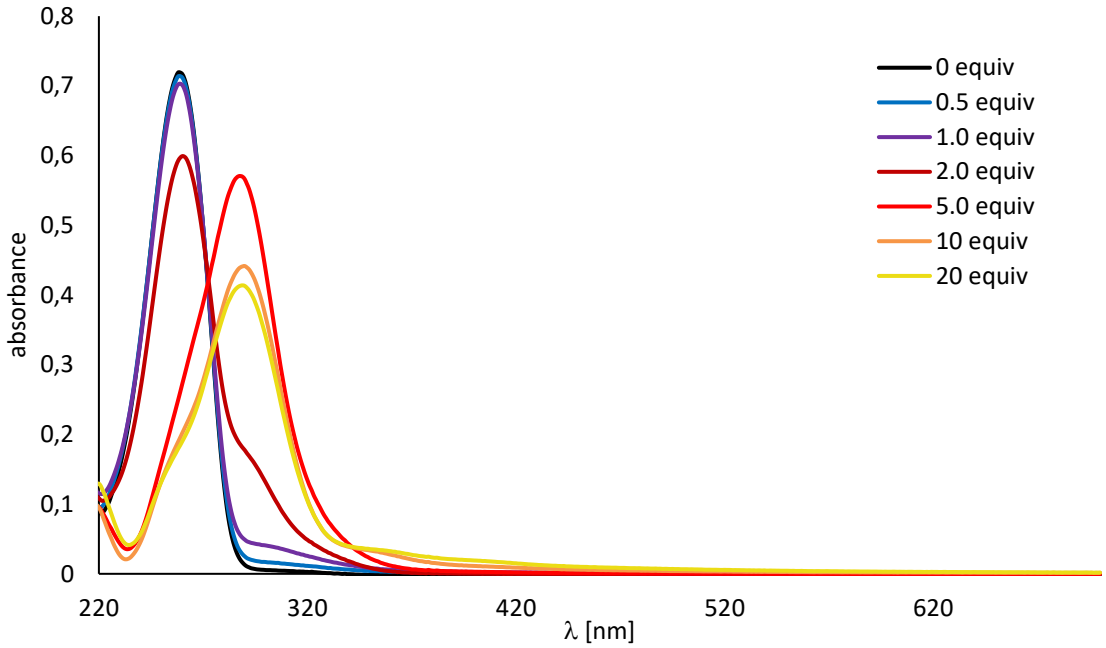
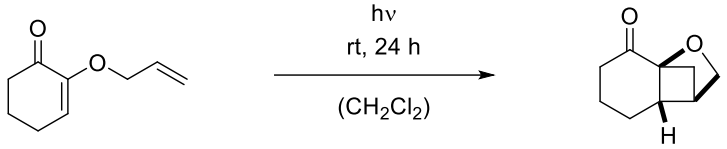


Figure 14. UV/vis titration of cyclohexenone **39** with different concentrations of $EtAlCl_2$ (*c* = 1.0 mM, CH_2Cl_2).

Next, different wavelengths (λ = 398 – 458 nm) were screened for a potential racemic background reaction (Table 9). No product formation was observed over the course of 24 h for λ = 458 and 437 nm, respectively (entries 1 – 2). Minimal amounts of product *rac*-**42** (4 – 6%) were detected when wavelength λ = 425 or 415 nm were employed (entries 3 – 4). Under the assumption that a catalyzed enantioselective reaction would require far less time this amount of product was determined as acceptable. In contrast, irradiation at λ = 405 or 398 nm afforded the product in almost 30% (entries 5 – 6) and therefore wavelengths below λ = 415 nm were in this case found to be unsuitable for the development of an enantioselective procedure. Overall an increase in background reaction was observed with an increase in photonic energy.

Table 9. Racemic background reaction of **39** in dependence of the irradiation wavelength.



39 *rac*-**42**

#	λ [nm]	c [mM]	t [h]	sm	prod
1	458	10	24	100	0
2	437	10	24	100	0
3	425	10	24	96	4
4	415	10	24	94	6
5	405	10	24	74	26
6	398	10	24	71	29

After UV/vis titration experiments had confirmed the complexation of substrate **39** with a *Lewis* acid and conditions to avoid a racemic background reaction had been established, it was clear, that enantioselective catalysis based on a bathochromic shift should in general be possible. In this context, a class of Pd-based chiral complexes came to our attention (Figure 15). In these complexes, the Pd is coordinated to chiral phosphine ligands and can be generated *in situ* prior to the reaction and no lengthy catalyst preparation is necessary.[90] These characteristics make complexes like **118** an ideal candidate, since tuning to the substrates needs is easily possible. Furthermore, this class of catalysts had been successfully employed in various thermal enantioselective reactions such as arylations, carbonyl-ene and cross coupling reactions or [3+2] cycloadditions by the group of *Mikami* with good yields and excellent enantioselectivities.[90,91]

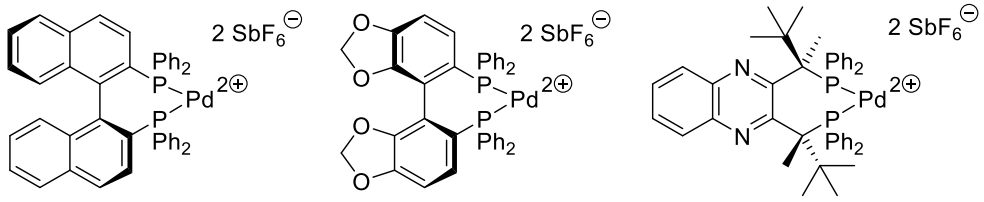


Figure 15. Structures of chiral Pd catalysts employed by the *Mikami* group.[90]

UV/vis spectra of the bright yellow compound **118** revealed a substantial absorption up to λ = 450 nm (Figure 16). As in the case of Δ-RhS (**27**) no bathochromic shift for model substrate **39** was observed because the relevant area was obscured by the catalyst's absorption. Nonetheless, the Pd complex was tested in the [2+2] photocycloaddition of enone **39** since *Lewis* acid complexation accompanied by a bathochromic shift was observed earlier.

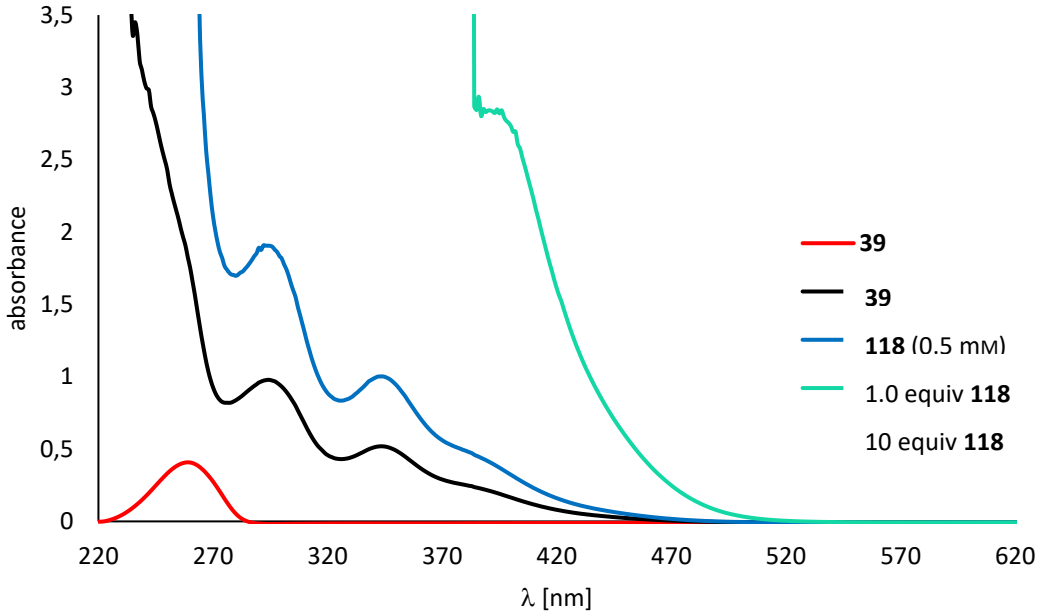
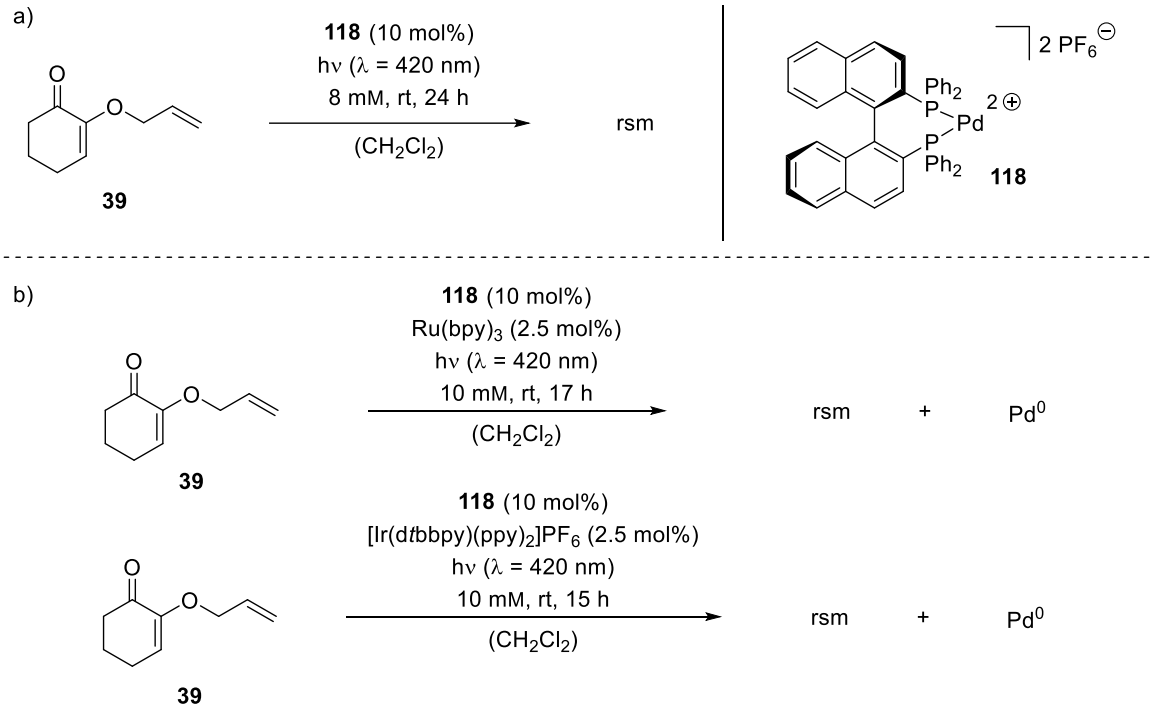


Figure 16. UV/vis spectra of **39** with different equivalents of chiral Pd complex **118** (*c* = 1.0 mM, CH_2Cl_2).

Unfortunately, for the irradiation of **39** with 10 mol% of catalyst **118** only starting material was recovered (Scheme 36, a). So a dual catalytic approach was followed next. It was assumed that coordination of the *Lewis* acid would not only provide a chiral environment but also decrease the triplet energy of the substrate. This would allow for selective excitation if a sensitizer with a triplet energy between the triplet energies of complexed and uncomplexed substrate [E_T(sub) > E_T(sens.) > E_T(LA-sub)] was employed. Thus, the sensitizer required a triplet energy below E_T(sub) = 237 kJmol^{-1} (*vide supra*). Reactions with

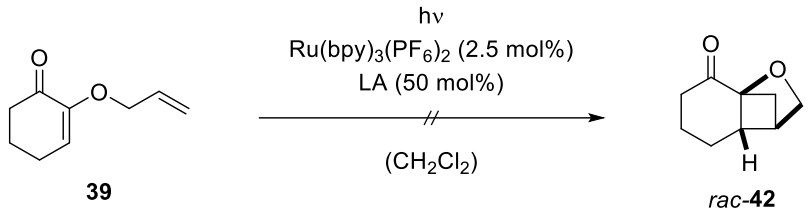
$Ru(bpy)_3$ (E_T = 193 kJmol^{-1})[67] and $[Ir(dtbbpy)(ppy)_2]PF_6$ (E_T = 206 kJmol^{-1})[92] were performed (Scheme 36, b). However, both reactions afforded the same results and only starting material was recovered together with Pd^0. This was attributed to potential photochemical redox processes between the two metal complexes. Since no product formation was observed at all, the Pd catalyst was not pursued further.



Scheme 36. [2+2] Photocycloaddition of **39** in the presence of chiral *Lewis* acid **118** without (a) and with an additional sensitizer (b).

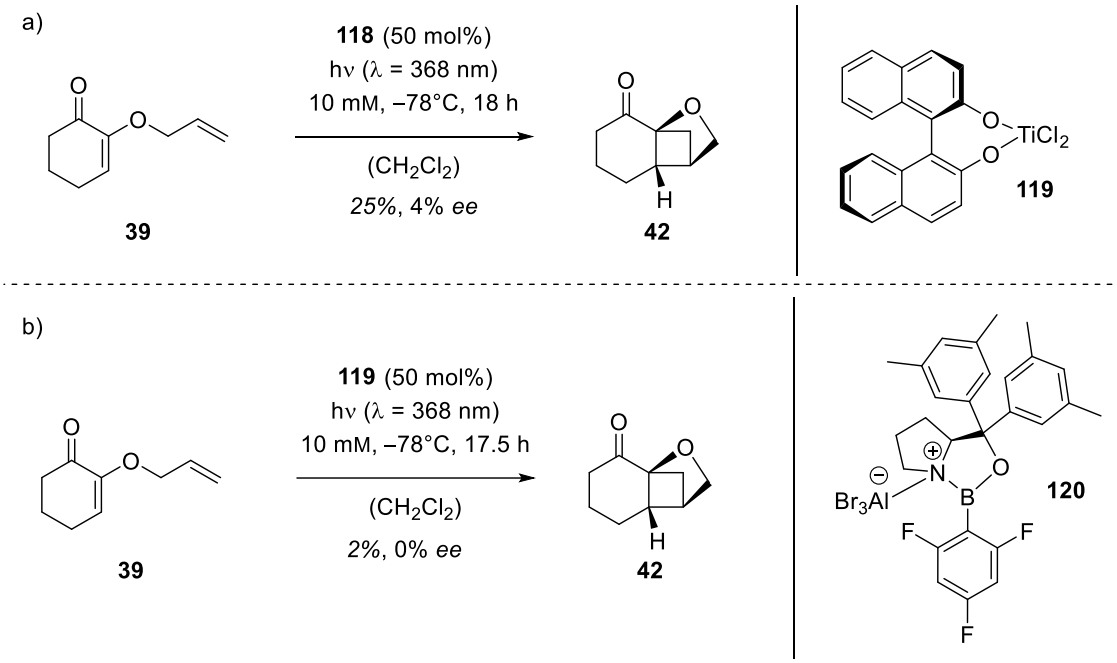
Nevertheless, dual catalysis by reduction of the substrate's triplet energy combined with the appropriate sensitizer to catalyze the photochemical reaction remained a promising concept. Therefore, different achiral *Lewis* acids (50 mol%) were screened as their metal triflates (Table 10) paired with 2.5 mol% $Ru(bpy)_3(PF_6)_2$ at λ = 458 nm. However, neither of the tested metal salts led to a positive outcome and starting material was recovered quantitatively in all cases. Therefore, it was concluded that the difference in triplet energy between $Ru(bpy)_3(PF_6)_2$ and the coordinated enone **39** might still be too large and future research should be focused on sensitizers with slightly higher triplet energies.

Table 10. Variation of metal triflates tested in the dual catalytic approach towards an enantioselective [2+2] photocycloaddition.



#	λ [nm]	c [mM]	t [h]	LA	Y [%]
1	458	10	2.5	$Gd(OTf)_3$	rsm
2	458	10	2.5	$Cu(OTf)_2$	rsm
3	458	10	2.5	$Eu(OTf)_3$	rsm
4	458	10	2.5	$Ni(OTf)_2$	rsm
5	458	10	2.5	$Yb(OTf)_3$	rsm
6	458	10	2.5	$Fe(OTf)_3$	rsm

Lastly, the Ti-(*R*)-binol complex **119** and oxazaborolidine *Lewis* acid **120** were tested under standard reaction conditions for the latter chiral *Lewis* acid.[93] Irradiation at –78 °C at λ = 368 nm with 50 mol% of the Ti complex resulted in a low yield of 25% and a very low enantioselectivity of 4% (Scheme 37, a). Application of the oxazaborolidine **120** mainly led to decomposition and only 2% of product **42** was isolated as a racemic mixture (Scheme 37, b).



Scheme 37. [2+2] Photocycloaddition of **39** in the presence of a Ti-based chiral *Lewis* acid **119** (a) and oxazaborolidine catalyst **120** (b).

In summary, UV/vis titration of model substrate **39** with $EtAlCl_2$ confirmed the coordination of the compound to a *Lewis* acid. This was accompanied by a bathochromic shift of the absorption maximum of approximately 30 nm, which was assumed to allow for enantioselective catalysis. However, the application of different Pd, Ti and oxazaborolidine-based *Lewis* acids as well as an attempt in dual catalysis did not lead to a satisfactory enantioselective protocol. Yields and enantioselectivities remained low or the starting material was recovered quantitatively. Therefore we concluded our studies on the enantioselective intramolecular [2+2] photocycloaddition of 2-(2'-alkenyloxy)cyclohex-2-enones at this point and turned our attention to a possible modification of the coordination motif of these substrates to a *Lewis* acidic metal (Figure 17).

2.5.5 Expansion of the Coordination Motif

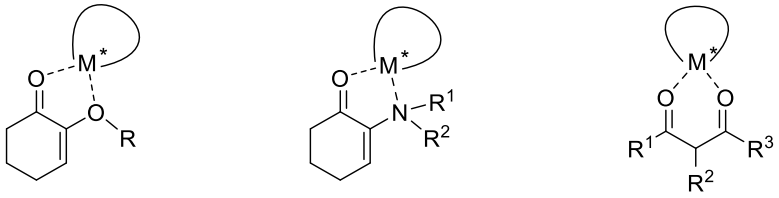
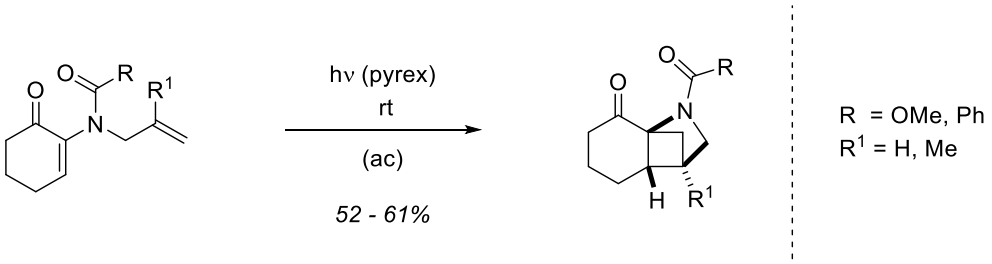


Figure 17. Structures of potential substrates with a new coordination motif.

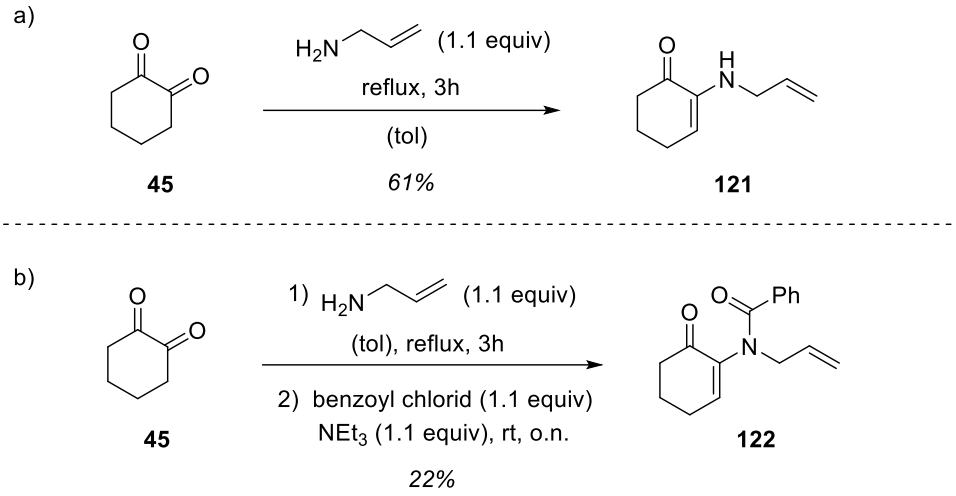
The employed chiral-at-metal Rh catalyst had previously been reported to catalyze a variety of photochemical reaction exquisitely when the substrate exhibited a nitrogen containing entity such as an imidazole or pyrazole (*vide supra*).[31] Therefore, nitrogen containing compounds were prepared next. *Ikeda* and co-workers had been the first group to publish the intramolecular crossed [2+2] photocycloaddition of the cyclohexenone compounds used above.[59,60] During the course of their research, they also briefly investigated the respective aza-analogues.[94] The protected 2-(*N*-acyl-*N*-alkylamino)cyclohex-2-enones were irradiated in ac with a 300 W high pressure mercury lamp upon application of a pyrex filter and gave the respective 2-azabicyclo[2.1.1]hexane derivatives in moderate yields (Scheme 38). However, the reaction did not proceed as cleanly as for the 2-(2'-alkenyloxy)cyclohex-2-enones and various side products were isolated and partially characterized.[94]



Scheme 38. [2+2] Photocycloadditions of 2-(*N*-acyl-*N*-alkylamino)cyclohex-2-enones performed by *Ikeda et al.*[94]

In this photochemical transformation we saw potential for improvement through *Lewis* acid catalysis and the substrates also beared a nitrogen moiety which could improve the coordination to Rh catalyst **27**. Therefore, compounds **121** and **122** were prepared in a procedure similar to method **A** that had been employed previously (*vide supra*). First the unprotected 2-(allylamino)cyclohex-2-enone (**121**) was synthesized from diketone **45** and allylamine under reflux in tol (Scheme 39, a). For compound **122** this first step was followed without

purification by treatment with benzoyl chloride under basic conditions. The final irradiation precursor **122** was obtained in 22% over two steps (Scheme 39, b).



Scheme 39. Synthesis of 2-(allylamino)cyclohexenones **121** and **122** from diketone **45**.

Before photochemical experiments were performed, the photophysical properties of this substrate class were investigated. The UV/vis spectra revealed a tremendous difference in absorption behavior between the protected and unprotected compounds **122** and **121** (Figure 18). The absorption maximum of **121** at λ = 311 nm (ε = 3966 $cm^{-1}M^{-1}$) is significantly bathochromically shifted compared to the protected derivative **122**. The UV/vis spectrum of **122** does not show an explicit absorption maximum but a shoulder at about λ = 260 nm (ε = 4414 $cm^{-1}M^{-1}$). Fortunately, no tailing in the visible region was detected and substrates **121** and **122** promised to be viable candidates for enantioselective catalysis at λ = 420 nm or above.

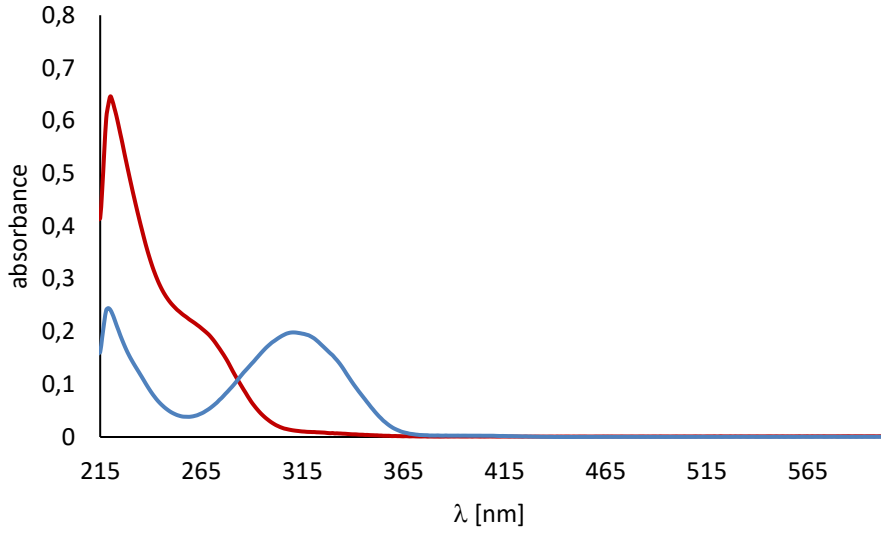
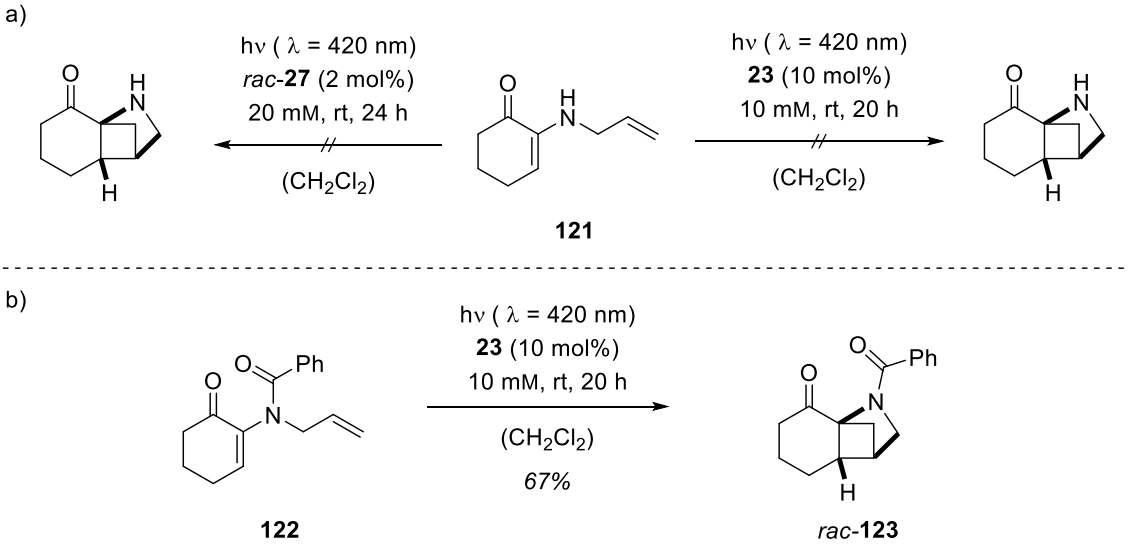


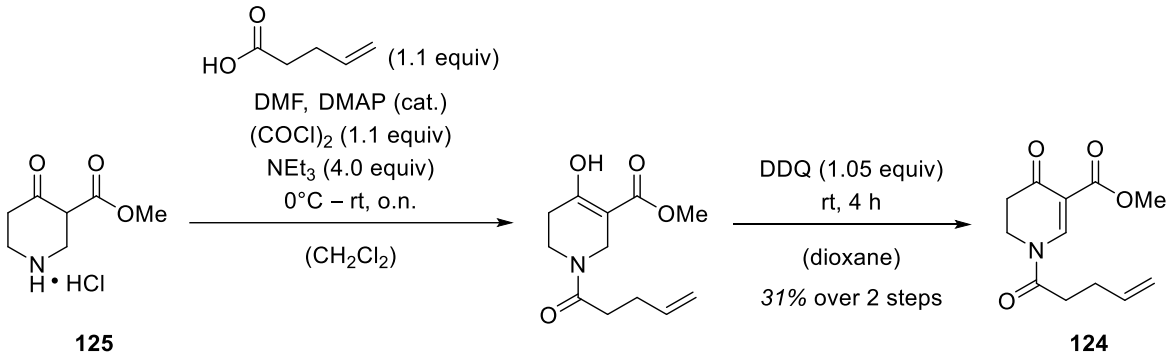
Figure 18. UV/vis spectra of unprotected (blue) and protected 2-(allylaminino)cyclohexenones (red) **121** (blue) and **122** (red) (c = 0.5 mM, CH_2Cl_2).

Next, this hypothesis was initially tested by irradiation of the 2-(allylamino)cyclohex-2-enones **121** and **122** with visible light in the presence of achiral sensitizers txt (**23**) or *rac*-**27** (Scheme 40). No conversion was observed for the photochemical reaction of unprotected compound **121** with either **23** or *rac*-**27**. Nevertheless, the protected derivative **122** readily underwent intramolecular [2+2] photocycloaddition to cyclobutane *rac*-**123** with a promising yield of 67%. The different photochemical behaviors of both substrates **121** and **122** indicated a strong influence of the protecting group on the reactivity of the respective compound, which is in accordance with the literature.[94]



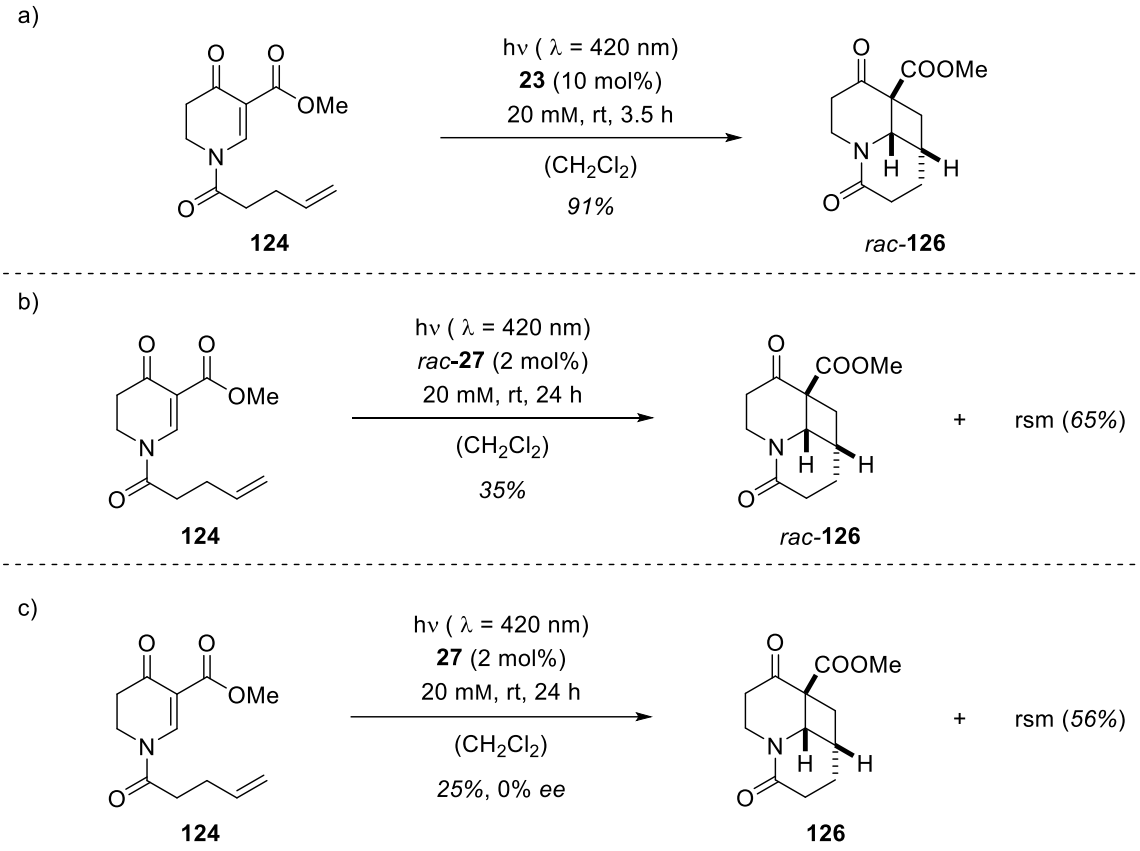
Scheme 40. [2+2] Photocycloaddion reactions of compounds **121** (a) and **122** (b).

In a second approach the coordination motif was altered from a five-membered to a six-membered ring system, while the two complexing atoms remained oxygen atoms. This coordination is for example possible in a 1,3-diketone (Figure 17). Therefore, dihydropyridone **124** was chosen for preliminary examination. The compound was prepared from the commercially available hydrochloride **125** in two steps.[95] Treatment with 4-pentenoic acid chloride, followed by a DDQ oxidation afforded **124** in 31% yield over two steps (Scheme 41).



Scheme 41. Synthesis of irradiation precursor **124** (DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone).

Sensitized irradiation of compound **124** with 10 mol% **23** reached full conversion after 3.5 h and the tricyclic product *rac*-**126** was isolated in 91% yield (Scheme 42, a). In contrast, the reaction with 2 mol% of *rac*-**27** under otherwise unchanged conditions was stopped after 24 h, because full conversion had not been reached at this time (Scheme 42, b) and gave 35% *rac*-**126**. This represents a significant drop in reaction rate for the chiral-at-metal catalyst. However, the overall mass balance was very good since 65% of starting material were recovered. Despite the lower reactivity the enantiomerically pure catalyst **27** was applied under the same reaction conditions (Scheme 42, c). In this case the mass balance was slightly worse since only 56% of **124** were recovered and 25% of the product **126** were isolated. Unfortunately, **126** was obtained as a racemic mixture.



Scheme 42. [2+2] Photocycloadditon reactions of compound **124** in the presence of txt (**23**) and Rh catalysts *rac*-**27** and **27**.

From the experiments performed with dihydropyridone **124**, we concluded that the coordination *via* a 1,3-diketone is not a feasible approach for our purpose of an enantioselective [2+2] photocycloaddition. Instead we focused on reaction kinetics and the determination of quantum yields.

2.6 Reaction Kinetics and Quantum Yield Determination

In order to get a better insight into the two reaction types ([2+2] photocycloaddition, cyclization/hydrogen abstraction cascade) that were observed during the extension of the cyclohexenone substrate scope, photochemical reactions of compounds **39** and **51** were monitored over time by calibrated GC. This was done by taking and analyzing small aliquots of the reaction solution over a certain period of time. For this purpose undecane was chosen as an internal standard because it did not interfere with the integration of all starting material and product signals.

The starting material depletion and product formation were monitored for both reaction types for the sensitized reaction (10 mol% **23**, λ = 420 nm) as well as for direct irradiation (λ = 350 nm). The results are depicted in Figure 19 and Figure 20, respectively. In the sensitized case (Figure 19), both reaction types show a linear increase in product concentration paired with a linear decrease in starting material, which is indicative of a zero order reaction kinetic.[96] This is due to sensitization and the efficiency of **23** as triplet sensitizer, since energy transfer from txt (**23**) to an enone system is fast.[97] Thus, the reaction rate is independent of the concentration of starting material (**39** or **51**). In contrast, an exponential curve was observed for the consumption of starting material and for product formation in the cases of direct irradiation (Figure 20), which implies a first order kinetic. Herein, the concentration of starting material directly affects the reaction rate, which decreases with depletion of starting material as a productive reaction becomes less likely.[96]

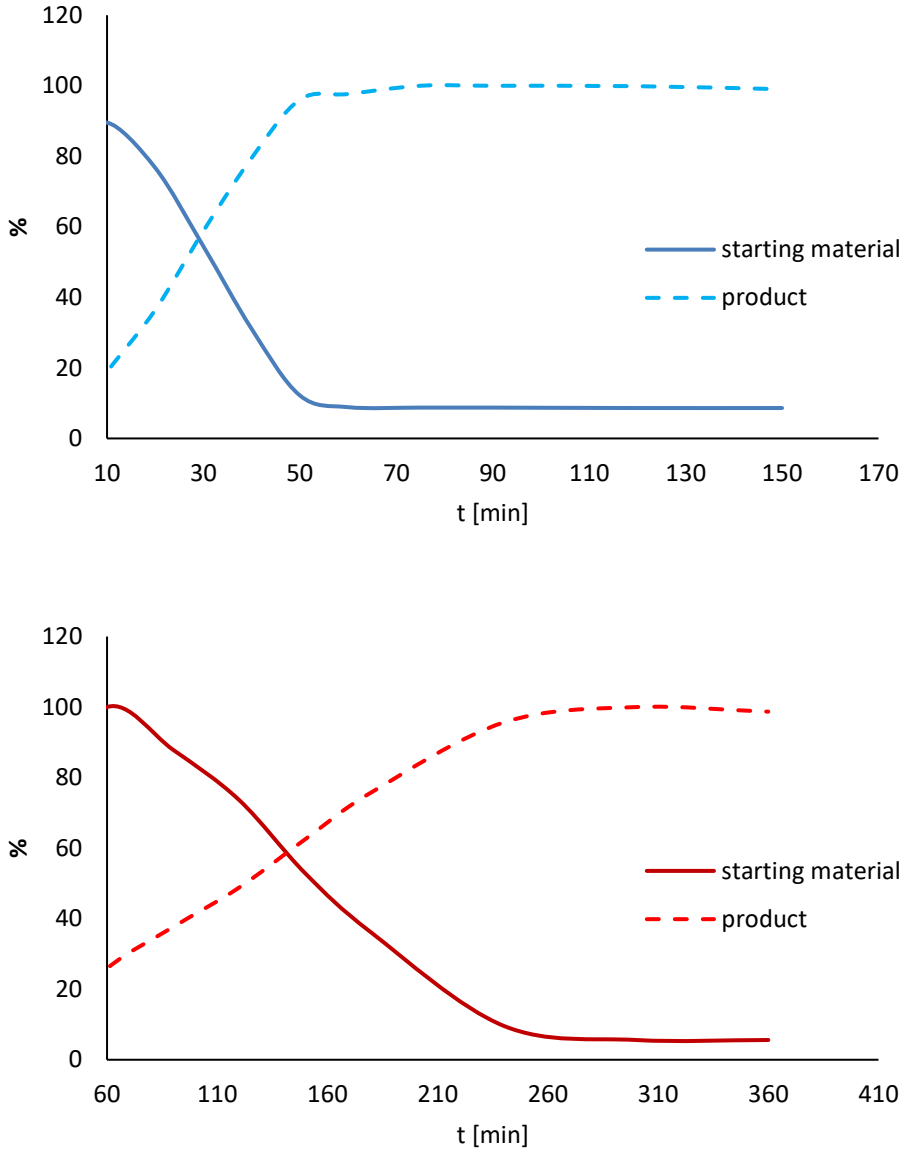


Figure 19. Reaction course of the [2+2] photocycloaddition of **39** (blue) and hydrogen abstraction reaction of **51** (red) catalyzed by **23** at λ = 420 nm. Concentrations were normalized to the highest value.

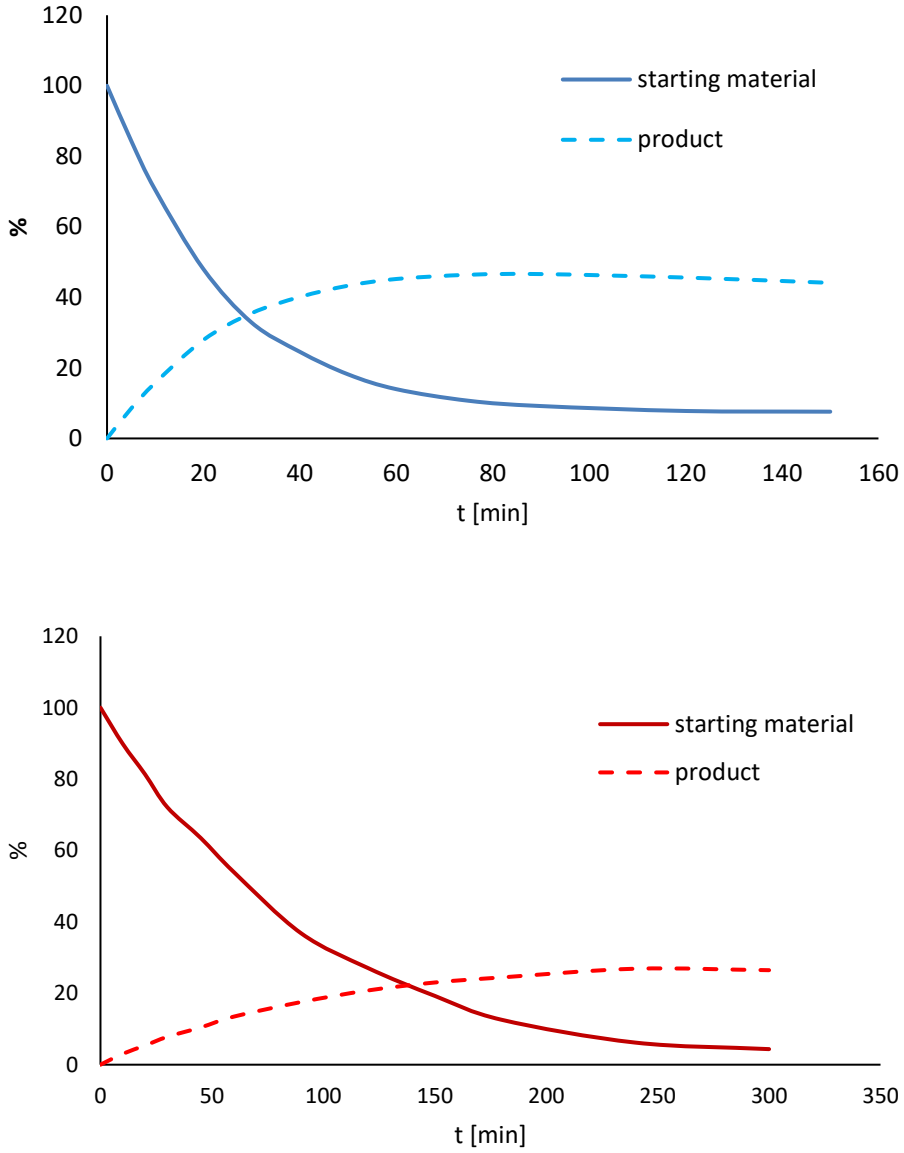


Figure 20. Reaction course of the [2+2] photocycloaddition of **39** (blue) and hydrogen abstraction reaction of **51** (red) at direct irradiation (λ = 350 nm). Concentrations were normalized to the highest value.

After evaluation of the reaction kinetics, we were further interested in the influence of sensitization on the quantum yield of the [2+2] photocycloaddition of **39** as well as the difference in quantum yield depending on the reaction type.

The quantum yield Φ is defined as the percentage of molecules A undergoing a defined photochemical process x such as the formation of product B (A → B) upon absorption of a photon.[98]

$$\Phi = \frac{n_x}{n_p} = \frac{\text{number of photochemical or photophysical events x}}{\text{number of photons absorbed}}$$

The value of Φ has a range of $0 \leq \Phi \leq 1$ if no radical chain mechanism is involved. A value of 1 would indicate formation of a product molecule for every absorbed photon, which is improbable since product formation competes with decay pathways such as other non-radiative processes or fluorescence and phosphorescence. In the case of a radical chain mechanism, values above 1 are possible as the photochemical process often acts as radical initiation.[98,99] Small conversions are beneficial for determining quantum yields in order to avoid corruption of the experimental results by secondary photoreaction. These can become more prominent for higher conversions.[98,99] In our case the quantum yields for the [2+2] photocycloaddition of **39** and the photochemical hydrogen abstraction reaction of **51** in the presence of txt (**23**, 10 mol%) were determined at λ = 382 nm by measuring small increments of Δn_x and Δn_p after short time intervals Δt. Based on the assumption of a linear increase of product concentration, the quantum yield of each segment was calculated and the average over all segments was determined as the reaction's quantum yield.

For the calculation of Φ of the intramolecular [2+2] photocycloaddition referred to the product *rac*-**42**, the amount of photons can be derived from the difference in intensity of the light source ΔI before and after passing through the reaction solution (*vide infra*). This intensity is defined by its power output per surface area.[100]

$$\Delta I = I_0 - I = \frac{P}{A_{surf}}$$

ΔI = intensity difference; P = power; A_{surf} = surface area

Therefore, the energy used for excitation of substrate molecules for a defined time increment can be determined by using the physical relations between power P, work W and energy E.[100]

$$P = \frac{\Delta W}{\Delta t} = \frac{E}{\Delta t}$$

$$E = P \cdot \Delta t = \Delta I \cdot A_{surf} \cdot \Delta t$$

P = power; W = work; A_{surf} = surface area; E = energy difference obtained from ΔI

Further, the energy of one photon at λ = 382 nm was calculated to be $5.18 \cdot 10^{-19}$ J by application of the quantum mechanical definition of light as an electromagnetic wave.[100]

$$E_p = h \cdot \nu = \frac{h \cdot c}{\lambda} = \frac{6.62 \cdot 10^{-34}\text{Js} \cdot 2.99 \cdot 10^{8}\,\frac{\text{m}}{\text{s}}}{382 \cdot 10^{-9}\text{m}} = 5.18 \cdot 10^{-19}\text{J}$$

E_p = energy of a photon at a certain wavelength; h = *Planck*'s constant = $6.62 \cdot 10^{-34}$ Js; ν = photon frequency; c = speed of light = $2.99 \cdot 10^{8}$ ms^{-1}

By application of the *Avogadro* constant N_A, the amount of photons Δn_p can be determined as follows:[100]

$$\Delta n_p = \frac{N_p}{N_A} = \frac{\frac{E}{E_p}}{N_A} = \frac{E}{N_A \cdot E_p} = \frac{E}{6.022 \cdot 10^{23}\,\frac{1}{\text{mol}} \cdot 5.18 \cdot 10^{-19}\text{J}} = \frac{E}{3.12 \cdot 10^{5}\,\frac{\text{J}}{\text{mol}}}$$

$$\Delta n_p = \frac{\Delta I \cdot A_{surf} \cdot \Delta t}{3.12 \cdot 10^{5}\,\frac{\text{J}}{\text{mol}}} = \frac{\Delta I \cdot 1\ \text{cm}^2 \cdot \Delta t}{3.12 \cdot 10^{5}\,\frac{\text{J}}{\text{mol}}}$$

N_A = *Avogadro* constant = $6.022 \cdot 10^{23}$ mol^{-1}

For the of quantum yield determination of the sensitized [2+2] photocycloaddition of enone **39**, a value of $2.70 \cdot 10^{-2}$ Wcm^{-2} was measured for ΔI. Therefore Δn_p for the first time increment (t = 0 – 60 s) was calculated to be $5.19 \cdot 10^{-6}$ mol.

$$\Delta n_p(60\ s) = \frac{\Delta I \cdot A_{surf} \cdot \Delta t}{3.12 \cdot 10^5 \frac{J}{mol}} = \frac{2.70 \cdot 10^{-2} \frac{W}{cm^2} \cdot 1\ cm^2 \cdot 60\ s}{3.12 \cdot 10^5 \frac{J}{mol}} = 5.19 \cdot 10^{-6} mol$$

1 W = 1 Js^{-1}

Consequently, the quantum yield Φ was determined by use of the amount of product that was formed within the first 60 s according to GC calibration ($\Delta n_x = 1.31 \cdot 10^{-6}$ mol):

$$\Phi\ (60\ s) = \frac{n_x}{n_p} = \frac{\Delta n_x}{5.19 \cdot 10^{-6} mol} = \frac{1.31 \cdot 10^{-6} mol}{5.19 \cdot 10^{-6} mol} = 0.252$$

According to this method the quantum yield for the [2+2] photocycloaddition of cyclohexenone **39** was determined to be Φ = 0.233 ± 0.023 as the mean value over all increments up to t = 15 min (Figure 21). The analysis of the photochemical cyclization/hydrogen abstraction cascade of **51** (t = 0 – 60 min) gave a considerably lower quantum yield of Φ = 0.050 ± 0.002 (Figure 22). Therefore it can be concluded that the intramolecular [2+2] photocycloaddition is over four times more efficient than the alternative reaction pathway.

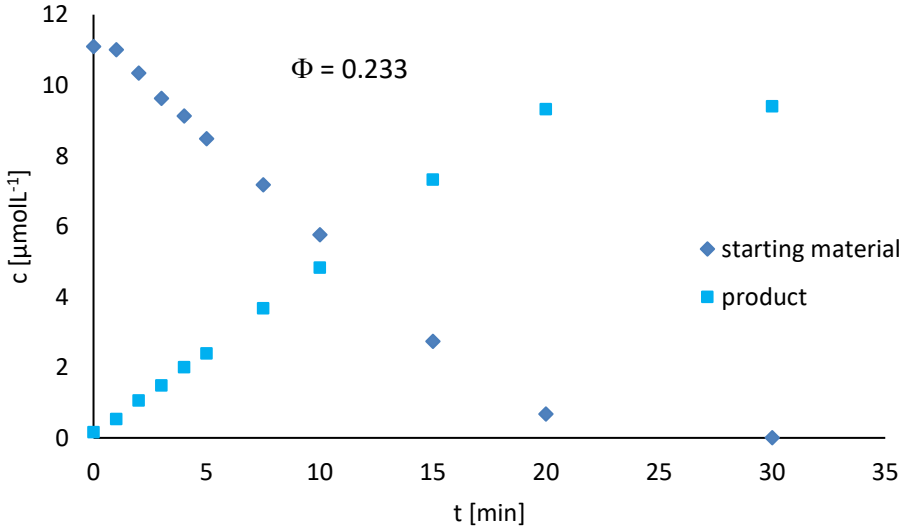


Figure 21. Quantum yield determination of the sensitized [2+2] photocycloaddition of **39** (10 mol% **23**, 10 mM, CH_2Cl_2, λ = 382 nm, concentration determined by GC).

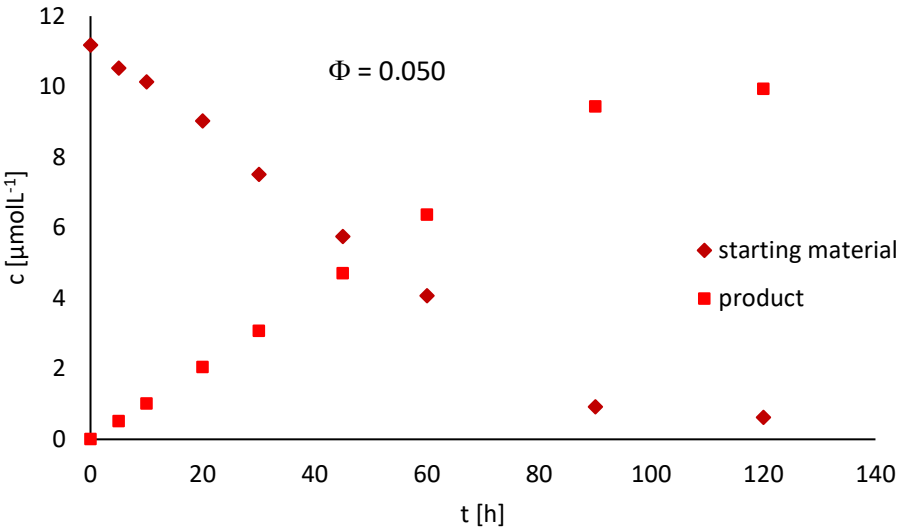


Figure 22. Quantum yield determination of the sensitized cyclization/hydrogen abstraction cascade of **51** (10 mol% **23**, 10 mM, CH_2Cl_2, λ = 382 nm, concentration determined by GC).

The quantum yield for direct irradiation of **39** was determined to be Φ = 0.231± 0.001 according to the same experimental method, but measurements were conducted at λ = 368 nm. A decrease in absorbance of the reaction solution was observed with decreasing substrate concentration. To account for this change of absorbance, an additional factor was implemented that reflected this decrease. Subsequently, this factor was used for quantum yield determination as an additional variable in a first order kinetic model. To obtain Φ, the deviation between theoretical model and experimental data was minimized by the Generalized Reduced Gradient (GRG) nonlinear solving method. Overall the accuracy of the calculated values is mainly limited by the GC calibration. The value indicates that the reaction at direct irradiation is similarly efficient concerning product formation but slower ($t_{sens} << t_{direct}$) as the sensitized version. However, considerably less product and no side products were isolated for direct irradiation, even though, full conversion was achieved, which can be explained by decomposition of starting material becoming a prominent non-productive decay pathway from the singlet excited state. It stands to reason that by sensitization the singlet state is avoided while the triplet state is reached, from which product formation can occur but other decay pathways such as phosphorescence and IC are also likely.

2.7 Summary

An extended series of 2-(2'-alkenyloxy)cycloalk-2-enones (**39** – **41** and **51** – **68**) was prepared starting either from the respective diketones **45** – **48** or epoxides *rac*-**49** and *rac*-**50**. The substrates were subjected to standard visible light irradiation conditions (10 mol% **23**, 10 mM, CH_2Cl_2, rt) and a range of structurally diverse products was obtained (Figure 23).

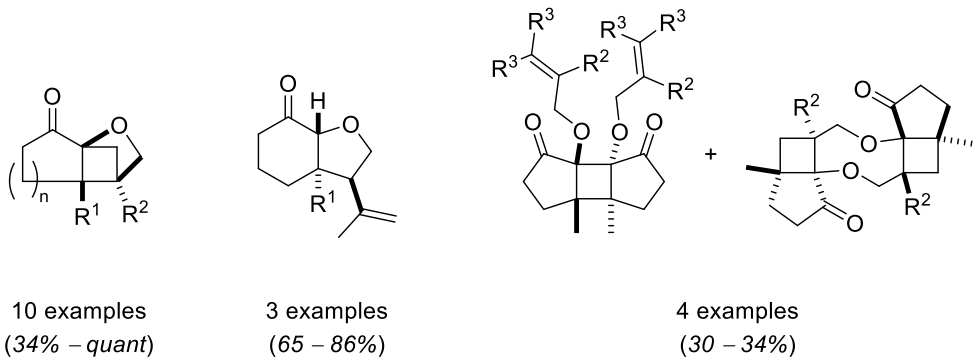
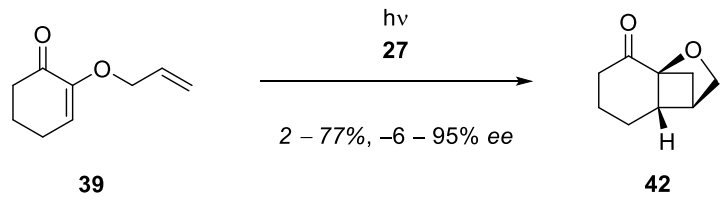


Figure 23. Structures of the diverse photoproducts formed in this work (R^1 = H, Me; R^2 = H, Me; R^3 = H, Me; n = 1, 2).

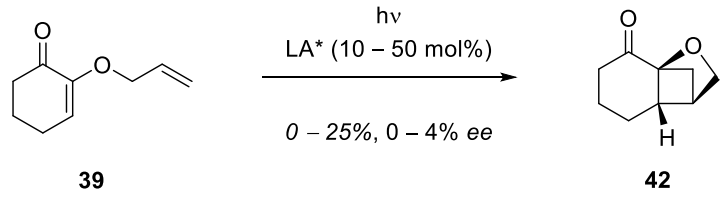
The crossed [2+2] photocycloaddition proceeded in high regio- and excellent diasteroselectivity. If the olefinic tether was trisubstituted, no cycloaddition but a cascade of cyclization followed by hydrogen abstraction occurred. This observation is consistent with the formation of a 1,4-diradical intermediate upon irradiation, indicating a reaction on the triplet hypersurface. In the case of cyclopent-2-enones **62** – **68**, decomposition or [2+2] photodimerization predominated over an intramolecular reaction. Two main dimerization products were isolated which were either formed by a HH [2+2] photocycloaddition or a twofold [2+2] photocycloaddition of the enone to the olefin tether. The latter afforded products **101** and **103** containing a central [1,5]dioxocane ring system. The structure assignment of the two types of dimeric product was verified by single-crystal X-ray analysis.

Subsequently, intense studies on the development of an enantioselective protocol were undertaken. At first, reaction conditions (t, T, catalyst loading and solvent) in the presence of chiral-at-metal catalyst **27** were screened (Scheme 43). Some promising conditions were found. However, mostly either high yields or high enantioselectivities were achieved and reproducibility remained the main issue.



Scheme 43. Enantioselective [2+2] photocycloaddition of model substrate **39** with ΔRhS (**27**).

During the course of this work, a selection of other chiral *Lewis* acids (Pd- or Ti-based (*R*)-binol complexes and an oxazaborolidine) were tested in the [2+2] photocycloaddition as well (Scheme 44). However, the starting material was either recovered quantitatively or the yields and *ee*s of the isolated product were very low. A dual catalytic approach was also pursued but did not give any conversion.



Scheme 44. Enantioselective [2+2] photocycloaddition of model substrate **39** with other *Lewis* acids.

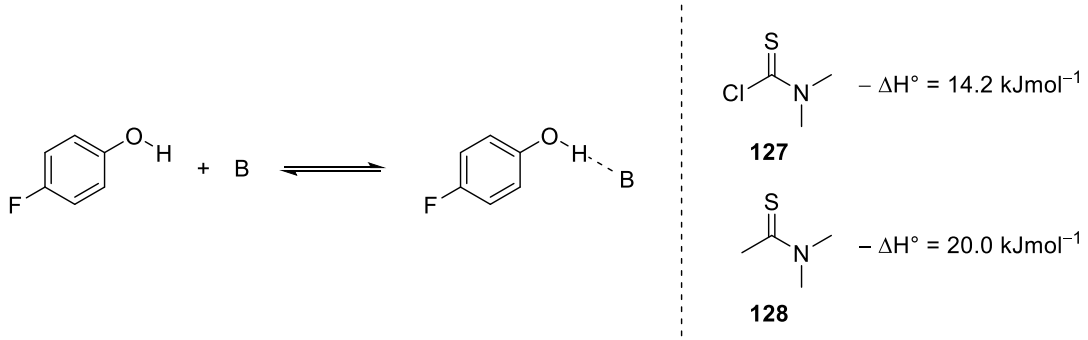
Lastly, the kinetics of the two types of intramolecular photoreactions were monitored for visible light-mediated (10 mol% **23**, λ = 420 nm) and direct irradiation conditions (λ = 350 nm) for substrates **39** and **51**. The quantum yields of the [2+2] photocycloaddition and cyclization/hydrogen abstraction cascade were determined in the presence of **23** at λ = 382 nm to be Φ = 0.233 ± 0.023 and Φ =0.050 ± 0.002, respectively. Therefore the [2+2] photocycloaddition is more than four times more efficient. The quantum yield for the uncatalyzed [2+2] photocycloaddition of **39** at λ = 368 nm was Φ = 0.231± 0.001. Hence, irrespective of a sensitizer the reaction is similarly efficient concerning product formation. However, without the catalyst the reaction time increased drastically and decomposition of the starting material became a predominant decay pathway.

3. Photochemical Reactions of Thiocarbonyl Compounds

3.1 Literature Background

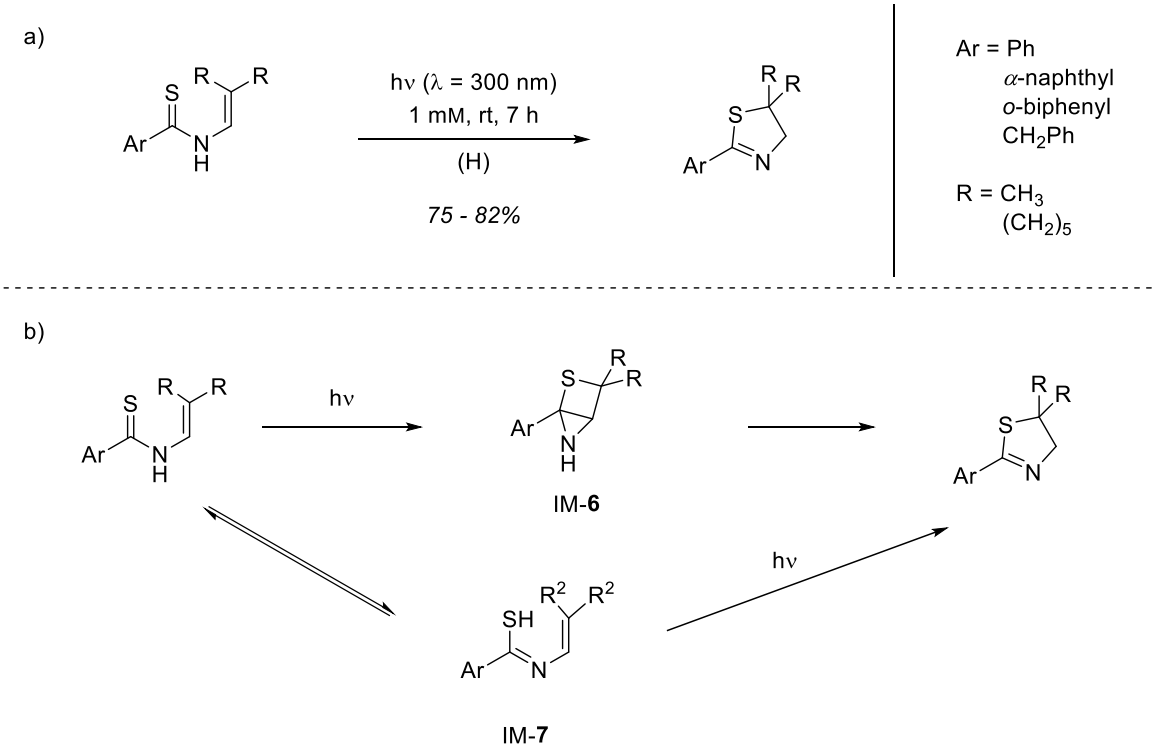
In contrast to their oxygen counterparts, the photoreactivity of thiocarbonyl compounds has not been studied extensively.[101] However, literature shows reports highlighting the differences in reactivity of thiocarbonyl compounds compared to the respective carbonyl compounds as their photophysical and thermodynamic properties differ significantly.[101-104] The lowest excited state energy of C=S compounds is considerably lower than for the respective C=O molecules[101,104] and e.g. $R_2\dot{C}$-SR radicals exhibit a different reactivity than $R_2\dot{C}$-OR radicals. Further, thiocarbonyl compounds are able to efficiently trap radicals or act as dienophiles. In general, most photochemical reactions occur from the first singlet (S_1) or triplet (T_1) state, nevertheless, thiocarbonyl compounds have also been known to react from their S_2 ($\pi\pi^*$) state which is accessible by excitation in the UV range (λ = 300 – 400 nm). Therefore different reaction types are commonly observed for visible light compared to UV irradiation.[101] This class of irradiation precursors exhibits a very weak $n\pi^*$ absorption which appears at very long wavelengths ($\lambda \geq 500$ nm). This makes selective excitation of the S_2 state possible and since the energy gap between S_1 and S_2 is quite large (up to 200 kJmol^{-1}) fluorescence can be observed from the S_2 state.[101,103,104] However, in numerous cases the formation of multiple compounds upon excitation has been observed instead of a defined photochemical transformation.[101-104]

In 2010 *Laurence et al.* investigated the hydrogen bonding between the aromatic alcohol *p*-fluorophenol (*p*-FPhOH) and different hydrogen bond acceptors.[105] The group determined the thermodynamics of the O-H···B hydrogen bond by FTIR spectroscopy by monitoring the change in the O-H band. The screening of a plethora of carbon π bases, oxygen bases and first- to fourth-row bases allowed them to establish a scale for *p*-FPhOH affinity which can be interpreted as a common hydrogen bond basicity scale. Their study included the two thiocarbonyl compounds **127** and **128** which gave negative enthalpies of hydrogen bonding with *p*-FPhOH of 14.2 kJmol^{-1} and 20.0 kJmol^{-1}, respectively (Scheme 45).[105] This outlines the possibility to involve at least thioamides into hydrogen bonding. If this interaction induced a shift in $\pi\pi^*$ absorption, enantioselective catalysis by selective excitation would become feasible.



Scheme 45. *p*-FPhOH affinity of two thiocarbonyl compounds **127** and **128**.[105]

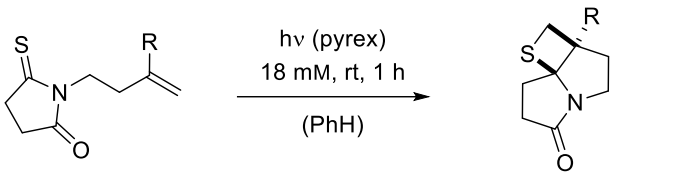
Potentially suitable photochemical cyclizations have been published by *Couture et al.*[106] or by *Padwa* and co-workers.[107,108] In the work by *Couture et al.* a cyclization of aromatic thioamides in hexane (H) upon irradiation with UV light afforded 5,5-dialkylthiazoline derivatives in good yields (75 – 82%) (Scheme 46, a).[106]



Scheme 46. a) Photochemical cyclization of aromatic thioamides; b) Mechanistic proposal for the formation of thiazoline products.[106]

Additionally, the group proposed two potential mechanisms for product formation (Scheme 46, b). A first pathway features thietane formation (intermediate IM-**6**) followed by ring opening of the highly strained intermediate IM-**6**. The second pathway takes the specific properties of the thiocarbonyl moiety into account as it has been shown to tautomerize to thioenol IM-**7** under similar reaction conditions. In this case a photochemically induced intramolecular attack of the thiol onto the double bond is presumed to form the five-membered heterocyclic compounds.[106]

Padwa and co-workers reported a [2+2] photocycloaddition under UV irradiation conditions. They probed two *N*-alkylated thioxopyrrolidinones **129** and **130**, which afforded the spirocyclic amidothietanes *rac*-**131** and *rac*-**132** in good yields of 68 – 73% (Scheme 47).[108] In the same work they conducted extensive research concerning the subsequent functionalization of the obtained photoproducts as well as the photoreactivity of analogous thiophtalimide and thioxopyrroline compounds.[108]



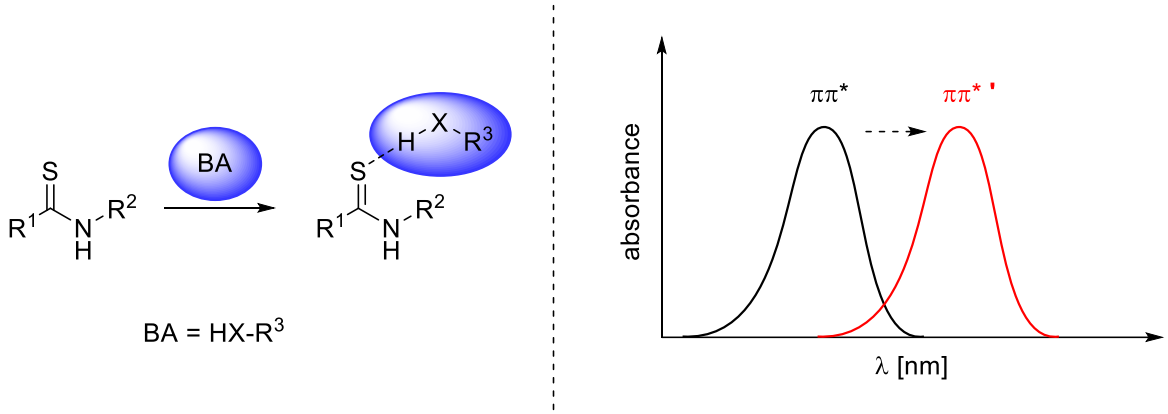
129 R = H
130 R = Me

rac-**131** R = H 68%
rac-**132** R = Me 73%

Scheme 47. Photochemical thietane formation from thioimides **129** and **130**.[108]

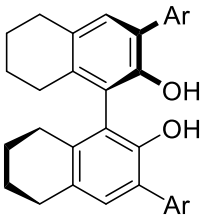
3.2 Project Aims

As stated earlier, on the ground of a common hydrogen bond basicity scale (*vide supra*), it seemed possible to involve thioamides into hydrogen bonding with *Brønsted* acids. This would ideally result in a bathochromic shift of the absorption maximum of the thiocarbonyl compound (Scheme 48). Hence, detailed UV/vis studies on the influence of the acidic strength of a *Brønsted* acid on the ππ*-transition were envisioned.



Scheme 48. Envisioned bathochromic shift of the ππ*-transition of thiocarbonyl compounds upon *Brønsted* acid (BA, HX-R^3) coordination.

In the case of a coordination-induced red shift of the absorption maximum, we aspired to develop a general procedure for the enantioselective photocatalysis of thiocarbonyl compounds. For this purpose we envisioned a selective long wavelength excitation of model substrates **130** and **133** in the presence of a chiral *Brønsted* acid such as binol derivatives **134** (Figure 24) which have previously been employed in an asymmetric *Morita-Baylis-Hillman* reaction.[109]

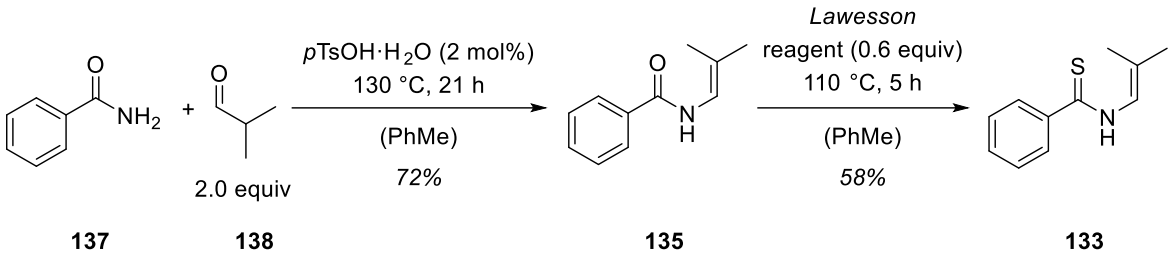


134

Figure 24. Structure of chiral binol-based *Brønsted* acids tentatively suggested for enantioselective photochemical reactions of thiocarbonyl compounds.

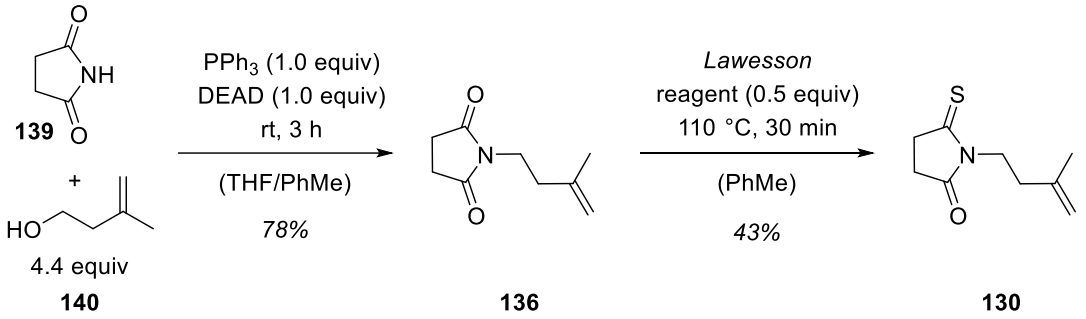
3.3 Substrate Synthesis

Both model substrates **129** and **133** were prepared from the respective carbonyl compounds **135** and **136** according to literature-known procedures.[106,108,110,111] First, benzamide (**137**) was refluxed with *i*-butyraldehyde (**138**) under acidic conditions in a *Dean-Stark* apparatus[111] to afford amide **135** in 72% yield. Subsequent treatment with *Lawesson* reagent [2,4-bis(4-methoxyphenyl)-2,4-dithioxo-1,3,2,4-dithiadiphosphetane][106] gave the desired thiocarbonyl compound **133** in 58% yield (Scheme 49).



Scheme 49. Synthesis of substrate **133** from benzamide (**137**).

For the preparation of irradiation precursor **130** a *Mitsunobu* reaction of succinimide (**139**) with 3-methylbut-3-en-1-ol (**140**) was used,[110] which gave the *N*-alkylated succinimide **136** in 78% yield. This compound was then treated with *Lawesson* reagent[108] and the thiocarbonyl substrate **130** was obtained in 43% yield (Scheme 50).



Scheme 50. Synthesis of substrate **130** from succinimide (**139**).

Initially, UV/vis spectra of the prepared substrates **130** and **133** were recorded in CH_2Cl_2 (Figure 25) and revealed a significant difference between the photophysical properties of both compounds. Thioamide **133** showed two equally intense absorption maxima at $\lambda = 272$ nm ($\varepsilon = 9134\ cm^{-1}M^{-1}$) and $\lambda = 332$ nm ($\varepsilon = 8528\ cm^{-1}M^{-1}$). These absorption

bands can be assigned to the nσ* and ππ* transition, respectively.[112] In contrast, for thioimide **130** only one major absorption maximum (ππ*) at λ = 277 nm (ε = 18 968 $cm^{-1}M^{-1}$) was detected. Spectroscopy at a higher concentration in CyH (*c* = 20 mM) revealed a very weak nπ* transition at λ = 396 nm (ε = 35 $cm^{-1}M^{-1}$) (Figure 26). In CH_2Cl_2 this nπ* transition was located at λ = 386 nm (ε = 44 $cm^{-1}M^{-1}$).

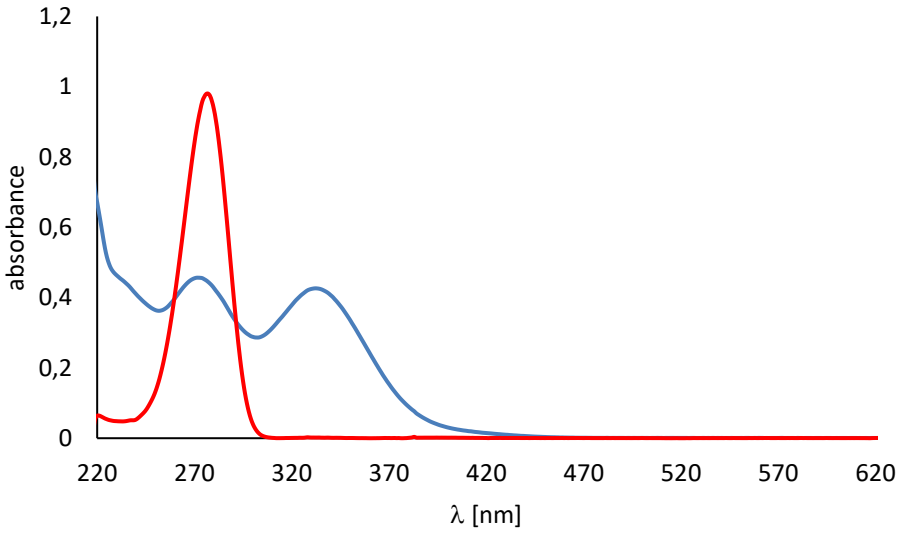


Figure 25. UV/vis spectra of thiocarbonyl compounds **133** (blue) and **130** (red) (*c* = 0.5 mM, CH_2Cl_2).

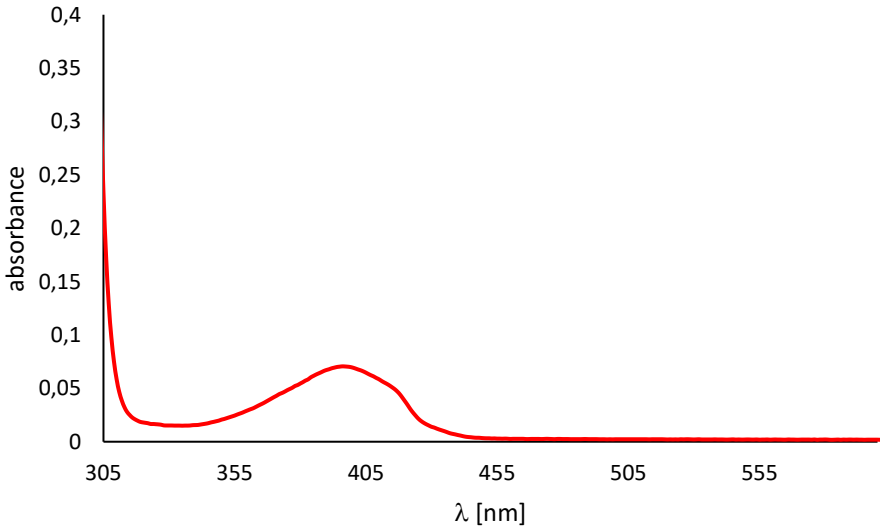


Figure 26. UV/vis spectrum of thiocarbonyl compound **130** (*c* = 20 mM, CyH).

3.4 UV/vis Studies and Irradiation Experiments with Thioamide 133

In the case of substrate **133** these initial measurements were followed by UV/vis spectroscopy performed upon addition of one equivalent of pentafluorophenol (F_5-PhOH), which was chosen as model hydrogen bond donor. The reason for this was the structural similarity to *p*-FPhOH, which had been used by *Laurence et al.* in their study (*vide supra*).[105] Compared to *p*-FPhOH the fully fluorinated phenol was assumed to have better hydrogen bonding properties due to the influence of five instead of one electronegative fluoro substituent. However, the obtained UV/vis spectra appeared to be merely an addition of the individual spectra of **133** and F_5-PhOH. No bathochromic shift was observed (Figure 27). Thus, hydrogen bonding for our system was not detectable by UV/vis spectroscopy. Nonetheless, a change in chemical shift of either the O-H proton of F_5-PhOH or the N-H proton of substrate **133** was anticipated if hydrogen bonding occurred due to an alteration of the electron density in either molecule upon coordination. However, no signal shift was observed for ^{1}H NMR spectra recorded in $CDCl_3$ at rt (Figure 28). Therefore, hydrogen bonding between **133** and F_5-PhOH remained without proof.

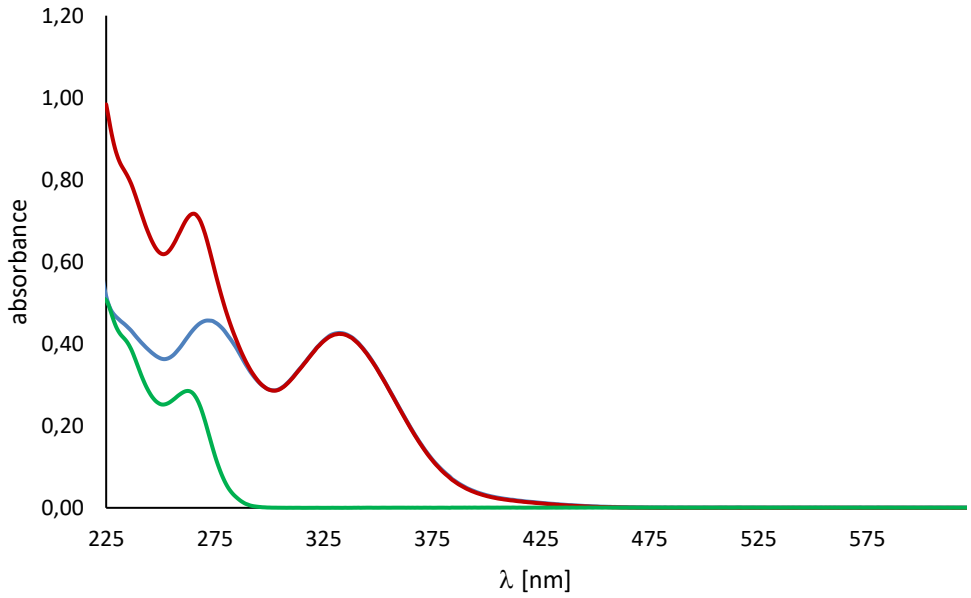


Figure 27. UV/vis spectra of F_5-PhOH (green) and thioamide **133** with (red) and without (blue) 1.0 equiv of C_6F_5OH (c = 0.5 mM, CH_2Cl_2).

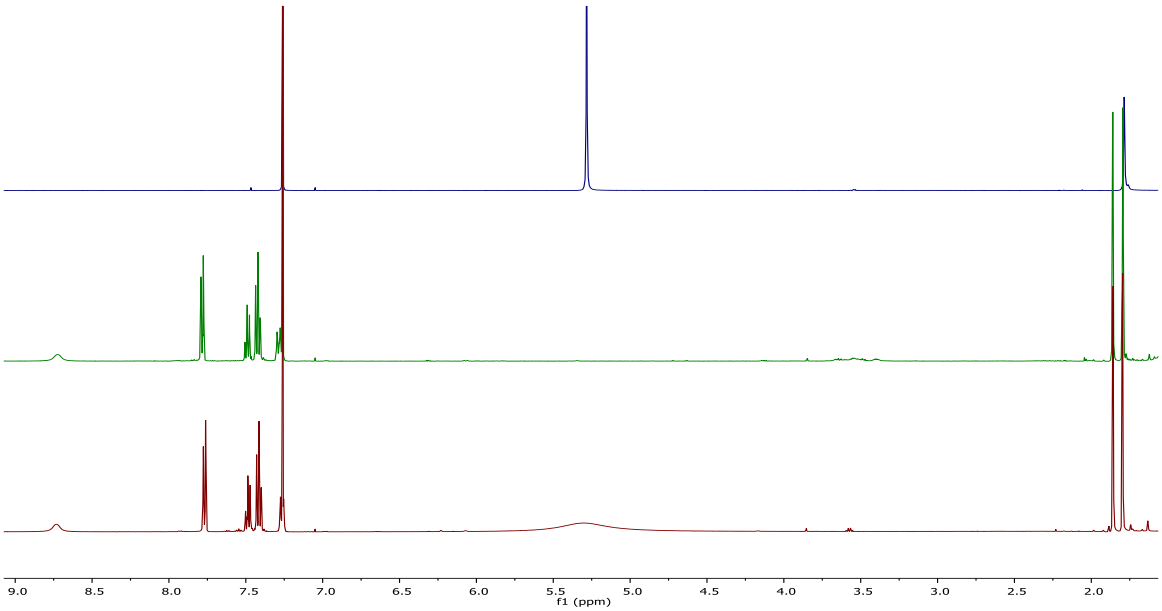


Figure 28. ^{1}H NMR spectra of F_5-PhOH (blue), thioamide **133** (green) and a mixture of both compounds (red).

In order to get a better insight into whether bonding to this thioamide **133** is in general detectable by UV/vis methods a broad variety of potential coordinating agents such as thioureas,[113] *Brønsted* and *Lewis* acids as well as two halogen bond donors (HD) (Figure 29) were investigated. It has been shown by *Huber* and co-workers that halogen bond-based organocatalysis is possible[114] and the structural features of these compounds seemed also intriguing for photocatalysis. The obtained spectra of measurements in CH_2Cl_2 are depicted in Figure 30 and Figure 31. The results are summarized in Table 11.

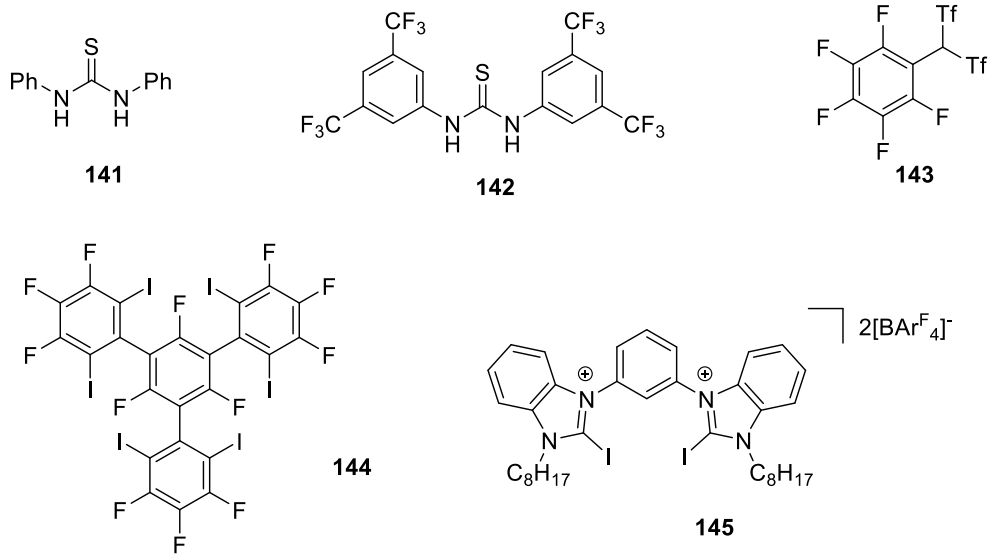


Figure 29. Strucutre of thioureas **141** and **142**, *Brønsted* acid **143** and HDs **144** and **145** tested for bonding to thiocarbonyl compounds **130** and **133**.

Upon addition of an excess of (*RS*)-binol, thioureas **141** and **142** (also known as *Schreiner's* catalyst),[113,115] *Brønsted* acid **143** as well as *p*-FPhOH, no bathochromic shift was observed (Figure 30, Table 11, entries 2 – 5, 13). Similar results were obtained for UV/vis spectra of thioamide **133** in the presence of the two HDs **144** and **145** as well as the *Lewis* acidic Au(I) and Cu(I) salts (Figure 30, Table 11, entries 8, 10 – 12). In the case of (*RS*)-binol and the HDs **144** and **145** the substrate spectrum was partially or fully obscured by the absorption bands of the respective additives (add.) (Figure 30).

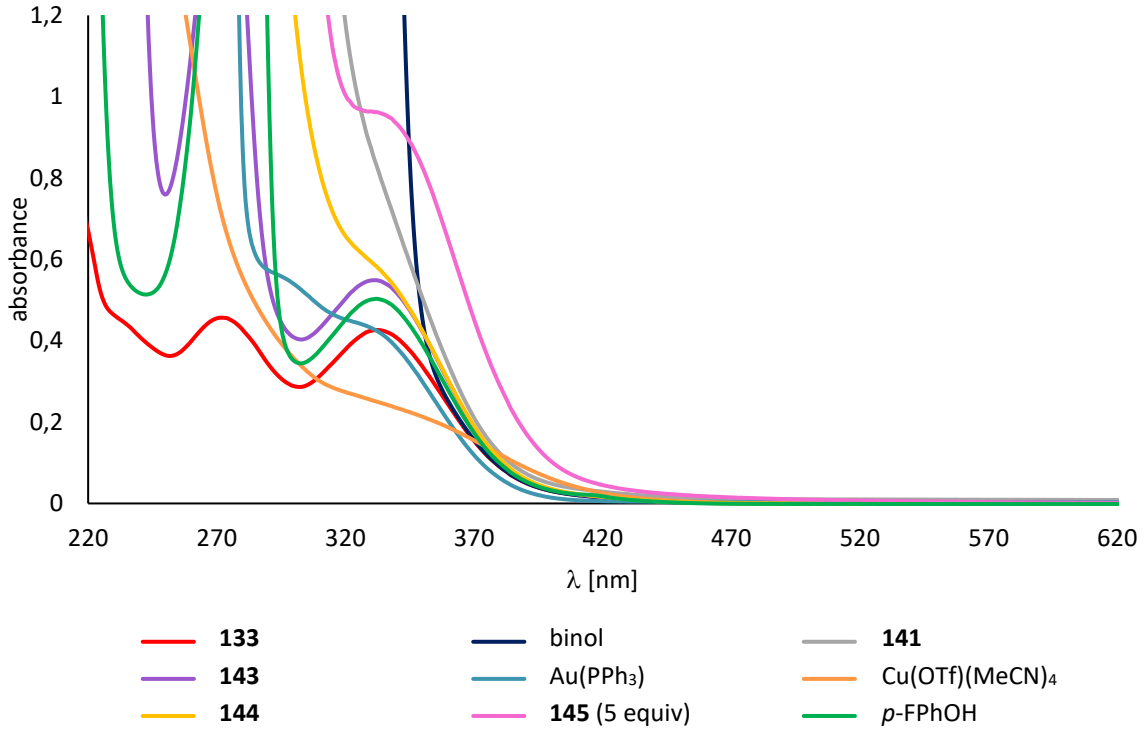


Figure 30. UV/vis spectra of thioamide **133** in the presence of a high excess (15 equiv) of different additives with no effect on the absorption of **133** (c = 0.5 mM, CH_2Cl_2).

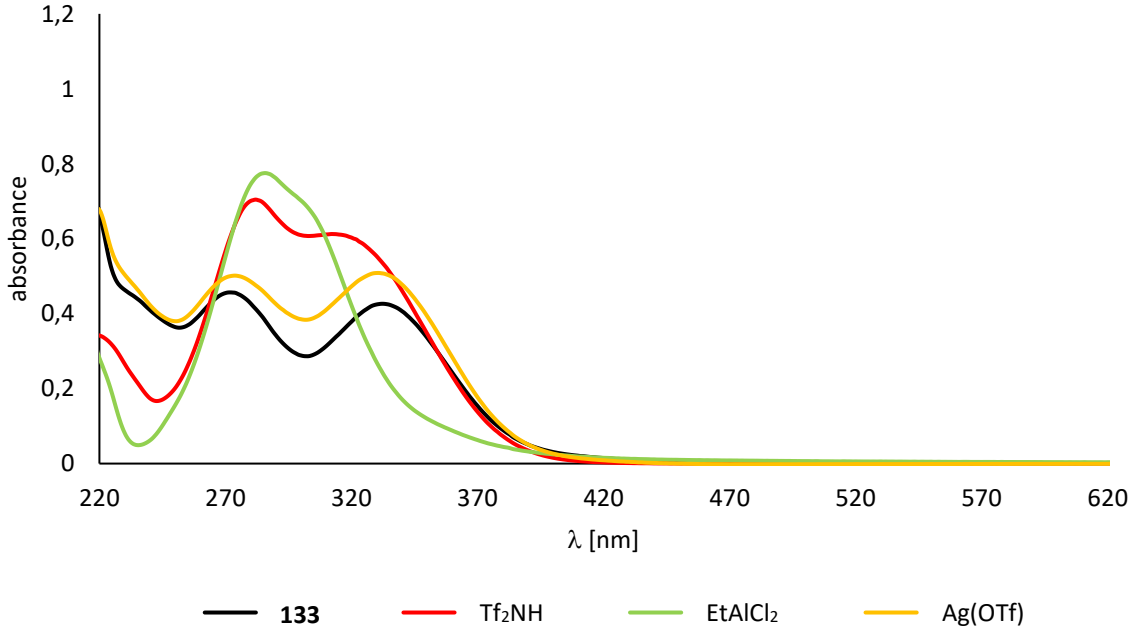
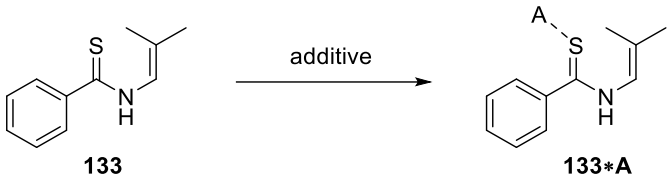


Figure 31. UV/vis spectra of thioamide **133** in the presence of a high excess (15 equiv) of *Brønsted* and *Lewis* acids with effect on the absorption of **133** (c = 0.5 mM, CH_2Cl_2).

Table 11. Variation of additives employed in the UV/vis studies on thioamide **133** in CH_2Cl_2.



133 **133∗A**

#	solv.	add. (15 equiv)	bath. shift	comment
1	CH_2Cl_2	F_5-PhOH	-	-
2	CH_2Cl_2	binol	-	-
3	CH_2Cl_2	thiourea **141**	-	minimal tailing
4	CH_2Cl_2	thiourea **142**	-	-
5	CH_2Cl_2	BA **143**	-	-
6	CH_2Cl_2	Tf_2NH	-	λ = 282 nm, ε = 14 088 $cm^{-1}M^{-1}$
7	CH_2Cl_2	$EtAlCl_2$	-	λ = 286 nm, ε = 15 502 $cm^{-1}M^{-1}$
8	CH_2Cl_2	$Cu(OTf)(MeCN)_4$	-	minimal tailing
9	CH_2Cl_2	Ag(OTf)	-	λ = 274 nm, ε = 10 030 $cm^{-1}M^{-1}$ λ = 286 nm, ε = 10 172 $cm^{-1}M^{-1}$
10	CH_2Cl_2	$Au(PPh_3)$	-	-
11	CH_2Cl_2	HD **144**	-	-
12	CH_2Cl_2	HD **145**[a]	-	-
13	CH_2Cl_2	*p*-FPhOH	-	-

[a] addition of 5 equiv

In contrast, a significant change in the absorption bands of **133** was detected for the *Brønsted* acid Tf_2NH and *Lewis* acids Ag(OTf) and $EtAlCl_2$ (Table 11, entries 6 – 7, 9). Interestingly, against our assumptions, the two absorption maxima started to merge (Figure 31). This trend became more pronounced, the stronger the employed acid was. It had been

determined by *Petiau* and *Fabian* that for thiocarbonyl compounds the spectral shift of the nπ* and ππ* transitions are dependent on the substitution. The two bands undergo opposite spectral shifts with a change in substitution pattern to larger (ππ*) and lower (nπ*) transition energies and consequently the two absorption bands approach each other.[112] Therefore, it can be assumed that the coordination of a *Lewis* or *Brønsted* acid affects the transition energies in a similar way for the ππ* and nσ* transitions. Unfortunately, the merger of absorption bands can be viewed as a hypsochromic shift of the electronic transition that is used for excitation. Thus, selective excitation of a substrate-catalyst complex becomes impossible and these acids are not applicable to an enantioselective photochemical transformation of **133** in CH_2Cl_2.

To probe the influence of solvent polarity, a selection of *Brønsted* acids was tested with **133** in CyH as an unpolar solvent (Figure 32). However, as in the previous study no bathochromic shift was observed for the two fluorinated phenols and thiourea **142** (Table 12). However, thiourea **142** was poorly soluble which most likely influenced this specific result (Table 12, entry 2). The spectrum of **133** in the presence of Tf_2NH exhibited great similarity to the spectrum measured in CH_2Cl_2 and not two distinct maxima but a merger of the latter became visible (Table 12, entry 3). Nonetheless, significant tailing in the visible light region ($\lambda > 400$ nm) was observed, which seemed promising for an application in catalytic photochemistry as there are reports by the *List* group on multiple catalytically active chiral *Brønsted* acids with a similar structural motif.[116]

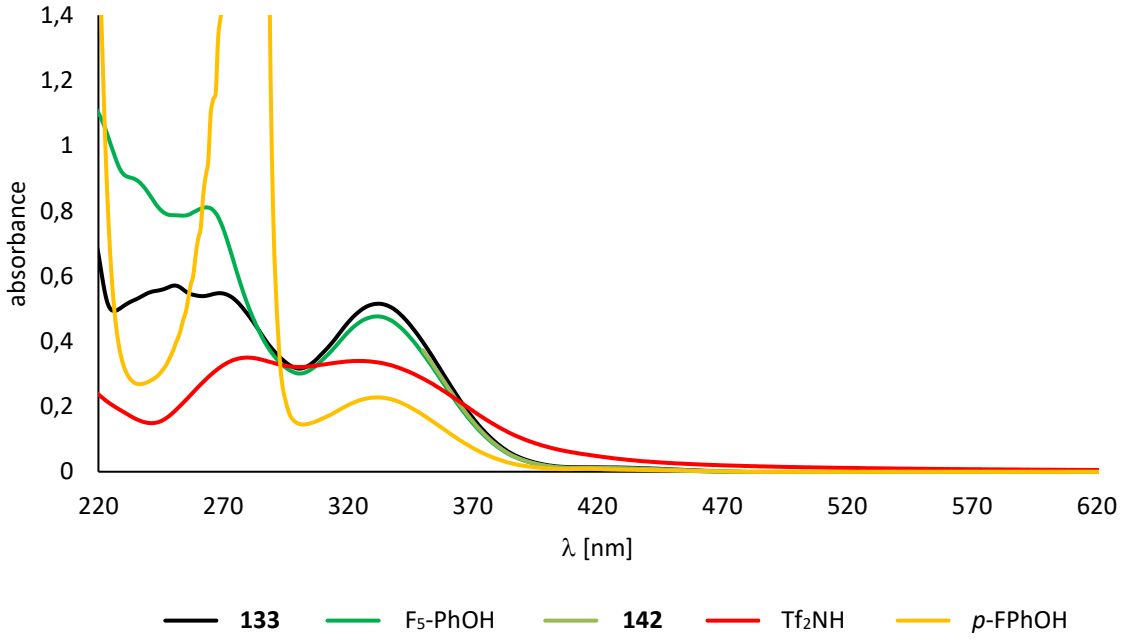
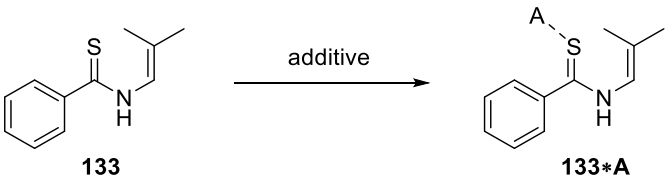


Figure 32. UV/vis spectra of thioamide **133** in the presence of a high excess (15 equiv) of different *Brønsted* acids (c = 0.5 mM, CyH).

Table 12. Variation of additives employed in the UV/vis studies on thioamide **133** in CyH.

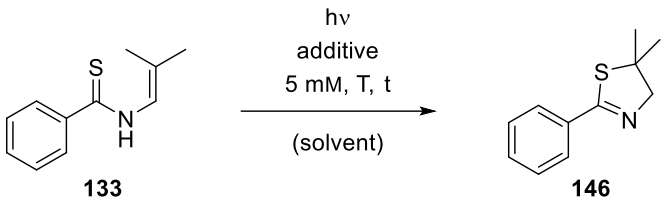


133 **133∗A**

#	solv.	add. (15 equiv)	bath. shift	comment
1	CyH	F_5-PhOH	-	-
2	CyH	thiourea **142**	-	poor solubility of **142**
3	CyH	Tf_2NH	-	broad tailing
4	CyH	*p*-FPhOH	-	-

With this set of UV/vis studies concluded we focused our further research on the photochemical cyclization of thioamide **133** (Table 13). In a first irradiation experiment the original conditions by *Couture et al.* at λ = 300 nm in H were reproduced and the thiazoline product **146** was isolated in 47% yield (entry 1). Compared to the literature the result was not satisfactory. Irradiation at λ = 420 nm under otherwise unchanged conditions gave an improved yield of 78% (entry 2) which is in the range of the 75% reported by *Couture et al.*[106] However, in both cases the product contained a small amount of undefined impurities. A change of solvent to CyH eliminated this issue, the reaction reached full conversion after 3 h for both wavelengths and the thiazoline **146** was obtained in very good yields (86 – 95%) (entries 3 – 4). Because full conversion was reached at λ = 420 nm after a short period of time, reaction conditions were screened in order to find a wavelength that would only allow for exclusive product formation upon addition of a catalyst. For this reason, λ was varied and the reaction solution irradiated for 14 – 15 h. Below λ = 500 nm over 70% conversion was observed by ^{1}H NMR spectroscopy (entry 5). At λ = 517 nm the conversion was still at 23%. However, this is the longest wavelength accessible by LEDs in our laboratories. It was therefore used for a test reaction in the presence of Tf_2NH, which resulted in a similar ratio of thioamide **133** to thiazoline **146** (sm/prod = 74/26) compared to the uncatalyzed conditions (entry 7).

Table 13. Variation of reaction conditions in the photochemical cyclization of thioamide **133** in CyH.



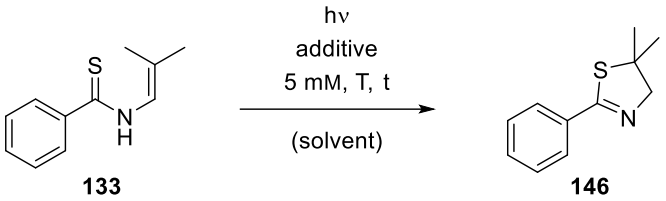
133 **146**

#	solv.	λ [nm]	add.	T [°C]	t [h]	Y [%][a]	sm/prod[b]
1	H	300	-	rt	14	47[c]	-
2	H	420	-	rt	14	78[c]	-
3	CyH	300	-	rt	3	95	-
4	CyH	420	-	rt	3	86	-
5	CyH	495	-	rt	14	-	22/78
6	CyH	517	-	rt	14.5	-	77/23
7	CyH	517	Tf_2NH[d]	rt	14.5	-	74/26

[a] isolated yield; [b] determined by ^{1}H NMR; [c] product contained impurities; [d] 15 equiv

Finally, irradiation in CH_2Cl_2 was performed for substrate **133** (Table 14). Full conversion was achieved at λ = 425 nm after 3 h and the product **146** was isolated in 65% yield (entry 1). Subsequently, longer wavelengths were screened and for λ = 470 nm still 27% conversion was observed by ^{1}H NMR. At λ = 497 nm no product was isolated (entry 3) and starting material was recovered quantitatively at λ = 517 nm after 14.5 h of irradiation (entry 5). Both wavelengths appeared to be suitable for a catalytic reaction in the presence of HD **145**. However, no product formation was detected in either experiment and the starting material was fully recovered in the latter case (entries 5 – 6).

Table 14. Variation of reaction conditions in the photochemical cyclization of thioamide **133** in CH_2Cl_2.



133 **146**

#	solv.	λ [nm]	add.	T [°C]	t [h]	Y [%][a]	sm/prod[b]
1	CH_2Cl_2	425	-	rt	3	65	-
2	CH_2Cl_2	470	-	rt	14.5	-	73/27
3	CH_2Cl_2	497	-	rt	14.5	-	-
4	CH_2Cl_2	497	HD **145** (10 mol%)	rt	14.5	-	-
5	CH_2Cl_2	517	-	rt	14.5	quant. rsm	-
6	CH_2Cl_2	517	HD **145** (2.5 mol%)	rt	14.5	quant. rsm	-

In general, an excitation wavelength of λ = 517 nm beared an inherent problem, since the very weak nπ* transition that was not observed by UV/vis is responsible for the excitation of the molecule. However, due to the efficiency of excitation at long wavelength it became difficult to exclude background reactions due to contamination by sun light. Therefore, it was doubtful whether this substrate is suitable for the visible light-induced enantioselective photocyclization we envisioned. Hence, we focused our research on 1-(3-methylbut-3-en-1-yl)pyrrolidine-2,5-dione (**130**) as a test substrate.

3.5 UV/vis Studies and Irradiation Experiments with Thioimide 130

For thiocarbonyl compound **130** the same array of additives was investigated by UV/vis spectroscopy (Figure 33, Figure 34). As for compound **133** no bathochromic shift was observed for most *Brønsted* and *Lewis* acids as well as the HDs **144** and **145** (Figure 33, Table 15, entries 1 – 4, 7 – 8 and 10 – 13).

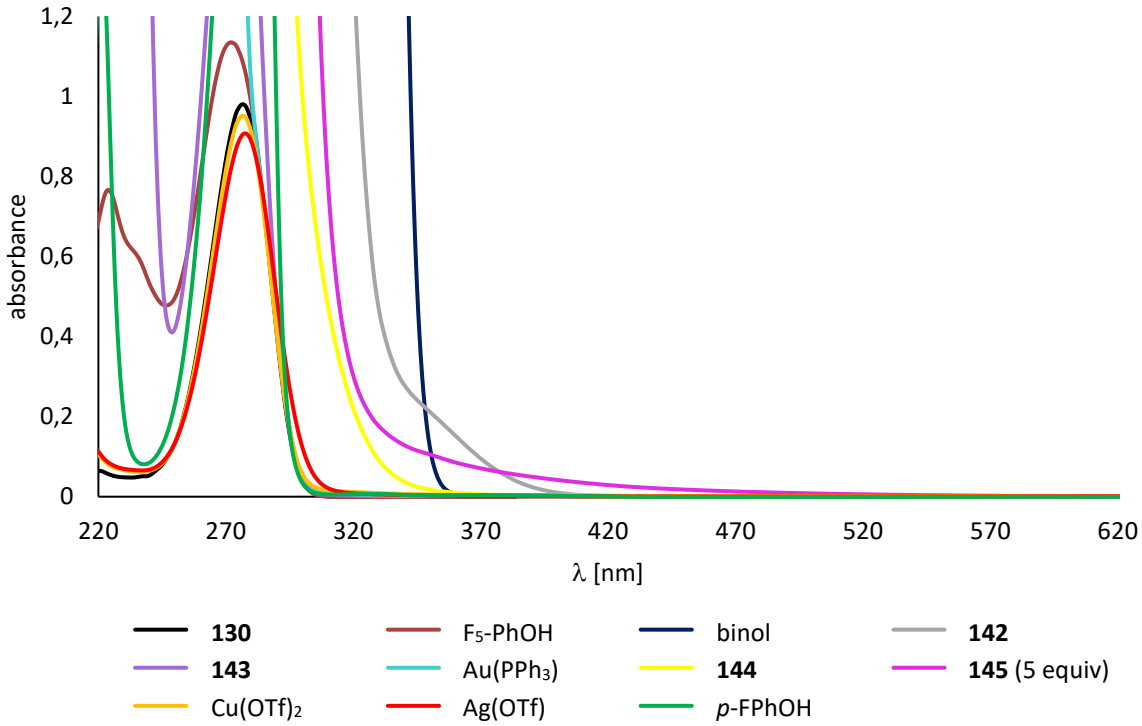


Figure 33. UV/vis spectra of thioimide **130** in the presence of a high excess (15 equiv) of different additives with no effect on the absorption of **130** (c = 0.5 mM, CH_2Cl_2).

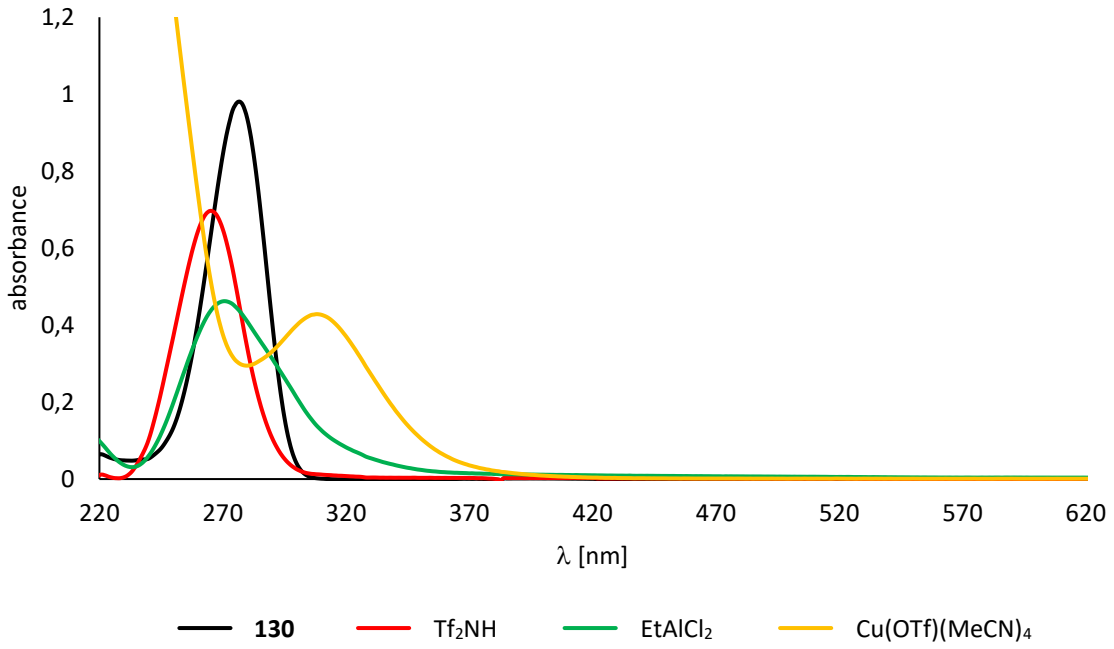
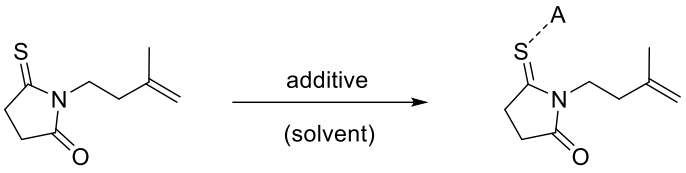


Figure 34. UV/vis spectra of thioimide **130** in the presence of a high excess (15 equiv) of *Brønsted* and *Lewis* acids with no effect on the absorption of **130** (c = 0.5 mM, CH_2Cl_2).

Similar to the previously investigated thioamide **133** Tf_2NH and $EtAlCl_2$ induced a hypsochromic shift of the absorption maximum of **130** (Table 15, entries 5 – 6). Additionally, a broad tailing was observed in the presence of $EtAlCl_2$ (Figure 34). To our delight, the addition of Cu(I) salt $Cu(OTf)(MeCN)_4$ to thioimide **130** resulted in a desired bathochromic shift of 31 nm as well as some broadening of the absorption band (Figure 34, Table 15, entry 9).

Table 15. Variation of additives employed in the UV/vis studies on thioimide **130** in CH_2Cl_2.



130 **130∗A**

#	solv.	add. (15 equiv)	bath. shift	comment
1	CH_2Cl_2	F_5-PhOH	-	-
2	CH_2Cl_2	binol	-	-
3	CH_2Cl_2	thiourea **142**	-	-
4	CH_2Cl_2	BA **143**	-	-
5	CH_2Cl_2	Tf_2NH	-	λ = 265 nm, ε = 13 938 $cm^{-1}M^{-1}$
6	CH_2Cl_2	$EtAlCl_2$	-	λ = 265 nm, ε = 13 938 $cm^{-1}M^{-1}$ tailing
7	CH_2Cl_2	HD **144**	-	-
8	CH_2Cl_2	HD **145**[a]	-	-
9	CH_2Cl_2	$Cu(OTf)(MeCN)_4$	31 nm	λ = 308 nm, ε = 8 570 $cm^{-1}M^{-1}$
10	CH_2Cl_2	$Cu(OTf)_2$	-	-
11	CH_2Cl_2	Ag(OTf)	-	-
12	CH_2Cl_2	$Au(PPh_3)$	-	-
13	CH_2Cl_2	*p*-FPhOH	-	-

[a] addition of 5 equiv

Additional UV/vis studies in CyH with the same selection of *Brønsted* acids that were used in previous experiments (*vide supra*) were conducted for substrate **130** (Figure 35). Also in accordance with the data obtained for compound **133** no change in the photophysical properties of **130** was observed by UV/vis for either *Brønsted* acid (Table 16).

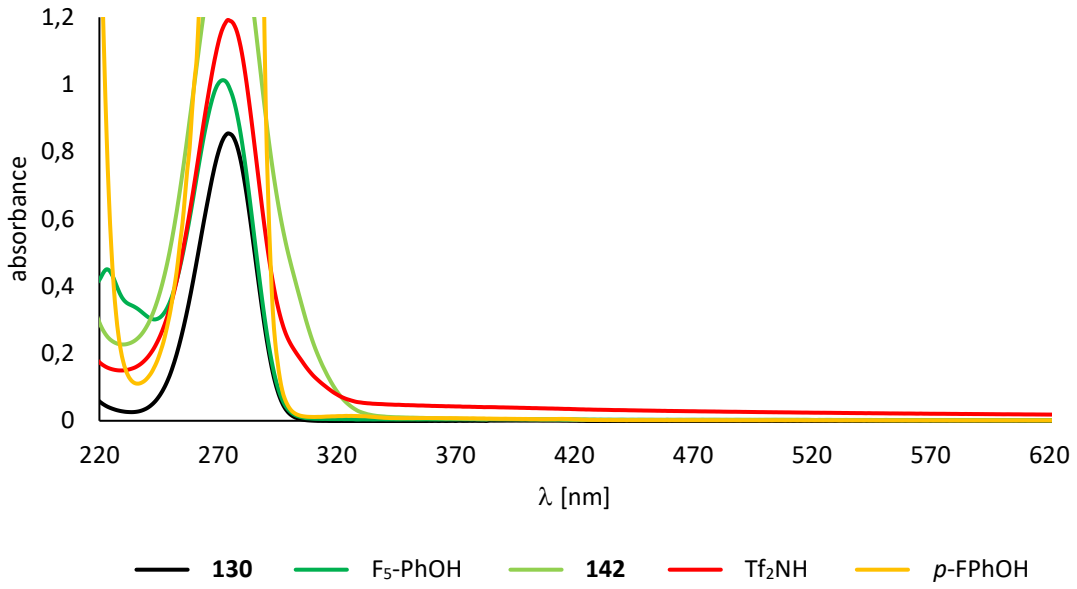
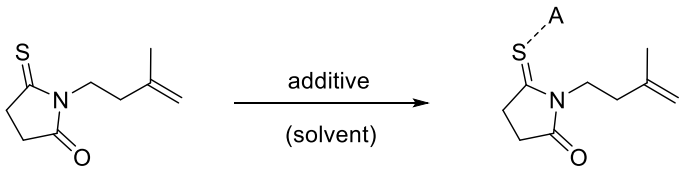


Figure 35. UV/vis spectra of thioimide **130** in the presence of a high excess (15 eq) of different *Brønsted* acids (*c* = 0.5 mM, CyH).

Table 16. Variation of additives employed in the UV/vis studies on thioimide **130** in CyH.

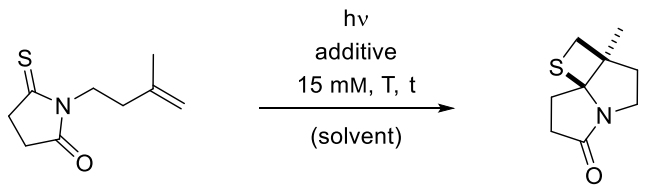


130 **130∗A**

#	solv.	add. (15 equiv)	bath. shift	comment
1	CyH	F_5-PhOH	-	-
2	CyH	thiourea **142**	-	poor solubility of **142**
3	CyH	Tf_2NH	-	broad tailing
4	CyH	*p*-FPhOH	-	-

In a next step, reaction conditions for the thioxetane formation were screened in order to obtain ideal parameters for an application of $Cu(OTf)(MeCN)_4$ and eventually chiral Cu(I) complexes (Table 17).

Table 17. Variation of reaction conditions in the photochemical cyclization of thioimide **130**.



130 *rac*-**132**

#	solv.	λ [nm]	add. (1.0 equiv)	T [°C]	t [h]	Y [%][a]
1	CH_2Cl_2	300 (quartz)	-	rt	2.3	66
2	CyH	300 (quartz)	-	rt	2.3	56
3	CH_2Cl_2	300 (duran)	-	rt	2.5	55
4	CyH	300 (duran)	-	rt	2.5	79
5	CH_2Cl_2	368	-	rt	2.5	96
6	CyH	368	-	rt	2.5	quant.
7	CH_2Cl_2	405	-	rt	2.5	63
8	CH_2Cl_2	424	-	rt	2.5	96[b]
9	CH_2Cl_2	424	$Cu(OTf)(MeCN)_4$	rt	2.5	71% rsm
10	CH_2Cl_2	368	$Cu(OTf)(MeCN)_4$	rt	2.5	94% rsm

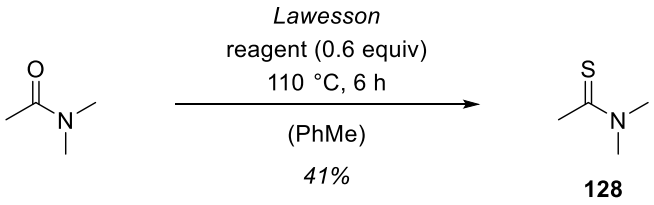
[a] isolated yield; [b] product contained impurities

Irradiation of compound **130** at λ = 300 nm in CH_2Cl_2 or CyH under application of either a quartz or duran filter resulted in full conversion after 2.3 h and afforded the heterocyclic product *rac*-**132** in moderate to good yields (55 – 79%) (Table 17, entries 1 – 4). The yield for both solvents could be further improved (96% – quant.) by an increase in wavelength (entries 5 – 6). Furthermore, the reaction occurred uncatalyzed upon irradiation with visible

light (λ = 405 or 424 nm) and product *rac*-**132** was isolated in 63% and 96% yield, respectively (entries 7 – 8). Nonetheless, the influence of $Cu(OTf)(MeCN)_4$ on the reaction rate was investigated at λ = 424 nm, but only starting material was recovered (71%) (entry 9). A similar result was obtained for irradiation with UV light (λ = 368 nm) at otherwise unchanged conditions as 94% of the starting material was recovered (entry 10). In contrast to our assumption, the addition of the Cu(I) salt did not accelerate but inhibit the photochemical transformation of thioimide **130**. Consequently, **130** was classified as unsuitable for our purposes as well.

3.6 UV/vis Studies on *N,N*-Dimethylthioacetamide (128)

Both compounds that were initially chosen for the UV/vis studies did not exhibit the behavior that was assumed for hydrogen bonding to the thiocarbonyl moiety. For this reason one of the compounds used by *Laurence et al.*[105] was prepared in 41% yield from the commercially available *N,N*-dimethylacetamide by treatment with *Lawesson* reagent (Scheme 51). The thiocarbonyl compound **128** showed an absorption maximum of λ = 273 nm and an extinction of ε = 13 000 – 15 000 $cm^{-1}M^{-1}$ depending on the solvent (Figure 36, Figure 37).



Scheme 51. Synthesis of thiocarbonyl compound **128**.

For this compound hydrogen bonding had been established by means of IR spectroscopy,[105] however, it could not be visualized by UV/vis spectroscopy in either CH_2Cl_2 (Figure 36) or CyH (Figure 37) with our set-up. Neither F_5-PhOH, nor *p*-FPhOH induced a bathochromic shift when added to *N,N*-thioacetamide (**128**) (Table 18). Hence, it was concluded that even though hydrogen bonding with thiocarbonyl compounds was empirically confirmed, it cannot be applied to their photochemistry in a beneficial way and is therefore unsuitable for the development of an enantioselective protocol that we had envisioned. Consequently, this area of research was not further pursued at this point.

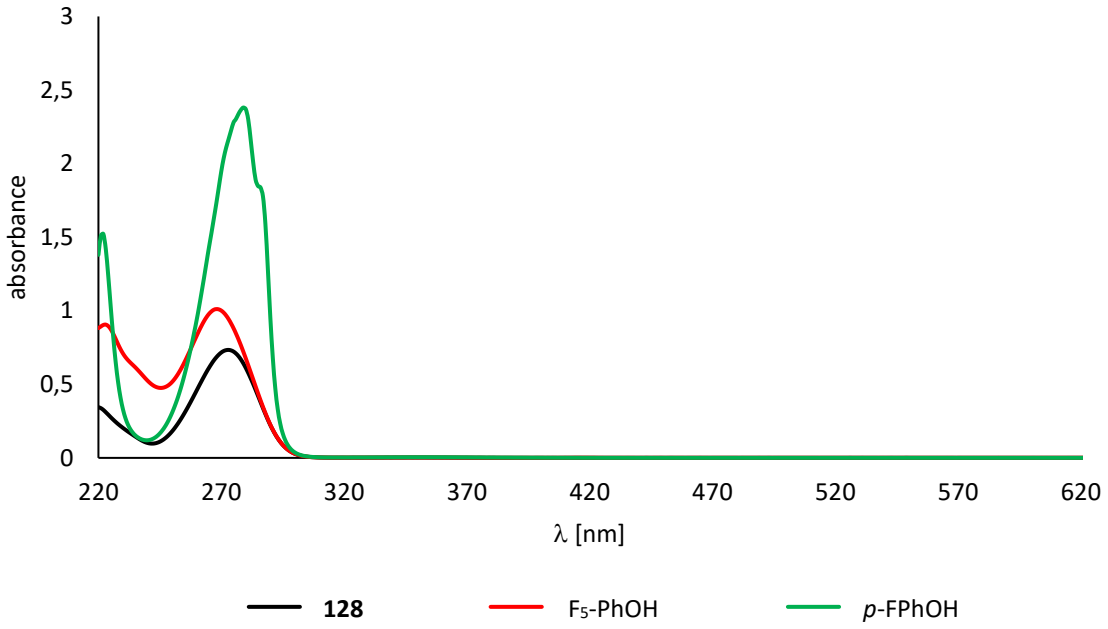


Figure 36. UV/vis spectra of thiocarbonyl compound **128** in the presence of a high excess (15 equiv) of F_5-PhOH and *p*-FPhOH (*c* = 0.5 mM, CH_2Cl_2).

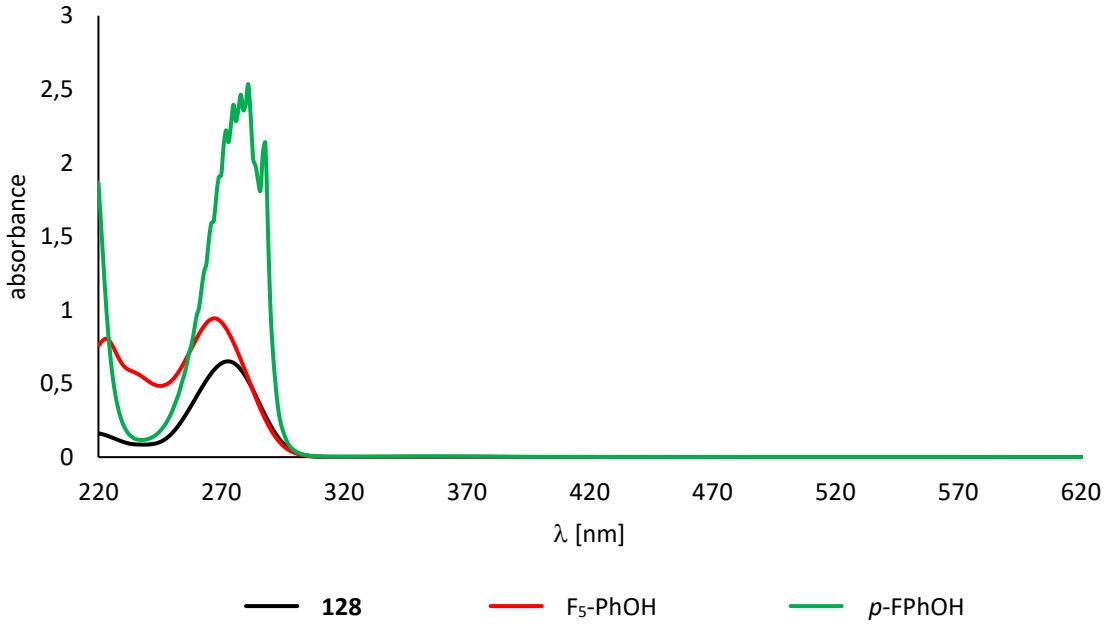
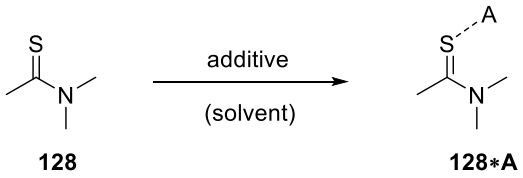


Figure 37. UV/vis spectra of thiocarbonyl compound **128** in the presence of a high excess (15 equiv) of F_5-PhOH and *p*-FPhOH (*c* = 0.5 mM, CyH).

Table 18. Variation of additives employed in the UV/vis studies on thiocarbonyl compound **128** in CH_2Cl_2 and CyH.



128 **128∗A**

#	solv.	Add. (15 equiv)	bath. Shift	comment
1	CH_2Cl_2	-	-	λ = 273 nm, ε = 14 674 $cm^{-1}M^{-1}$
2	CH_2Cl_2	F_5-PhOH	-	-
3	CH_2Cl_2	*p*-FPhOH	-	-
4	CyH	-	-	λ = 273 nm, ε = 13 016 $cm^{-1}M^{-1}$
5	CyH	F_5-PhOH	-	-
6	CyH	*p*-FPhOH	-	-

3.7 Summary

The three thiocarbonyl compounds **128**, **130** and **133** (Figure 38) were prepared starting from the respective carbonyl species by treatment with *Lawesson* reagent. The UV/vis properties of these compounds were intensively studied in the presence of several *Brønsted* and *Lewis* acids as well as HDs. Irrespective of the additive the UV/vis spectra closely resembled each other in most cases and no bathochromic shifts were observed. In all but one [addition of Cu(I) to **130**] of the cases in which addition of an acidic compound led to a shift of the absorption maximum, this shift was hypsochromic and consequently not viable for enantioselective catalysis in the sense of selective excitation of a coordinated thiocarbonyl moiety.

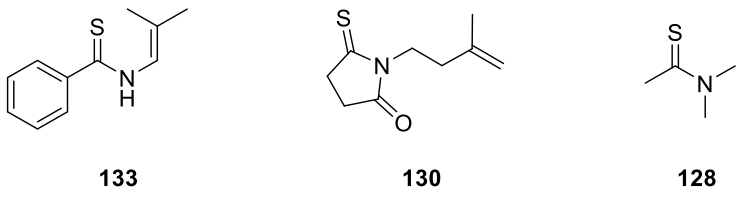
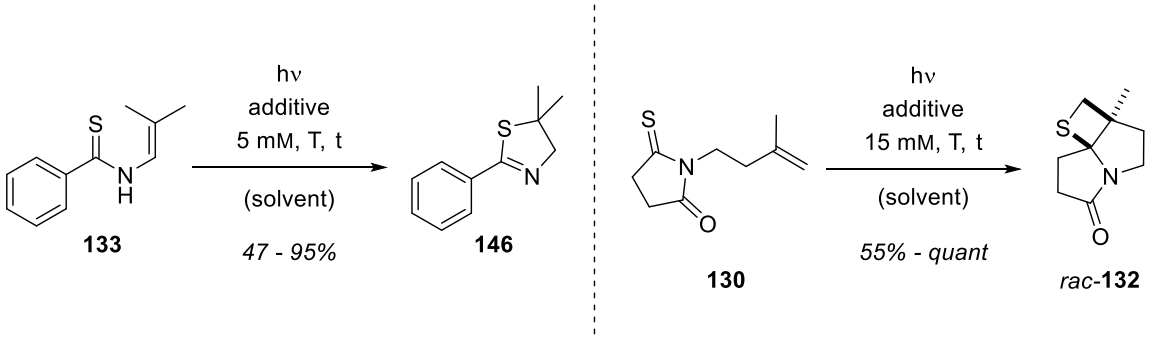


Figure 38. Structure of the thiocarbonyl compounds **128**, **130** and **133** employed in this work.

Nonetheless, reaction conditions for two photochemical reactions were screened and moderate to excellent yields were obtained depending on the reaction parameters (Scheme 52). A selection of *Brønsted* and *Lewis* acids was tested under optimized conditions, however, no beneficial influence of the acids on product formation was observed.



Scheme 52. Photochemical cyclization reactions of thiocarbonyl compounds **133** and **130** that were optimized in this work.

4. Experimental Part

4.1 General Information

All air and moisture sensitive reactions were carried out in flame-dried glassware under an argon atmosphere using standard *Schlenk* techniques. Commercially available chemicals were used without further purification unless otherwise mentioned. For moisture sensitive reactions, tetrahydrofuran (THF), diethylether (Et_2O) and dichloromethane (CH_2Cl_2) were dried using a MBSPS 800 *MBraun* solvent purification system. The following columns were used:

THF:	2 × MB-KOL-M type 2 (3 Å molecular sieve)
Et_2O:	1 × MB-KOL-A type 2 (aluminum oxide),
	1 × MB-KOL-M type 2 (3 Å molecular sieve)
CH_2Cl_2:	2 × MB-KOL-A type 2 (aluminum oxide)

Cyclohexane (CyH) was dried over neutral aluminum oxide and stored over 4Å molecular sieve. The following dry solvents are commercially available and were used without further purification:

N,N-Dimethylformamide :	*Acros Organics*, 99.5% extra dry, over molecular sieves
Toluene:	*Acros Organics*, 99.8% extra dry, over molecular sieves

For photochemical reactions, dry dichloromethane was degassed by three freeze-pump-thaw cycles. Technical solvents [1,2-dichloroethane (DCE), pentane (P), Et_2O, CH_2Cl_2, methanol (MeOH), ethyl acetate (EtOAc), CyH] were distilled prior to use. Flash column chromatography was performed on silica 60 (*Merck*, 230-400 mesh) with the indicated eluent mixtures. Cooling baths used were ice/water (0°C) and dry ice/ethanol (–78°C).

Photochemical experiments at 300, 350, 366 or 420 nm were carried out in flame-dried duran tubes (ø 1, 2 or 3 cm) in a positive geometry setup (cylindrical array of 16 *Southern New England Ultraviolet Company* Rayonet RPR-3000A fluorescent light tubes, 8 W nominal power, λ_{max} = 300 nm; *Hitachi/Luzchem* LZC-UVA fluorescent light tubes, 8 W nominal power, λ_{max} = 350 nm; *Rayonet* UV-A fluorescent light tubes, 8 W nominal power, λ_{max} = 366 nm or *Luzchem* LZC-420 fluorescent light tubes, 8 W nominal power,

λ_{max} = 420 nm) with the sample placed in the center of the illumination chamber. Photochemical experiments at wavelengths other than 300, 350, 366 or 420 nm were carried out in an LED *Schlenk* tube (ø 1 cm) with a polished quartz rod as an optical fiber, which was attached to the LED at one end and roughened by sandblasting at the other end. The roughed end had to be fully submerged in the solvent in order to guarantee optimal and reproducible reaction conditions.

4.2 Analytical Methods

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 [$KMnO_4$] followed by heat treatment.
$KMnO_4$-staining solution: potassium permanganate (3.00 g), potassium carbonate (20.0 g) and 5% aqueous sodium hydroxide solution (5.00 mL) in water (300 mL).

Infrared Spectra (IR) were recorded on a *Perkin Elmer* Frontier IR-FTR spectrometer by ATR technique. The signal intensity is assigned using the following abbreviations: vs (very strong), s (strong), m (medium), w (weak).

Nuclear Magnetic Resonance Spectra were recorded at rt 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) or benzene-d_6 (δ = 7.16 ppm). ^{13}C NMR spectra were referenced to the ^{13}C-D triplet of $CDCl_3$ (δ = 77.16 ppm) or the ^{13}C-D triplet of C_6D_6 (δ = 128.06 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: s-singlet, d-doublet, t-triplet, q-quartet, quint-quintet. Assignment and multiplicity of the ^{13}C NMR signals were determined by two-dimensional NMR experiments (COSY, HSQC, HMBC).

Melting Points were determined using a *Kofler* („Thermopan“, Fa. *Reichert*) melting point apparatus and were not corrected.

Mass Spectroscopy (MS) and High Resolution Mass Spectroscopy (HRMS) was measured on a *Thermo Scientific* DFS-HRMS spectrometer (EI).

UV/vis Spectra were measured on a *Perkin Elmer* Lambda 35 UV/vis spectrometer. Spectra were recorded using a *Hellma* precision cell made of quartz SUPRASIL® with a pathway of 1 mm. Solvents and concentrations are given for each spectrum.

4.3 Synthetic Procedures and Analytical Data

General procedure 1:
To a solution of the respective 1,2-cyclohexadione (1.0 equiv) in dry CyH (40 mL/g starting material) was added *p*-TsOH·H_2O (3.0 mol%) and the corresponding allylic alcohol (4.0 equiv). The reaction mixture was heated at reflux in a *Dean-Stark* apparatus for 15 – 17 h. The solution was cooled to rt, washed with brine (2 × 50 mL/g), dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was purified using flash column chromatography (P/Et_2O).

General procedure 2:
To a solution of the respective 1,2-cyclohexadione (1.0 equiv) in dry DMF (40 mL/g starting material) was added K_2CO_3 (1.2 equiv) and the respective allylbromide (1.2 equiv). The reaction mixture was stirred at rt for 4.5 – 21 h. The reaction was quenched by the addition of H_2O (20 mL/g). Subsequently, Et_2O (40 mL/g) was added and the layers were separated. The organic layer was washed with H_2O (4 × 40 mL/g) and brine (1 × 60 mL/g), dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (P/Et_2O).

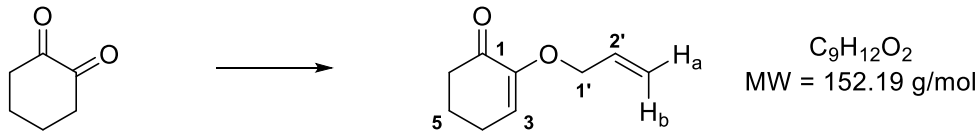
General procedure 3:
A round bottom flask charged with NaH (60 wt%, 1.2 equiv) was cooled to 0 °C and the respective allylic alcohol (30 equiv) was added dropwise. The reaction mixture was stirred for 10 min and subsequently the corresponding epoxide (1.0 equiv) was added dropwise. The reaction mixture was allowed to warm to rt and stirred for 20 – 24 h. The mixture was diluted with Et_2O (75 mL/g) and quenched by the addition of H_2O (35 mL/g). The layers were separated and the organic layer was washed with H_2O (1 × 35 mL/g) and brine (1 × 75 mL/g), dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (P/Et_2O).

General procedure 4:

To a solution of the respective 1,2-cyclopentadione (1.0 equiv) in dry DMF (40 mL/g starting material) was added K_2CO_3 (1.2 equiv) and the respective allylbromide (1.2 equiv). The reaction mixture was stirred at rt for 17 – 22 h. The reaction was quenched by the addition of H_2O (20 mL/g). Subsequently, Et_2O (40 mL/g) was added and the layers were separated. The organic layer was washed with H_2O (4 × 40 mL/g) and brine (1 × 60 mL/g), dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (P/Et_2O).

4.3.1 2-(2'-Alkenyloxy)cyclohex-2-en-1-ones

2-(Allyloxy)cyclohex-2-en-1-one (39)



45 **39**

According to general procedure 1, compound **39** was synthesized starting from diketone **45** (1.14 g, 10.2 mmol, 1.0 equiv), allylic alcohol (2.80 mL, 2.39 g, 41.2 mmol, 4.0 equiv) and *p*-TsOH·H_2O (65.2 mg, 343 µmol, 3.4 mol%). Purification by flash column chromatography (SiO_2, P/Et_2O = 5/1, UV) afforded the product (815 mg, 5.36 mmol, 53%) as a colorless oil.

TLC: R_f = 0.18 (P/Et_2O = 3/1) [UV, $KMnO_4$].

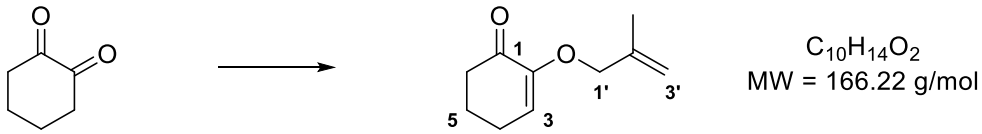
^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.97 (*virt.* quint. $^3J \approx {}^3J$ = 6.2 Hz, 2H, H-5), 2.41 (td, ^3J = 6.0, 4.7 Hz, 2H, H-4), 2.48 – 2.53 (m, 2H, H-6), 4.31 (*virt.* dt ^3J = 5.5 Hz, $^4J \approx {}^4J$ = 1.5 Hz, 2H, H-1'), 5.25 (ddt, ^2J = 1.5 Hz, ^3J = 10.6 Hz, ^4J = 1.5 Hz, 1H, H_a-3'), 5.33 (ddt, ^2J = 1.5 Hz, ^3J = 17.4 Hz, ^4J = 1.5 Hz, 1H, H_b-3'), 5.89 (t, ^3J = 4.7 Hz, 1H, H-3), 5.98 (ddt, ^3J = 17.4, 10.6, 5.5 Hz, 1H, H-2').

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 23.1 (t, C-5), 24.7 (t, C-4), 39.0 (t, C-6), 68.8 (t, C-1'), 118.1 (t, C-3'), 118.7 (d, C-3), 133.1 (d, C-2'), 150.5 (s, C-2), 194.5 (s, C-1).

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 259 nm (ε = 3736 $cm^{-1}M^{-1}$), 305 nm (ε = 99 $cm^{-1}M^{-1}$).

Data of this compound were in accordance with the literature.[60]

2-[(2-Methylallyl)oxy]cyclohex-2-en-1-one (40)



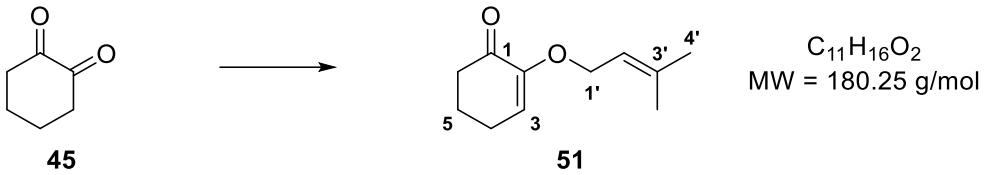
45 **40**

According to general procedure 1, compound **40** was synthesized starting from diketone **45** (1.00 g, 8.92 mmol, 1.0 equiv), methallylic alcohol (3.00 mL, 2.57 g, 35.7 mmol, 4.0 equiv) and *p*-TsOH·H_2O (52.3 mg, 275 µmol, 3.0 mol%). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1 → 4/1, UV) afforded the product (682 mg, 4.10 mmol, 46%) as a colorless oil.

TLC: R_f = 0.19 (P/Et_2O = 3/1) [UV, $KMnO_4$].
^{1}H NMR (500 MHz, C_6D_6, 300 K): δ [ppm] = 1.36 (*virt.* quint. $^3J \approx {}^3J$ = 6.1 Hz, 2H, H-5), 1.66 [s, 3H, C-2'(CH_3)], 1.74 (td, ^3J = 6.0, 4.6 Hz, 2H, H-4), 2.05 – 2.21 (m, 2H, H-6), 3.90 (s, 2H, H-1'), 4.86 (s, 1H, H-3'), 5.11 (s, 1H, H-3'), 5.30 (t, ^3J = 4.6 Hz, 1H, H-3).
^{13}C NMR (75 MHz, C_6D_6, 300 K): δ [ppm] = 19.8 (q, CH_3), 23.5 (t, C-5), 24.8 (t, C-4), 39.6 (t, C-6), 71.9 (t, C-1'), 113.0 (t, C-3'), 118.1 (d, C-3), 141.6 (s, C-2'), 151.5 (s, C-2), 190.4 (s, C-1).
UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 259 (ε = 4518 $cm^{-1}M^{-1}$).

Data of this compound were in accordance with the literature.[60]

2-[(3-Methylbut-2-en-1-yl)oxy]cyclohex-2-en-1-one (51)



45 **51**

According to general procedure 2, compound **51** was synthesized starting from diketone **45** (1.00 g, 8.92 mmol, 1.0 equiv), 3,3-dimethylallyl bromide (1.24 mL, 1.60 g, 10.7 mmol, 1.2 equiv) and K_2CO_3 (1.48 g, 10.7 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1 → 4/1 → 3/1, UV) afforded the product (227 mg, 1.26 mmol, 14%) as a colorless oil.

TLC: R_f = 0.15 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2926 (w, $C_{sp3}H$), 1686 (vs, C=O), 1622 (m, C=C), 1444 (w, $C_{sp3}H$), 1375 (w, $C_{sp3}H$), 1259 (m, C-O), 1184 (s, $C_{sp3}H$), 1148 (vs, C-O), 1003 (m, C=C), 874 (w, $C_{sp2}H$).

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.64 [s, 3H, C-3'(CH_3)*], 1.71 (s, 3H, H-4'*), 1.86 – 1.99 (m, 2H, H-5), 2.39 (td, ^3J = 6.1, 4.7 Hz, 2H, H-4), 2.47 (dd, ^3J = 7.4, 6.0 Hz, 2H, H-6), 4.23 (d, ^3J = 5.9 Hz, 2H, H-1'), 5.38 (*virt.* ddq, ^3J = 8.2, 5.9 Hz, $^4J \approx {}^4J$ = 1.5 Hz, 1H, H-2'), 5.85 (t, ^3J = 4.7 Hz, 1H, H-3).

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 18.2 [q, C-3'(CH_3)*], 23.0 (t, C-5), 24.6 (t, C-4), 25.8 (q, C-4'*), 38.9 (t, C-6), 64.6 (t, C-1'), 117.9 (d, C-3), 119.6 (d, C-2'), 137.6 (s, C-3'), 150.7 (s, C-2), 194.5 (s, C-1).

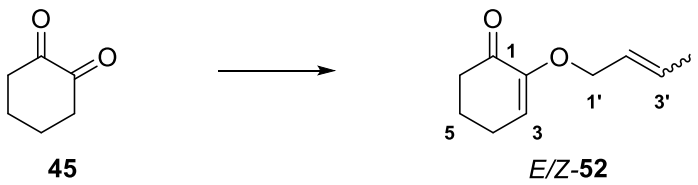
MS (EI, 70 eV): *m/z* (%) = 180 (27) [M^+], 147 (11), 134 (8), 118 (57), 112 (100) [M^+–C_5H_8], 99 (12), 95 (7) [$C_6H_7O^+$], 84 (27) [$C_5H_8O^+$].

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O_2$ [M]$^+$: 180.1148; found: 180.1145,
calc. for $C_{10}{}^{13}C_1H_{16}O_2$ [M]$^+$: 181.1185; found: 181.1178.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 261 nm (ε = 4126 $cm^{-1}M^{-1}$).

* Assignment is interconvertible.

(*E/Z*)-2-(But-2-en-1-yloxy)cyclohex-2-en-1-one (*E/Z*-52)



According to general procedure 1, compound *E/Z*-**52**[117] was synthesized starting from diketone **45** (1.00 g, 8.92 mmol, 1.0 equiv), crotyl alcohol (*E*/*Z* = 1/1) (3.00 mL, 2.55 g, 35.4 mmol, 4.0 equiv) and *p*-TsOH·H_2O (51.7 mg, 272 µmol, 3 mol%). Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, UV) afforded the product (510 mg, 3.07 mmol, 34%) as a colorless oil.

TLC: R_f = 0.14 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2939 (w, $C_{sp3}H$), 1686 (vs, C=O), 1622 (m, C=C), 1439 (w, $C_{sp3}H$), 1365 (w, $C_{sp3}H$), 1259 (m, C-O), 1185 (s, $C_{sp3}H$), 1149 (vs, C-O), 1006 (m, C=C), 965 (s, C=C), 872 (w, $C_{sp2}H$).

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.72 (dd, ^3J = 6.3 Hz, ^4J = 1.1 Hz, 3H, H-4'), 1.96 (*virt.* quint. $^3J \approx {}^3J$ = 6.2 Hz, 2H, H-5), 2.41 (*virt.* td, $^3J \approx {}^3J$ = 5.9 Hz, ^3J = 4.6 Hz, 2H, H-3), 2.50 (dd, ^3J = 7.4, 6.0 Hz, 2H, H-6), 4.20 (d, ^3J = 6.3 Hz, 2H, H-1'), 5.62 – 5.71 (m, 1H, H-2'*), 5.71 – 5.83 (m, 1H, H-3'*), 5.88 (t, ^3J = 4.6 Hz, 1H, H-3).

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 17.9 (q, C-4'), 23.1(t, C-5), 24.7 (t, C-4), 39.0 (t, C-6), 68.6 (t, C-1'), 118.1 (d, C-3), 125.9 (d, C-2'*), 130.9 (d, C-3'*), 150.6 (s, C-2), 194.5 (s, C-1).

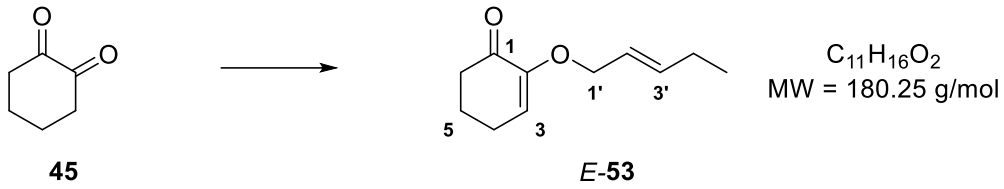
MS (EI, 70 eV): *m/z* (%) = 166 (21) [M^+], 112 (100) [M^+–C_4H_6], 95 (6) [$C_6H_7O^+$], 84 (32) [$C_5H_8O^+$].

HRMS (EI, 70 eV): calc. for $C_{10}H_{14}O_2$ [M]$^+$: 166.0988; found: 166.0988,
calc. for $C_9{}^{13}C_1H_{14}O_2$ [M]$^+$: 167.1022; found: 167.1025.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 260 nm (ε = 4882 $cm^{-1}M^{-1}$).

* Assignment is interconvertible.

(*E*)-2-(Pent-2-en-1-yloxy)cyclohex-2-en-1-one (*E*-53)



According to general procedure 1, compound *E*-**53** was synthesized starting from diketone **45** (250 mg, 2.23 mmol, 1.0 equiv), (*E*)-pent-2-en-1-ol (0.90 mL, 770 mg, 8.92 mmol, 4.0 equiv) and *p*-TsOH·H_2O (12.7 mg, 70.0 µmol, 3 mol%). Purification by flash column chromatography (SiO_2, P/Et_2O = 6/1 → 3/1, P/Et_2O = 6/1, UV) afforded the product (152 mg, 840 µmol, 38%) as a colorless oil.

TLC: R_f = 0.18 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2933 (w, $C_{sp3}H$), 1686 (vs, C=O), 1623 (m, C=C), 1458 (w, $C_{sp3}H$), 1365 (w, $C_{sp3}H$), 1259 (m, C-O), 1185 (s, $C_{sp3}H$), 1149 (vs, C-O), 1123 (s, C-O), 1007 (m, C=C), 967 (s, C=C), 880 (w, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.00 (t, ^3J = 7.5 Hz, 3H, H-5'), 1.96 (dt, ^2J = 12.4 Hz, ^3J = 6.0 Hz, 2H, H-5), 2.02 – 2.13 (m, 2H, H-4'), 2.41 (*virt.* td, $^3J \approx {}^3J$ = 6.0 Hz, ^3J = 4.6 Hz, 2H, H-4), 2.50 (dd, ^3J = 7.4, 6.0 Hz, 2H, H-6), 4.22 (dd, ^3J = 6.3 Hz, ^4J = 1.4 Hz, 2H, H-1'), 5.64 (dtt, ^3J = 15.5, 6.3 Hz, ^4J = 1.6 Hz, 1H, H-2'), 5.75 – 5.85 (m, 1H, H-3'), 5.88 (t, ^3J = 4.6 Hz, 1H, H-3).

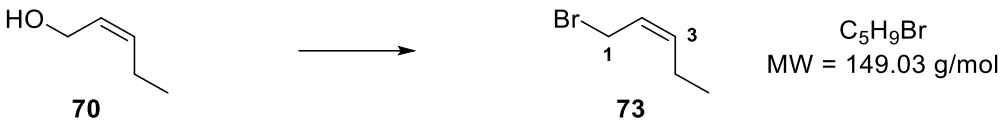
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 13.3 (q, C-5'), 23.1 (t, C-5), 24.7 (t, C-4), 25.5 (t, C-4'), 39.0 (t, C-6), 68.7 (t, C-1'), 118.2 (d, C-3), 123.5 (d, C-2'), 137.6 (d, C-3'), 150.5 (s, C-2), 194.6 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 180 (11) [M^+], 145 (93), 129 (11), 113 (16), 99 (100), 83 (23).

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O_2$ [$M]^+$: 180.1145; found: 180.1143.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 260 nm (ε = 4760 $cm^{-1}M^{-1}$).

(*Z*)-1-Bromopent-2-ene (73)[75]

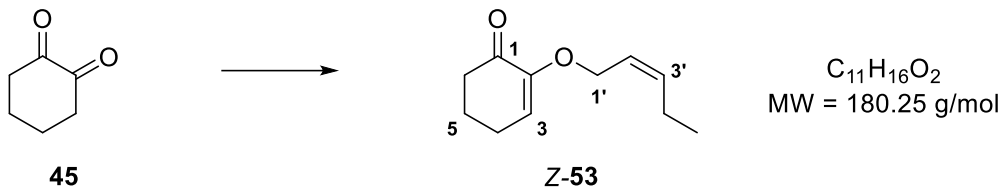


(*Z*)-Pent-2-en-1-ol (**70**) (0.81 mL, 689 mg, 8.00 mmol, 1.0 equiv) was dissolved in 16 mL of dry Et_2O and cooled to 0 °C. PBr_3 (0.90 mL, 2.60 g, 9.60 mmol, 1.2 equiv) was added dropwise, the reaction mixture was allowed to warm to rt and stirred for 4 h. The reaction was quenched by addition of 20 mL of H_2O and the layers were separated. The organic layer was washed with $NaHCO_{3(aq.)}$ (1 × 20 mL), H_2O (1 × 20 mL) and brine (1 × 20 mL), dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P, UV) the product **73** (119 mg, 0.80 mmol, 10%) was obtained as a colorless oil.

TLC: R_f = 0.67 (P) [UV, $KMnO_4$].
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.03 (t, ^3J = 7.5 Hz, 3H, H-5), 2.16 (*virt.* quint.d $^3J \approx {}^3J$ = 7.5 Hz, ^4J = 1.5 Hz, 2H, H-4), 4.00 (dd, ^3J = 8.3 Hz, ^4J = 0.7 Hz, 2H, H-1), 5.60 (dt, ^3J = 10.6, 7.4 Hz, 1H, H-3), 5.70 (m, 1H, H-2).
^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 13.9 (q, C-5), 20.4 (t, C-4), 27.4 (t, C-1), 124.8 (d, C-3), 137.7 (d, C-2).

Data of this compound were in accordance with the literature.[75]

(*Z*)-2-(Pent-2-en-1-yloxy)cyclohex-2-en-1-one (*Z*-53)



45 *Z*-**53**

According to general procedure 2, compound *Z*-**53** was synthesized starting from diketone **45** (520 mg, 4.64 mmol, 1.0 equiv), allyl bromide **73** (830 mg, 5.57 mmol, 1.2 equiv) and K_2CO_3 (770 mg, 5.57 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, H/EtOAc = 24/1 → 7/3 → 0/1, UV) afforded the product (133 mg, 737 µmol, 17%) as a colorless oil.

TLC: R_f = 0.19 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2933 (w, $C_{sp3}H$), 1687 (vs, C=O), 1622 (m, C=C), 1457 (w, $C_{sp3}H$), 1374 (w, $C_{sp3}H$), 1259 (m, C-O), 1185 (m, $C_{sp3}H$), 1149 (vs, C-O), 1123 (s, C-O), 1007 (m, C=C), 873 (w, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.99 (t, ^3J = 7.5 Hz, 3H, H-5'), 1.89 – 2.03 (m, 2H, H-5), 2.03 – 2.15 (m, 2H, H-4'), 2.42 (*virt.* td, $^3J \approx {}^3J$ = 6.0 Hz, ^3J = 4.6 Hz, 2H, H-4), 2.51 (dd, ^3J = 7.5, 6.0 Hz, 2H, H-6), 4.36 (d, ^3J = 5.1 Hz, 2H, H-1'), 5.43 – 5.67 (m, 2H, H-2', H-3'), 5.87 (t, ^3J = 4.6 Hz, 1H, H-3).

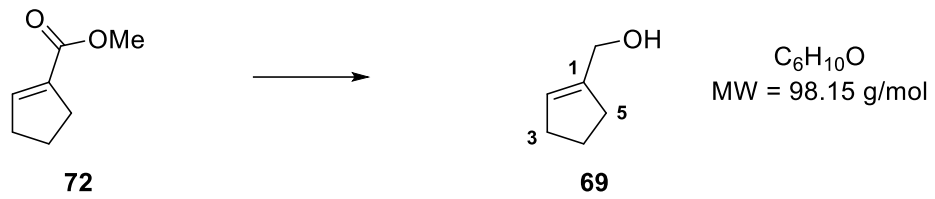
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.2 (q, C-5'), 21.3 (t, C-4'), 23.1 (t, C-5), 24.7 (t, C-4), 39.0 (t, C-6), 63.8 (t, C-1'), 118.2 (d, C-3), 124.0 (d, C-2'), 135.7 (d, C-3'), 150.5 (s, C-2), 194.6 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 180 (17) [M^+], 145 (58), 129 (11), 113 (100), 99 (87), 84 (40) [$C_5H_8O^+$].

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O_2$ [$M]^+$: 180.1145; found: 180.1145,
calc. for $C_{10}{}^{13}C_1H_{16}O_2$ [$M]^+$: 181.1178; found: 181.1183.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 259 nm (ε = 3754 $cm^{-1}M^{-1}$).

Cyclopent-1-en-1-ylmethanol (69)



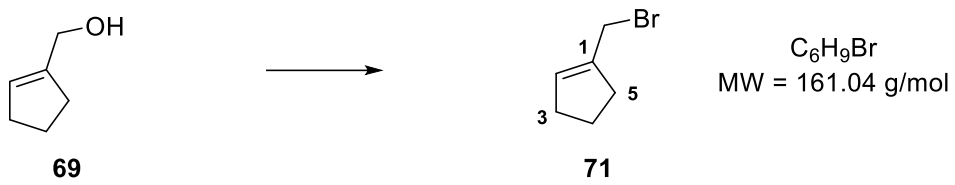
72 **69**

A solution of methyl cyclopent-1-ene-1-carboxylate (**72**) (200 µL, 200 mg, 1.60 mmol, 1.0 equiv) in 2.0 mL of dry tol was cooled to 0 °C and sodium bis(2-methoxyethoxy)aluminum hydride (60 wt% in tol, 0.75 mL, 712 mg, 3.52 mmol, 2.2 equiv) was added dropwise. The reaction mixture was stirred at this T for 2 h. Subsequently, the reaction was quenched by the addition of 2.0 mL saturated *Rochelle* salt solution and the aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layers were washed with brine (1 × 15 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P → P/Et_2O = 1/1, $KMnO_4$) the product **69** (65.7 mg, 688 µmol, 43%) was obtained as a colorless oil.

TLC: R_f = 0.38 (P/Et_2O = 1/1) [UV, $KMnO_4$].
^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.83 – 2.01 (m, 2H, H-4), 2.22 – 2.44 (m, 4H, H-3, H-5), 4.19 (s, 2H, C*H*$_2$OH), 5.61 (dd, ^3J = 3.6, 1.7 Hz, 1H, H-2).
^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 23.6 (t, C-4), 32.5 (t, C-5), 32.7 (t, C-3), 62.4 (t, CH_2OH), 125.6 (d, C-2), 144.4 (s, C-1).

Data of this compound were in accordance with the literature.[73]

1-(Bromomethyl)cyclopent-1-ene (71)



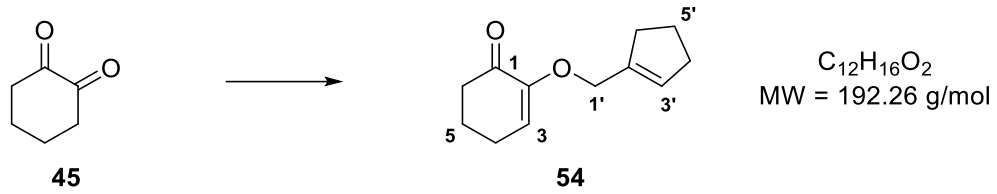
69 **71**

A solution of compound **69** (730 mg, 7.44 mmol, 1.0 equiv) in 30 mL of dry Et_2O was cooled to −78 °C and a solution of PBr_3 (350 µL, 1.01 g, 3.72 mmol, 0.5 equiv) in 5.5 mL of dry Et_2O was added dropwise. The reaction mixture was stirred at this T for 2 h, allowed to warm to rt and stirred for further 16 h. The reaction was diluted with 30 mL of Et_2O, quenched by addition of 8.0 mL of H_2O and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with brine (1 × 50 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P, $KMnO_4$) the product **71** (817 mg, 5.07 mmol, 68%) was obtained as colorless oil.

TLC: R_f = 0.84 (P/Et_2O = 3/1) [UV, $KMnO_4$].
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.95 (*virt.* quint., $^3J \approx {}^3J$ = 7.5 Hz, 2H, H-4), 2.33 – 2.39 (m, 2H, H-5), 2.40 – 2.46 (m, 2H, H-3), 4.09 (s, 2H, CH_2Br), 5.79 (t, ^3J = 5.8 Hz, 1H, H-2).
^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 23.6 (t, C-4), 31.8 (t, C-3), 33.0 (t, C-5), 33.4 (t, CH_2Br), 131.2 (d, C-2), 140.6 (s, C-1).

Data of this compound were in accordance with the literature.[74]

2-(Cyclopent-1-en-1-ylmethoxy)cyclohex-2-en-1-one (54)



According to general procedure 2, compound **54** was synthesized starting from diketone **45** (139 mg, 1.24 mmol, 1.0 equiv), allyl bromide **71** (130 mg, 1.18 mmol, 1.0 equiv) and K_2CO_3 (206 mg, 1.49 mmol, 1.3 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1 → 4/1 → 0/1, UV) afforded the product (46.8 mg, 243 μmol, 21%) as a colorless oil.

TLC: R_f = 0.20 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2926 (w, $C_{sp3}H$), 2847 (m, $C_{sp3}H$), 1686 (vs, C=O), 1622 (s, C=C), 1362 (w, $C_{sp3}H$), 1260 (m, C-O), 1185 (s, $C_{sp3}H$), 1149 (vs, C-O), 1122 (s), 1013 (m), 1002 (m, C=C), 872 (m, $C_{sp2}H$).

^{1}H NMR (400 MHz, C_6D_6, 300 K): δ [ppm] = 1.32 – 1.44 (m, 2H, H-5), 1.68 – 1.82 (m, 4H, H-4, H-5'), 2.11 – 2.17 (m, 2H, H-6), 2.22 (*virt.* ddt, ^2J = 9.9 Hz, ^3J = 6.5 Hz, $^3J \approx {}^4J$ = 2.2 Hz, 2H, H-6'), 2.32 (dddd, ^2J = 8.7 Hz, ^3J = 5.6, 2.5 Hz, ^4J = 1.3 Hz, 2H, H-4'), 4.08 (s, 2H, H-1'), 5.34 (t, ^3J = 4.5 Hz, 1H, H-3), 5.66 (*virt.* hept., $^3J \approx {}^4J$ = 1.8 Hz, 1H, H-3').

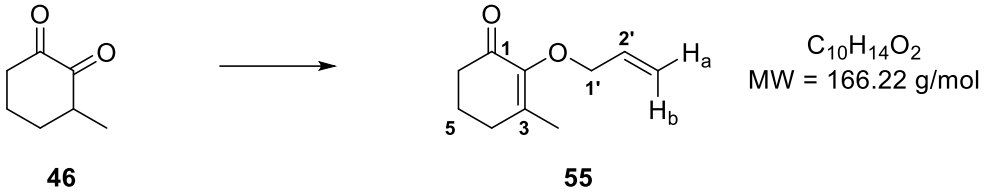
^{13}C NMR (101 MHz, C_6D_6, 300 K): δ [ppm] = 23.2 (t, C-5), 23.6 (t, C-5'), 24.5 (t, C-4), 32.8 (t, C-6'), 33.2 (t, C-4'), 39.3 (t, C-6), 66.9 (t, C-1'), 117.3 (d, C-3), 127.9 (d, C-3'), 140.5 (s, C-2'), 151.3 (s, C-2), 192.2 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 192 (9) [M^+], 113 (9), 80 (100) [$C_6H_8^+$], 67 (8) [$C_5H_7^+$], 55 (8), 41 (12) [$C_3H_5^+$].

HRMS (EI, 70 eV): calc. for $C_{12}H_{16}O_2$ $[M]^+$: 192.1145; found: 192.1137,
calc. for $C_{11}{}^{13}C_1H_{16}O_2$ $[M]^+$: 193.1178; found: 193.1168.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 260 nm (ε = 6728 $cm^{-1}M^{-1}$).

2-(Allyloxy)-3-methylcyclohex-2-en-1-one (55)



46 **55**

According to general procedure 2, compound **55**[56,58] was synthesized starting from diketone **46** (500 mg, 3.96 mmol, 1.0 equiv), allyl bromide (410 µL, 580 mg, 4.76 mmol, 1.2 equiv) and K_2CO_3 (670 mg, 4.85 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1, UV) afforded the product (259 mg, 1.56 mmol, 39%) as a colorless oil.

TLC: R_f = 0.30 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2928 (w, $C_{sp3}H$), 1672 (vs, C=O), 1631 (m, C=C), 1431 (w, $C_{sp3}H$), 1379 (w, $C_{sp3}H$), 1304 (w), 1193 (s, $C_{sp3}H$), 1153 (s, C-O), 985 (s, C=C), 926 (s, C=C).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.92 [s, 3H, C-3(CH_3)], 1.92 – 1.97 (m, 2H, H-5), 2.38 (t, ^3J = 6.1 Hz, 2H, H-4), 2.41 – 2.47 (m, 2H, H-6), 4.34 (*virt.* dt, ^3J = 6.0 Hz, $^2J \approx {}^4J$ = 1.4 Hz, 2H, H-1'), 5.18 (*virt.* dt, ^3J = 10.3 Hz, $^2J \approx {}^4J$ = 1.4 Hz, 1H, H_a-3'), 5.28 (*virt.* dtd, ^3J = 17.2 Hz, $^2J \approx {}^4J$ = 1.6 Hz, ^4J = 1.5 Hz, 1H, H_b-3'), 5.99 (ddt, ^3J = 17.0, 10.3, 6.0 Hz, 1H, H-2').

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 18.1 [q, C-3(*C*H_3)], 22.3 (t, C-5), 31.7 (t, C-4), 38.9 (t, C-6), 73.0 (t, C-1'), 117.8 (t, C-3'), 134.5 (d, C-2'), 146.4 (s, C-2*), 147.9 (s, C-3*), 194.9 (s, C-1).

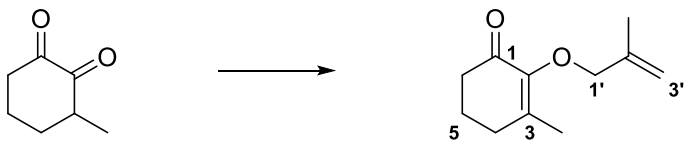
MS (EI, 70 eV): *m/z* (%) = 166 (80) [M^+], 151 (100) [M^+–CH_3], 137 (13), 125 (17) [M^+–C_3H_5], 113 (38), 110 (93) [$C_6H_6O_2^+$], 95 (82) [$C_6H_7O^+$], 82 (78).

HRMS (EI, 70 eV): calc. for $C_{10}H_{14}O_2$ $[M]^+$: 166.0982; found: 166.0988.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 247 nm (ε = 8212 $cm^{-1}M^{-1}$), 313 nm (ε = 77 $cm^{-1}M^{-1}$).

* Assignment is interconvertible.

3-Methyl-2-[(2-methylallyl)oxy]cyclohex-2-en-1-one (56)



46 **56**

$C_{10}H_{14}O_2$
MW = 166.22 g/mol

According to general procedure 2, compound **56** was synthesized starting from diketone **46** (500 mg, 3.96 mmol, 1.0 equiv), methallyl bromide (480 µL, 640 mg, 4.76 mmol, 1.2 equiv) and K_2CO_3 (660 mg, 4.76 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1, UV) afforded the product (414 mg, 2.29 mmol, 58%) as a colorless oil.

TLC: R_f = 0.29 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2920 (w, $C_{sp3}H$), 1673 (vs, C=O), 1632 (m, C=C), 1433 (w, $C_{sp3}H$), 1378 (m, $C_{sp3}H$), 1304 (m), 1193 (s, $C_{sp3}H$), 1151 (vs, C-O), 993 (m, C=C), 895 (m, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.82 [s, 3H, C-2'(CH_3)], 1.90 – 1.98 [m, 5H, H-5, C-3(CH_3)], 2.38 (t, ^3J = 6.1 Hz, 2H, H-4), 2.44 (t, ^3J = 6.7 Hz, 2H, H-6), 4.22 (s, 2H, H-1'), 4.90 (*virt.* t, $^2J \approx {}^4J$ = 2.0 Hz, 1H, H-3'), 5.02 (s, 1H, H-3').

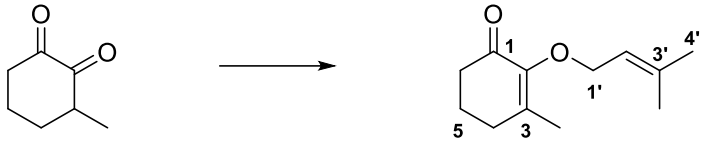
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 18.0 [q, C-3(*C*H_3)], 19.9 [q, C-2'(*C*H_3)], 22.3 (t, C-5), 31.7 (t, C-4), 38.9 (t, C-6), 75.7 (t, C-1'), 112.8 (t, C-3'), 142.0 (s, C-2'), 146.1 (s, C-3), 148.2 (s, C-2), 194.9 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 180 (100) [M^+], 165 (37) [M^+–CH_3], 137 (11), 123 (21), 110 (94) [$C_7H_{10}O^+$], 95 (74) [$C_6H_7O^+$].

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O_2$ [$M]^+$: 180.1145; found: 180.1145,
calc. for $C_{10}{}^{13}C_1H_{16}O_2$ [$M]^+$: 181.1185; found: 181.1178.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 248 nm (ε = 7196 $cm^{-1}M^{-1}$).

3-Methyl-2-[(3-methylbut-2-en-1-yl)oxy]cyclohex-2-en-1-one (57)



46 **57**

According to general procedure 2, compound **57**[57] was synthesized starting from diketone **46** (500 mg, 3.96 mmol, 1.0 equiv), 3,3-dimethylallyl bromide (550 µL, 710 mg, 4.76 mmol, 1.2 equiv) and K_2CO_3 (660 mg, 4.76 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1 → 3/1, UV) afforded the product (197 mg, 1.01 mmol, 26%) as a colorless oil.

TLC: R_f = 0.24 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2917 (w, $C_{sp3}H$), 1673 (vs, C=O), 1630 (m, C=C), 1433 (w, $C_{sp3}H$), 1381 (m, $C_{sp3}H$), 1301 (m), 1191 (s, $C_{sp3}H$), 1148 (s, C-O), 970 (m, C=C).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.68 [s, 3H, C-3'(CH_3)*], 1.75 (s, 3H, H-4'*), 1.86 – 2.03 [m, 5H, H-5, C-3(CH_3)], 2.38 (t, ^3J = 6.1 Hz, 2H, H-4), 2.41 – 2.45 (m, 2H, H-6), 4.32 (d, ^3J = 7.4 Hz, 2H, H-1'), 5.44 (*virt.* ddq, ^3J = 7.4, 5.9 Hz, $^4J \approx {}^4J$ = 1.4 Hz, 1H, H-2').

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 18.1 [q, C-3(CH_3), C-3'(CH_3)*], 22.3 (t, C-5), 26.0 (q, C-4'*), 31.6 (t, C-4), 38.9 (t, C-6), 68.3 (t, C-1'), 120.7 (d, C-2'), 138.2 (s, C-3'), 146.5 (s, C-3), 148.0 (s, C-2), 195.1 (s, C-1).

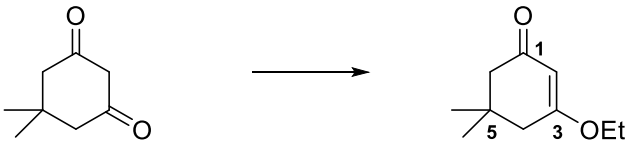
MS (EI, 70 eV): *m/z* (%) = 126 (100) [M^+–C_5H_8], 98 (11), 84 (23).

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O_2$ [M]$^+$: 194.1300; found:194.1301.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 248 nm (ε = 6640 cm^{-1} M^{-1}).

*Assignment is interconvertible.

3-Ethoxy-5,5-dimethylcyclohex-2-en-1-one (77)



76 **77**

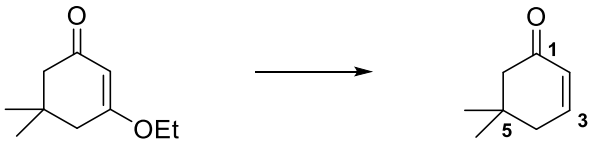
$C_{10}H_{16}O_2$
MW = 168.24 g/mol

According to a modified literature procedure:[22] To a solution of dimedone (**76**) (2.10 g, 15.0 mmol, 1.0 equiv) in 46 mL of dry tol were added EtOH (3.56 mL, 2.80 g, 61.0 mmol, 4.0 equiv) and *p*-TsOH·H_2O (139 mg, 0.73 mmol, 5.0 mol%). The reaction mixture was heated at reflux in a *Dean-Stark* apparatus for 90 min at which point EtOH (3.00 mL, 2.37 g, 50.3 mmol, 3.4 equiv) was added. Subsequently, the solution was refluxed for additional 14 h. It was allowed to cool to rt and the solvent was removed under reduced pressure. The crude product was filtered over a short plug of Al_2O_3 (Et_2O, UV) and the product **77** (2.52 g, 15.0 mmol, 100%) was obtained as a pale yellow oil.

TLC: R_f = 0.17 (P/Et_2O = 3/1) [UV, $KMnO_4$].
^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.07 (s, 6H, CH_3), 1.36 (t, ^3J = 7.0 Hz, 3H, CH_2CH_3), 2.21 (s, 2H, H-6), 2.27 (s, 2H, H-4), 3.90 (q, ^3J = 7.0 Hz, 2H, CH_2CH_3), 5.35 (s, 1H, H-2).
^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.3 (q, CH_2CH_3), 28.4 [q, C-5(CH_3)$_2$], 32.6 (t, C-5), 43.1 (t, C-6), 50.8 (t, C-4), 64.4 (t, CH_2CH_3), 101.6 (d, C-2), 176.5 (s, C-3), 199.8 (s, C-1).

Data of this compound were in accordance to the literature.[22]

5,5-Dimethylcyclohex-2-en-1-one (74)



77 **74**

$C_8H_{12}O$
MW = 124.18 g/mol

According to a modified literature procedure:[22] To an ice-cooled suspension of LAH (138 mg, 3.63 mmol, 0.4 equiv) in 4.0 mL of dry THF, a solution of 3-Ethoxy-5,5-dimethylcyclohex-2-en-1-one (**77**) (1.50 g, 8.92 mmol, 1.0 equiv) in 7.5 mL of dry THF was added. Subsequently, the reaction mixture was allowed to warm to rt and stirred for 3 h. The reaction mixture was then cooled to 0 °C and quenched by the addition of MeOH (approx. 10 mL) until no further gas evolution was observed. After addition of 14 mL 1M HCl the reaction was stirred for 30 min, the layers were separated and the aqueous layer was extracted wit Et_2O (3 × 30 mL). The combined organic layers were washed with brine (2 × 60 mL), dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 8/1, UV) the product **74** (663 mg, 5.34 mmol, 60%) was obtained as a colorless oil.

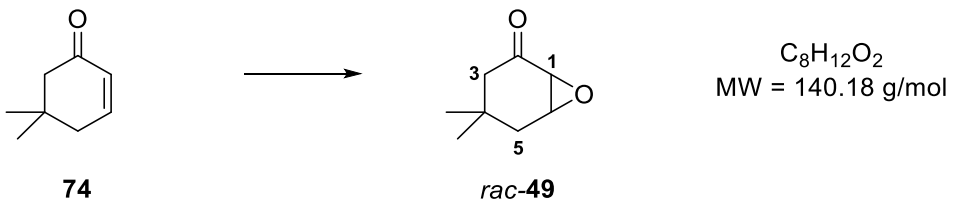
TLC: R_f = 0.29 (P/Et_2O = 1/1) [UV, $KMnO_4$].

^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.05 (s, 6H, CH_3), 2.24 (dd, ^3J = 4.1 Hz, ^4J = 2.1 Hz, 2H, H-4), 2.27 (s, 2H, H-6), 6.02 (dt, ^3J = 10.1 Hz, ^4J = 2.1 Hz, 1H, H-2), 6.86 (dt, ^3J = 10.1, 4.1 Hz, 1H, H-3).

^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 28.5 [q, C-5(CH_3)$_2$], 34.0 (s, C-5), 40.0 (t, C-4), 51.9 (t, C-6), 129.1 (d, C-2), 148.5 (d, C-3), 200.1 (s, C-1).

Data of the compound were in accordance with the literature.[22]

(1*SR*,6*SR*)-4,4-Dimethyl-7-oxabicyclo[4.1.0]heptan-2-one (*rac*-49)



74 *rac*-**49**

According to a modified literature procedure:[76] To an ice-cooled solution of 5,5-dimethyl-cyclohex-2-en-1-one[22] (**74**) (990 mg, 7.97 mmol, 1.0 equiv) in 16 mL of MeOH were dropwise added H_2O_2 (30-wt%, 3.30 mL, 1.10 g, 32.3 mmol, 4.1 equiv) and 6M NaOH (0.64 mL, 154 mg, 3.84 mmol, 0.5 equiv). The reaction mixture was allowed to warm to rt and stirred for 2 h. Subsequently, the reaction mixture was diluted with 32 mL of CH_2Cl_2 and H_2O was added until proper phase separation was achieved. The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (2 × 80 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 2/1, $KMnO_4$) the product *rac*-**49** (901 mg, 6.43 mmol, 80%) was obtained as a colorless oil.

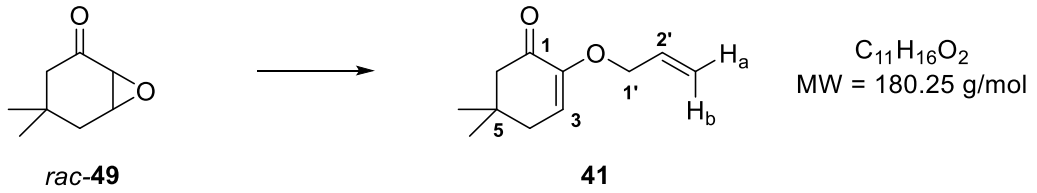
TLC: R_f = 0.56 (P/Et_2O = 2/1) [$KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.92 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.74 – 1.89 (m, 2H, H-5), 2.04 (d, ^2J = 14.3 Hz, 1H, H-3), 2.66 (d, ^2J = 14.3 Hz, 1H, H-3), 3.21 (*virt.* dt, ^3J = 3.8 Hz, $^3J \approx {}^3J$ = 1.0 Hz, 1H, H-6), 3.51 (dd, ^3J = 3.8, 4.7 Hz, 1H, H-1).

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 28.2 (q, CH_3), 31.2 (q, CH_3), 37.4 (t, C-3), 37.5 (t, C-5), 48.8 (s, C-4), 54.9 (d, C-1), 57.2 (d, C-6), 207.6 (s, C-2).

Data of this compound were in accordance with the literature.[118]

2-(Allyloxy)-5,5-dimethylcyclohex-2-en-1-one (41)



rac-**49** **41**

According to general procedure 3, compound **41**[56] was synthesized starting from epoxide *rac*-**49** (200 mg, 1.43 mmol, 1.0 equiv), allylic alcohol (3.00 mL, 2.55 g, 43.9 mmol, 31 equiv) and NaH (60 wt%, 72.0 mg, 1.80 mmol, 1.3 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1 → 6/1, UV) afforded the product (115 mg, 640 μmol, 45%) as a colorless oil.

TLC: R_f = 0.31 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2959 (m, $C_{sp3}H$), 1690 (vs, C=O), 1629 (m, C=C), 1467 (w, $C_{sp3}H$), 1368 (w, $C_{sp3}H$), 1165 (m, $C_{sp3}H$), 999 (m, C=C).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.06 [s, 6H, C-5(CH_3)$_2$], 2.31 (d, ^3J = 4.6 Hz, 2H, H-4), 2.37 (s, 2H, H-6), 4.32 (*virt.* dt, ^3J = 5.8 Hz, $^2J \approx {}^4J$ = 1.4 Hz, 2H, H-1'), 5.25 (*virt.* dq, ^3J = 10.6 Hz, $^2J \approx {}^4J$ = 1.3 Hz, 1H, H_a-3'), 5.33 (*virt.* dq, ^3J = 17.3 Hz, $^2J \approx {}^4J$ = 1.5 Hz, 1H, H_b-3'), 5.73 (t, ^3J = 4.6 Hz, 1H, H-3), 5.98 (ddt, ^3J = 17.2, 10.8, 5.5 Hz, 1H, H-2').

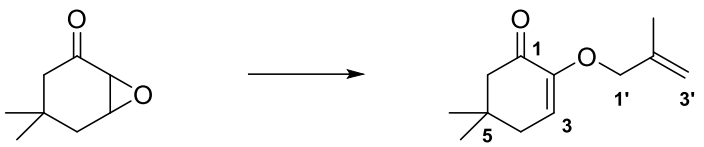
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 28.3 [q, C-5(CH_3)$_2$], 34.1 (s, C-5), 38.6 (t, C-4), 52.4 (t, C-6), 68.8 (t, C-1'), 116.1 (d, C-3), 118.2 (t, C-3'), 133.0 (d, C-2'), 149.8 (s, C-2), 194.5 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 180 (100) [M^+], 165 (10) [M^+–CH_3], 151 (10) [$C_9H_{11}O_2^+$], 127 (10), 124 (51) [$C_8H_{12}O^+$], 109 (49) [$C_7H_9O^+$], 95 (52) [$C_6H_7O^+$], 83 (19).

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O_2$ [M^+]: 180.1145; found: 180.1145.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 261 nm (ε = 5484 $cm^{-1}M^{-1}$).

5,5-Dimethyl-2-[(2-methylallyl)oxy]cyclohex-2-en-1-one (58)



rac-**49** **58**

$C_{12}H_{18}O_2$
MW = 194.27 g/mol

According to general procedure 3, compound **58** was synthesized starting from epoxide *rac*-**49** (200 mg, 1.43 mmol, 1.0 equiv), methallylic alcohol (2.40 mL, 2.06 g, 28.6 mmol, 20 equiv) and NaH (60 wt%, 70.0 mg, 1.75 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1, UV) afforded the product (102 mg, 527 µmol, 37%) as a colorless oil.

TLC: R_f = 0.40 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2958 (m, $C_{sp3}H$), 1691 (vs, C=O), 1629 (m, C=C), 1455 (w, $C_{sp3}H$), 1368 (w, $C_{sp3}H$), 1163 (m, $C_{sp3}H$), 902 (w, C=C).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.06 [s, 6H, C-5(CH_3)$_2$], 1.76 [s, 3H, C-2'(CH_3)], 2.29 (d, ^3J = 4.6 Hz, 2H, H-4), 2.36 (s, 2H, H-6), 4.25 (s, 2H, H-1'), 4.95 (s, 1H, H-3'), 5.00 (s, 1H, H-3'), 5.73 (t, ^3J = 4.6 Hz, 1H, H-3).

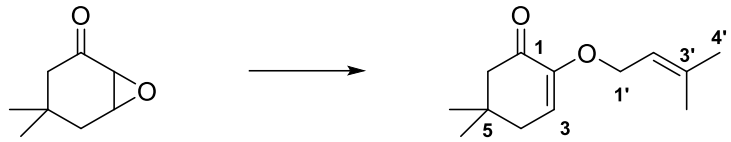
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 19.4 [q, C-2'(CH_3)$_2$], 28.3 [q, C-5(CH_3)], 34.2 (s, C-5), 38.5 (t, C-4), 52.4 (t, C-6), 71.6 (t, C-1'), 112.9 (t, C-3'), 116.3 (d, C-3), 140.5 (s, C-2'), 149.9 (s, C-2), 194.3 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 194 (57) [M^+], 179 (8) [M^+–CH_3], 151 (9) [$C_9H_{11}O_2^+$], 138 (22), 127 (14), 109 (100) [$C_7H_9O^+$], 95 (9) [$C_6H_7O^+$], 83 (14).

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O_2$ [M^+]: 194.1301; found: 194.1302.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 261 nm (ε = 4374 $cm^{-1}M^{-1}$).

5,5-Dimethyl-2-[(3-methylbut-2-en-1-yl)oxy]cyclohex-2-en-1-one (59)



rac-**49** **59**

$C_{13}H_{20}O_2$
MW = 208.30 g/mol

According to general procedure 3, compound **59** was synthesized starting from epoxide *rac*-**49** (200 mg, 1.43 mmol, 1.0 equiv), 3,3-dimethylallylic alcohol (4.50 mL, 3.83 g, 44.4 mmol, 31 equiv) and NaH (60 wt%, 69.0 mg, 1.73 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1, P/Et_2O = 9/1 → 6/1, UV) afforded the product (45.2 mg, 217 µmol, 15%) as a colorless oil.

TLC: R_f = 0.28 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2958 (m, $C_{sp3}H$), 1691 (vs, C=O), 1627 (m, C=C), 1452 (w, $C_{sp3}H$), 1368 (w, $C_{sp3}H$), 1162 (s, $C_{sp3}H$), 1108 (m, C-O), 1003 (w, C=C).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.06 [s, 6H, C-5(CH_3)$_2$], 1.68 (s, 3H, H-4'), 1.75 [s, 3H, C-3'(CH_3)], 2.31 (d, ^3J = 4.6 Hz, 2H, H-4), 2.36 (s, 2H, H-6), 4.28 (d, ^3J = 7.3 Hz, 2H, H-1'), 5.42 (ddd, ^3J = 7.3 Hz, ^4J = 4.1, 1.5 Hz, 1H, H-2'), 5.71 (t, ^3J = 4.6 Hz, 1H, H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 18.3 (q, C-4'*), 25.9 [q, C-3'(CH_3)$_2$], 28.3 [q, C-5(CH_3)], 34.1 (s, C-5), 38.6 (t, C-4), 52.4 (t, C-6), 64.6 (t, C-1'), 115.3 (d, C-3), 119.6 (d, C-2'), 137.7 (s, C-3'), 150.1 (s, C-2), 194.5 (s, C-1).

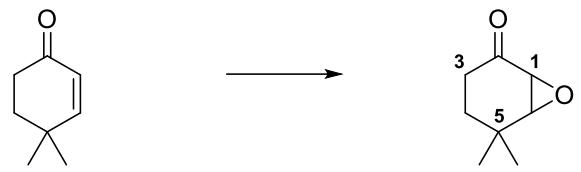
MS (EI, 70 eV): *m/z* (%) = 208 (28) [M^+], 175 (12), 146 (30), 140 (100) [M^+–C_5H_8], 125 (49), 112 (10), 98 (71), 84 (57).

HRMS (EI, 70 eV): calc. for $C_{13}H_{20}O_2$ $[M]^+$: 208.1458; found: 208.1445,
calc. for $C_{12}{}^{13}C_1H_{20}O_2$ $[M]^+$: 209.1491; found: 209.1482.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 263 nm (ε = 4500 $cm^{-1}M^{-1}$).

* Assignment is interconvertible.

(1*SR*,6*SR*)-5,5-Dimethyl-7-oxabicyclo[4.1.0]heptan-2-one (*rac*-50)



75 *rac*-**50**

$C_8H_{12}O_2$
MW = 140.18 g/mol

According to a modified literature procedure:[76] To an ice-cooled solution of 4,4-dimethyl-cyclohex-2-en-1-one (**75**) (2.00 g, 16.1 mmol, 1.0 equiv) in 32 mL of MeOH were dropwise added H_2O_2 (30-wt%, 8.23 mL, 80.5 mmol, 5.0 equiv) and 6M NaOH (1.33 mL, 8.05 mmol, 0.5 equiv). The reaction mixture was allowed to warm to rt and stirred for 3.5 h. Subsequently, the reaction mixture was diluted with 60 mL of CH_2Cl_2 and H_2O was added until proper phase separation was achieved. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 60 mL). The combined organic layers were washed with brine (1 × 120 mL), dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 6/1, $KMnO_4$) the product *rac*-**50** (1.67 g, 11.9 mmol, 74%) was obtained as a colorless oil.

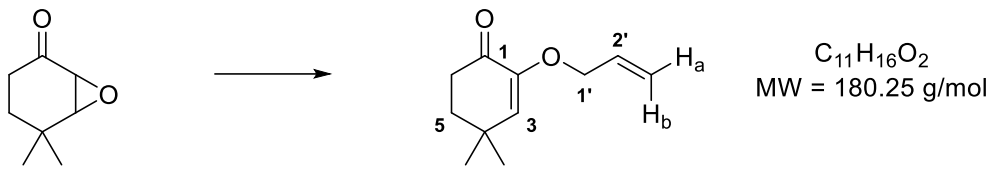
TLC: R_f = 0.68 (P/Et_2O = 2/1) [$KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.06 [s, 3H, C-5(CH_3)], 1.22 [s, 3H, C-5(CH_3)], 1.34 (dddd, ^2J = 13.7 Hz, ^3J = 7.1, 3.0 Hz, ^4J = 1.3 Hz, 1H, H-4), 1.90 (ddd, ^2J = 13.7 Hz, ^3J = 11.7, 6.4 Hz, 1H, H-4), 2.19 (ddd, ^2J = 18.9 Hz, ^3J = 11.7, 7.0 Hz, 1H, H-3), 2.40 (ddd, ^2J = 18.9 Hz, ^3J = 6.4, 3.0 Hz, 1H, H-3), 3.18 (dd, ^3J = 4.0 Hz, ^4J = 1.3 Hz, 1H, H-6), 3.23 (d, ^3J = 4.0 Hz, 1H, H-1).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 23.1 [q, C-5(*C*H_3)], 27.6 [q, C-5(*C*H_3)], 29.9 (t, C-4), 30.9 (s, C-5), 33.3 (t, C-3), 56.1 (d, C-1), 64.3 (d, C-6), 206.2 (s, C-2).

Data of this compound were in accordance with the literature.[118]

2-(Allyloxy)-4,4-dimethylcyclohex-2-en-1-one (60)



rac-**50** **60**

KOH (85 wt%, 94.2 mg, 1.43 mmol, 1.0 equiv) was dissolved in allylic alcohol (1.00 mL, 854 mg, 14.7 mmol, 10 equiv). A solution of epoxide *rac*-**50** (200 mg, 1.43 mmol, 1.0 equiv) in allylic alcohol (1.5 mL, 1.28 g, 22.1 mmol, 15 equiv) was then added dropwise, and the reaction mixture was stirred at rt overnight. Subsequently, the reaction mixture was diluted with 15 mL Et_2O and quenched by the addition of 15 mL H_2O. The layers were separated and the aqueous layer was extracted with Et_2O (2 × 15 mL). The combined organic layers were washed with brine (1 × 50 mL), dried over Na_2SO_4, filtered, and the solvent as well as the remaining allylic alcohol were removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 20/1 → 6/1, UV) product **60** (30.5 mg, 169 µmol, 12%) was obtained as a colorless oil.

TLC: R_f = 0.28 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2958 (m, $C_{sp3}H$), 1690 (vs, C=O), 1619 (s, C=C), 1458 (w, $C_{sp3}H$), 1362 (m, $C_{sp3}H$), 1261 (m), 1200 (s, $C_{sp3}H$), 1130 (s, $C_{sp3}H$), 1107 (s, C-O), 1014 (m, C=C), 925 (w, C=C).

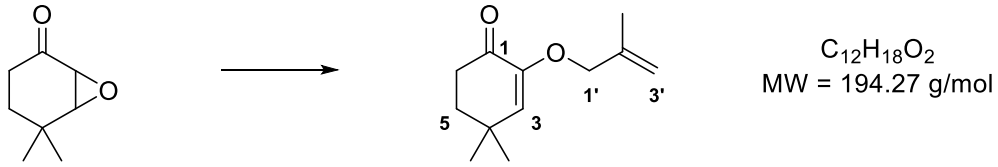
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.18 [s, 6H, C-4(CH_3)$_2$], 1.82 (t, ^3J = 6.5 Hz, 2H, H-5), 2.55 (t, ^3J = 6.5 Hz, 2H, H-6), 4.27 (*virt.* dt, ^3J = 5.6 Hz, $^4J \approx {}^4J$ = 1.5 Hz, 2H, H-1'), 5.24 (*virt.* dq, ^3J = 10.4 Hz, $^2J \approx {}^4J$ = 1.4 Hz, 1H, H_a-3'), 5.32 (*virt.* dq, ^3J = 17.2 Hz, $^2J \approx {}^4J$ = 1.6 Hz, 1H, H_b-3'), 5.59 (s, 1H, H-3), 5.97 (ddt, ^3J = 17.3, 10.8, 5.6 Hz, 1H, H-2').

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 29.2 [q, C-4(CH_3)$_2$], 33.0 (s, C-4), 35.0 (t, C-6), 36.0 (t, C-5), 68.7 (t, C-1'), 118.2 (t, C-3'), 128.7 (d, C-3), 132.9 (d, C-2'), 148.1 (s, C-2), 194.1 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 180 (24) [M^+], 165 (24) [M^+–CH_3], 137 (4), 124 (100) [$C_7H_8O_2^+$], 109 (23) [$C_6H_5O_2^+$], 96 (15), 83 (11).

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O_2$ $[M]^+$: 180.1145; found: 180.1144.
UV/vis (CH_2Cl_2, c = 0.5 mM): λ = 260 nm (ε = 7584 $cm^{-1}M^{-1}$).

4,4-Dimethyl-2-[(2-methylallyl)oxy]cyclohex-2-en-1-one (61)



rac-**50** **61**

KOH (85 wt%, 59.9 mg, 908 µmol, 1.0 equiv) was dissolved in methallylic alcohol (1.00 mL, 851 mg, 11.8 mmol, 13 equiv). A solution of epoxide *rac*-**50** (127 mg, 908 µmol, 1.0 equiv) in methallylic alcohol (1.0 mL, 851 mg, 11.8 mmol, 13 equiv) was then added dropwise and the reaction mixture was stirred at rt overnight. Subsequently, the reaction mixture was diluted with 15 mL Et_2O and quenched by the addition of 15 mL H_2O. The layers were separated and the aqueous layer was extracted with Et_2O (2 × 15 mL). The combined organic layers were washed with brine (1 × 50 mL), dried over Na_2SO_4, filtered, and the solvent as well as the remaining volatiles were removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 6/1, UV), product **61** (11.0 mg, 56.6 µmol, 6%) was obtained as a colorless oil.

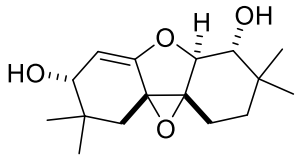
TLC: R_f = 0.37 (P/Et_2O = 3/1) [UV, $KMnO_4$].
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2958 (m, $C_{sp3}H$), 1692 (vs, C=O), 1619 (s, C=C), 1455 (w, $C_{sp3}H$), 1363 (m, $C_{sp3}H$), 1201 (s, $C_{sp3}H$), 1130 (s, $C_{sp3}H$), 1109 (s, C-O), 1014 (m, C=C), 901 (w).
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.17 [s, 6H, C-4(CH_3)$_2$], 1.76 [t, ^4J = 1.2 Hz, 3H, C-2'(CH_3)], 1.80 – 1.83 (m, 2H, H-5), 2.52 – 2.60 (m, 2H, H-6), 4.18 (s, 2H, H-1'), 4.94 (*virt.* quint., $^2J \approx {}^4J$ = 1.3 Hz, 1H, H-3'), 5.00 (*virt.* dq, ^2J = 2.1 Hz, $^4J \approx {}^4J$ = 1.2 Hz, 1H, H-3'), 5.60 (s, 1H, H-3).
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 19.5 [q, C-2'(CH_3)], 29.2 [q, C-4(CH_3)$_2$], 33.0 (s, C-4), 35.1 (t, C-6), 36.0 (t, C-5), 71.5 (t, C-1'), 113.1 (t, C-3'), 128.9 (d, C-3), 140.3 (s, C-2'), 148.2 (s, C-2), 194.1 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 194 (44) [M^+], 179 (31) [M^+–CH_3], 151 (14), 138 (100) [M^+–C_4H_8], 125 (20) [$C_7H_9O_2^+$], 109 (37) [$C_6H_5O_2^+$], 97 (22), 83 (10).

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O_2$ [M]$^+$: 194.1301; found:194.1301,
calc. for $C_{11}{}^{13}C_1H_{18}O_2$ [M]$^+$: 195.1335; found:195.1350.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 260 nm (ε = 6300 cm^{-1} M^{-1}), 338 nm (ε = 912 cm^{-1} M^{-1}).

(3*RS*,5a*SR*,6*RS*,9a*SR*,10a*RS*)-2,2,7,7-tetramethyl-2,3,5a,6,8,9-hexahydro-1*H*,7*H*-dibenzo[*b*,*d*]oxireno[2,3-*c*]furan-3,6-diol (78)

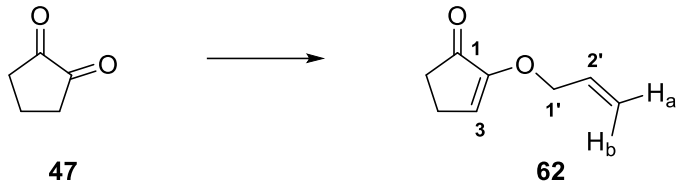


78

In analogy to compound **61**: KOH (85 wt%, 283 mg, 4.28 mmol, 1.0 equiv.) was dissolved in methallylic alcohol (1.5 mL, 1.29 mg, 17.9 mmol, 4.2 equiv.). A solution of epoxide *rac*-**50** (603 mg, 4.30 mmol, 1.0 equiv.) in methallylic alcohol (1.0 mL, 0.851 mg, 11.8 mmol, 2.8 equiv.) was then added dropwise and the reaction mixture was stirred at rt overnight. Subsequently, the reaction mixture was diluted with 15 mL CH_2Cl_2 and quenched by the addition of 15 mL H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (1 × 150 mL), dried over Na_2SO_4, filtrated and the solvent as well as the remaining volatiles were removed under reduced pressure. The irradiation precursor **61** was dissolved in a minimum of Et_2O and subjected to flash column chromatography. The remaining colorless solid was filtered off. It is insoluble in Et_2O and poorly soluble in CH_2Cl_2. Single crystals were obtained from a saturated solution of **78** in CH_2Cl_2. The structure and relative configuration of **78** were determined by data obtained from SC-XRD measurements.

4.3.2 2-(2'-Alkenyloxy)cyclopent-2-en-1-ones

2-(Allyloxy)cyclopent-2-en-1-one (62)



47 62

$C_8H_{10}O_2$
MW = 138.17 g/mol

To a solution of 1,2-cyclopentadione (**47**) (95.0 mg, 968 μmol, 1.0 equiv) in 5.0 mL of dry CyH was added *p*-TsOH·H_2O (6.10 mg, 32.1 μmol, 3.0 mol%) and allylic alcohol (210 μL, 178 mg, 3.06 mmol, 3.2 equiv). The reaction mixture was heated at reflux in a *Dean-Stark* apparatus for 23 h. The solution was allowed to cool to rt and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, UV) product **62** (100 mg, 720 μmol, 74%) was obtained as a colorless oil.

TLC: R_f = 0.14 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2925 (w, $C_{sp3}H$), 1715 (vs, C=O), 1624 (m, C=C), 1337 (w, $C_{sp3}H$), 1276 (w), 1119 (m, C-O), 1027 (w, C-O), 934 (w, C=C).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 2.38 – 2.48 (m, 2H, H-5), 2.52 (ddd, ^3J = 6.4, 4.2, 2.9 Hz, 2H, H-4), 4.43 (*virt.* dt, ^3J = 5.6 Hz, $^4J \approx {}^4J$ = 1.5 Hz, 2H, H-1'), 5.28 (*virt.* dq, ^3J = 10.6 Hz, $^2J \approx {}^4J$ = 1.4 Hz, 1H, H_a-3'), 5.36 (*virt.* dq, ^3J = 17.3 Hz, $^2J \approx {}^4J$ = 1.6 Hz, 1H, H_b-3'), 5.98 (ddt, ^3J = 17.3, 10.9, 5.6 Hz, 1H, H-2'), 6.39 (t, ^3J = 2.9 Hz, 1H, H-3).

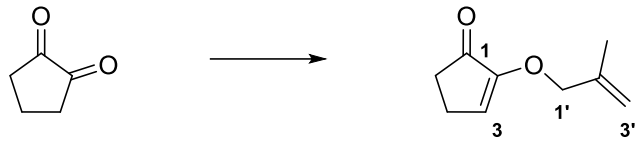
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 22.1 (t, C-4), 33.2 (t, C-5), 70.8 (t, C-1'), 118.7 (t, C-3'), 128.3 (d, C-3), 132.4 (d, C-2'), 156.4 (s, C-2), 202.7 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 138 (100) [M^+], 109 (15), 95 (11), 82 (52) [$C_5H_6O^+$].

HRMS (EI, 70 eV): calc. for $C_8H_{10}O_2$ [$M]^+$: 138.0675; found: 138.0677,
calc. for $C_7{}^{13}C_1H_{10}O_2$ [$M]^+$: 139.0709; found: 139.0712.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 248 nm (ε = 5180 $cm^{-1}M^{-1}$).

2-[(2-Methylallyl)oxy]cyclopent-2-en-1-one (63)



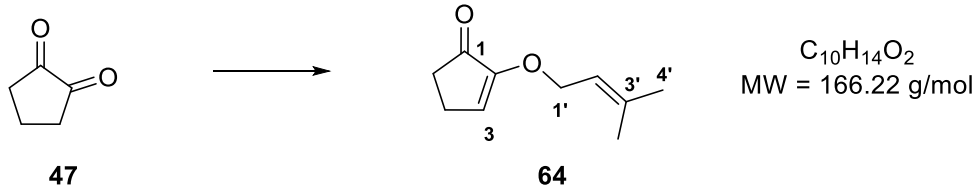
47 **63**

$C_9H_{12}O_2$
MW = 152.19 g/mol

In analogy to general procedure 4 compound **63**[58] was synthesized starting from diketone **47** (100 mg, 1.02 mmol, 1.0 equiv), methallyl bromide (150 µL, 207 mg, 1.53 mmol, 1.5 equiv) and K_2CO_3 (211 mg, 1.53 mmol, 1.5 equiv) in 4.0 mL dry DMF. The reaction was quenched by the addition of 5 mL H_2O and 10 mL Et_2O. The organic layer was washed with H_2O (4 × 10 mL) and brine (1 × 20 mL), dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, UV) afforded the product (55.1 mg, 360 µmol, 35%) as a colorless oil.

TLC: R_f = 0.30 (P/Et_2O = 1/1) [UV, $KMnO_4$].
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2922 (w, $C_{sp3}H$), 1708 (vs, C=O), 1623 (s, C=C), 1407 (w), 1336 (w, $C_{sp3}H$), 1273 (m, C-O), 1104 (vs, C-O), 1025 (m, C-O), 902 (m, C=C), 782 (m).
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.78 [s, 3H, C-2'(CH_3)], 2.40 – 2.44 (m, 2H, H-5), 2.50 (dt, ^3J = 6.1, 2.8 Hz, 2H, H-4), 4.34 (s, 2H, H-1'), 4.98 (s, 1H, H-3'), 5.03 (s, 1H, H-3'), 6.40 (t, ^3J = 2.8 Hz, 1H, H-3).
^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 19.4 [q, C-2'(*C*H_3)], 22.1 (t, C-4), 33.2 (t, C-5), 73.8 (t, C-1'), 113.7 (t, C-3'), 128.5 (d, C-3), 140.0 (s, C-2'), 156.5 (s, C-2), 202.6 (s, C-1).
MS (EI, 70 eV): *m/z* (%) = 152 (100) [M^+], 137 (16) [M^+–CH_3], 124 (10), 109 (21), 96 (90) [$C_5H_4O_2^+$], 82 (19) [$C_5H_6O^+$].
HRMS (EI, 70 eV): calc. for $C_9H_{12}O_2$ [$M]^+$: 152.0832; found: 152.0831.
UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 248 nm (ε = 6794 $cm^{-1}M^{-1}$).

2-[(3-Methylbut-2-en-1-yl)oxy]cyclopent-2-en-1-one (64)



47 **64**

In analogy to general procedure 4, compound **64** was synthesized starting from diketone **47** (170 mg, 1.73 mmol, 1.0 equiv), 3,3-dimethylallyl bromide (310 µL, 340 mg, 2.68 mmol, 1.5 equiv), and K_2CO_3 (377 mg, 2.73 mmol, 1.6 equiv) in 7.0 mL of dry DMF. The reaction was quenched by the addition of 7 mL H_2O and 15 mL Et_2O. The organic layer was washed with H_2O (4 × 15 mL) and brine (1 × 30 mL), dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, UV) afforded the product (60.0 mg, 360 µmol, 21%) as a colorless solid.

TLC: R_f = 0.35 (P/Et_2O = 1/1) [UV, $KMnO_4$].

Mp: 42 – 43 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2924 (w, $C_{sp3}H$), 1715 (vs, C=O), 1623 (s, C=C), 1449 (w, $C_{sp3}H$), 1342 (w, $C_{sp3}H$), 1275 (w, C-O), 1110 (s, C-O), 1026 (w, C-O), 964 (w, C=C), 782 (m).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.70 [s, 3H, C-3'(CH_3)], 1.76 (s, 3H, H-4'), 2.41 – 2.44 (m, 2H, H-5), 2.48 – 2.60 (m, 2H, H-4), 4.40 (d, ^3J = 6.8 Hz, 2H, H-1'), 5.43 (t, ^3J = 6.8 Hz, 1H, H-2'), 6.36 (*virt.* q, $^3J \approx {}^4J$ = 2.5 Hz, 1H, H-3).

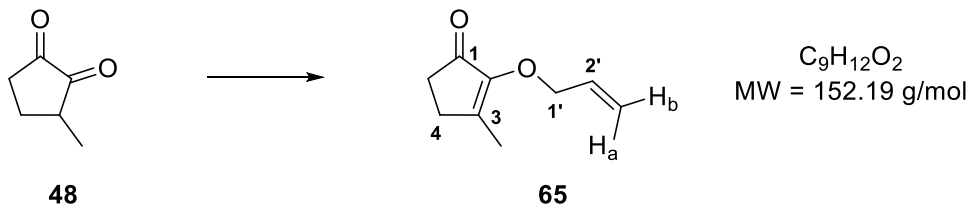
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 18.3 [q, C-3'(*C*H_3)], 22.2 (t, C-4), 25.9 (q, C-4'), 33.2 (t, C-5), 66.7 (t, C-1'), 119.1 (d, C-2'), 127.6 (d, C-3), 138.7 (s, C-3'), 156.6 (s, C-2), 202.9 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 166 (59) [M^+], 148 (21), 120 (11), 110 (23), 106 (28), 99 (100).

HRMS (EI, 70 eV): calc. for $C_{10}H_{14}O_2$ $[M]^+$: 166.0988; found: 166.0983,
calc. for $C_9{}^{13}C_1H_{14}O_2$ $[M]^+$: 167.1022; found: 167.1021.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 250 nm (ε = 5976 cm^{-1} M^{-1}).

2-(Allyloxy)-3-methylcyclopent-2-en-1-one (65)



48 **65**

According to general procedure 4, compound **65**[56] was synthesized starting from diketone **48** (500 mg, 4.46 mmol, 1.0 equiv), allyl bromide (460 µL, 650 mg, 5.35 mmol, 1.2 equiv) and K_2CO_3 (740 mg, 5.35 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, UV) afforded the product (387 mg, 2.54 mmol, 55%) as a colorless oil.

TLC: R_f = 0.24 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2917 (w, $C_{sp3}H$), 1699 (vs, C=O), 1643 (m, C=C), 1442 (w, $C_{sp3}H$), 1389 (w, $C_{sp3}H$), 1333 (m), 1204 (m, C-O), 1094 (s, C-O), 984 (m, C=C), 928 (m).

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.98 (s, 3H, CH_3), 2.30 – 2.39 (m, 2H, H-4), 2.43 (*virt.* dtd, ^2J = 7.1 Hz, $^3J \approx {}^3J$ = 2.5 Hz, ^3J = 1.2 Hz, 2H, H-5), 4.67 (*virt.* dt, ^3J = 5.9 Hz, $^2J \approx {}^2J$ = 1.4 Hz, 2H, H-1'), 5.18 (*virt.* dq, ^3J = 10.4 Hz, $^2J \approx {}^4J$ = 1.3 Hz, 1H, H_a-3'), 5.29 (*virt.* dq, ^3J = 17.2 Hz, $^2J \approx {}^4J$ = 1.6 Hz, 1H, H_b-3'), 5.94 (ddt, ^3J = 17.2, 10.4, 5.8 Hz, 1H, H-2').

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.1 (q, CH_3), 27.6 (t, C-5), 33.1 (t, C-4), 70.9 (t, C-1'), 117.9 (t, C-3'), 134.3 (d, C-2'), 151.7 (s, C-3*), 155.6 (s, C-2*), 203.3 (s, C-1).

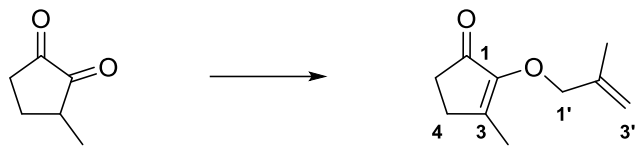
MS (EI, 70 eV): *m/z* (%) = 152 (49) [M^+], 137 (76) [M^+–CH_3], 123 (19), 112 (9) [$C_6H_8O_2^+$], 96 (22) [$C_6H_8O^+$], 84 (16), 81 (8), 69 (26), 67 (15), 55 (19), 41 (100) [$C_3H_5^+$].

HRMS (EI, 70 eV): calc. for $C_9H_{12}O_2$ [M^+]: 152.0827; found: 152.0832.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 246 nm (ε = 10132 cm^{-1} M^{-1}), 315 nm (ε = 140 cm^{-1} M^{-1}).

*Assignment is interconvertible.

3-Methyl-2-[(2-methylallyl)oxy]cyclopent-2-en-1-one (66)



48 66

$C_{10}H_{14}O_2$
MW = 166.22 g/mol

According to general procedure 4, compound **66** was synthesized starting from diketone **48** (500 mg, 4.46 mmol, 1.0 equiv), methallyl bromide (550 µL, 736 mg, 5.46 mmol, 1.2 equiv) and K_2CO_3 (740 mg, 5.35 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1, UV) afforded the product (621 mg, 3.74 mmol, 84%) as a colorless oil.

TLC: R_f = 0.28 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2917 (w, $C_{sp3}H$), 1700 (vs, C=O), 1646 (m, C=C), 1448 (w, $C_{sp3}H$), 1389 (m, $C_{sp3}H$), 1335 (m), 1204 (m, C-O), 1096 (s, C-O), 990 (m, C=C), 903 (m).

^{1}H NMR (300 MHz, C_6D_6, 300 K): δ [ppm] = 1.57 – 1.59 [m, 3H, C-3(CH_3)], 1.56 – 1.67 (m, 2H, H-4), 1.64 – 1.71 [m, 3H, C-2'(CH_3)], 1.85 – 1.90 (m, 2H, H-5), 4.79 – 4.86 (m, 2H, H-1'), 4.86 (*virt.* ddq, ^2J = 2.3 Hz, ^4J = 1.6, $^4J \approx {}^4J$ = 0.8 Hz, 1H, H-3'), 5.11 (*virt.* dq, ^2J = 2.3 Hz, $^4J \approx {}^4J$ = 1.1 Hz, 1H, H-3').

^{13}C NMR (75 MHz, C_6D_6, 300 K): δ [ppm] = 14.4 [q, C-3(*C*H_3)], 19.4 [q, C-2'(*C*H_3)], 26.8 (t, C-4), 33.1 (t, C-5), 73.0 (t, C-1'), 112.7 (t, C-3'), 142.5 (s, C-2'), 151.8 (s, C-3*), 152.1 (s, C-2*), 201.4 (s, C-1).

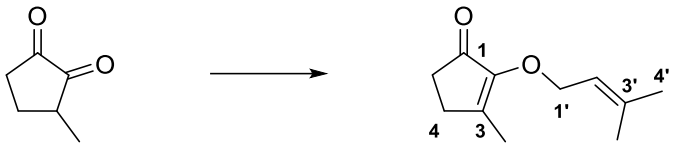
MS (EI, 70 eV): *m/z* (%) = 166 (56) [M^+], 151 (31) [M^+–CH_3], 137 (10), 110 (9) [$C_6H_6O_2^+$], 96 (12) [$C_6H_8O^+$], 84 (15), 69 (16), 55 (100) [$C_4H_7^+$], 41 (24).

HRMS (EI, 70 eV): calc. for $C_{10}H_{14}O_2$ $[M]^+$: 166.0988; found:166.0985,
calc. for $C_9{}^{13}C_1H_{14}O_2$ $[M]^+$: 167.1022; found:167.1026.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 248 nm (ε = 9284 cm^{-1} M^{-1}).

*Assignment is interconvertible.

3-Methyl-2-[(3-methylbut-2-en-1-yl)oxy]cyclopent-2-en-1-one (67)



48 **67**

$C_{11}H_{16}O_2$
MW = 180.25 g/mol

According to general procedure 4, compound **67**[57] was synthesized starting from diketone **48** (500 mg, 4.46 mmol, 1.0 equiv), 3,3-dimethylallyl bromide (620 µL, 800 mg, 5.35 mmol, 1.2 equiv) and K_2CO_3 (750 mg, 5.42 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1, UV) afforded the product (558 mg, 3.09 mmol, 69%) as a colorless oil.

TLC: R_f = 0.26 (P/Et_2O = 3/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2915 (w, $C_{sp3}H$), 1700 (vs, C=O), 1645 (m, C=C), 1443 (w, $C_{sp3}H$), 1390 (m, $C_{sp3}H$), 1338 (m), 1205 (m, C-O), 1092 (s, C-O), 969 (m, C=C), 905 (m).

^{1}H NMR (300 MHz, C_6D_6, 300 K): δ [ppm] = 1.55 [dd, ^4J = 1.4, 0.8 Hz, 6H, H-4', C-3'(CH_3)], 1.60 – 1.62 [m, 3H, C-3(CH_3)], 1.63 – 1.67 (m, 2H, H-4), 1.82 – 1.99 (m, 2H, H-5), 4.97 (*virt.* dquint., ^3J = 7.1 Hz, $^4J \approx {}^4J$ = 0.9 Hz, 2H, H-1'), 5.52 (*virt.* ddquint., ^3J = 8.4, 5.6 Hz, $^4J \approx {}^4J$ = 1.4 Hz, 1H, H-2').

^{13}C NMR (75 MHz, C_6D_6, 300 K): δ [ppm] = 14.5 [q, C-3(*C*H_3)], 18.0 [q, C-3'(*C*H_3)**], 25.8 (q, C-4'**), 33.1 (t, C-5), 66.4 (t, C-1'), 121.9 (d, C-2'), 137.4 (s, C-3'), 152.2 (s, C-3*), 152.7 (s, C-2*), 201.8 (s, C-1).

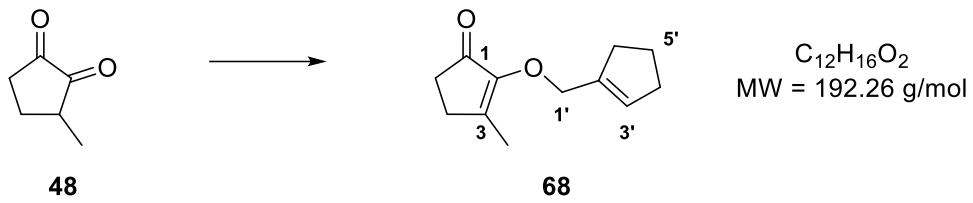
MS (EI, 70 eV): *m/z* (%) = 112 (90) [M^+–C_5H_8], 84 (32), 69 (100) [$C_5H_9^+$], 53 (9), 41 (74).

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O_2$ $[M]^+$: 180.1145; found: 180.1143.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 247 nm (ε = 9532 $cm^{-1}M^{-1}$).

* **Assignment is interconvertible.

2-(Cyclopent-1-en-1-ylmethoxy)-3-methylcyclopent-2-en-1-one (68)



48 **68**

According to general procedure 2, compound **68** was synthesized starting from diketone **48** (425 mg, 3.79 mmol, 1.1 equiv), allyl bromide **71** (405 mg, 3.49 mmol, 1.0 equiv) and K_2CO_3 (572 mg, 4.14 mmol, 1.2 equiv). Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1, UV) afforded the product (383 mg, 1.99 mmol, 58%) as a colorless oil.

TLC: R_f = 0.31 (P/Et_2O = 3/1) [$KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2930 (w, $C_{sp3}H$), 2849 (w, $C_{sp3}H$), 1700 (vs, C=O), 1643 (m, C=C), 1444 (w, $C_{sp3}H$), 1391 (m, $C_{sp3}H$), 1334 (m), 1204 (s, C-O), 1098 (s, C-O), 951 (m, C=C).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.89 (*virt.* quint., $^3J \approx {}^3J$ = 7.5 Hz, 2H, H-5'), 1.98 [s, 3H, C-3(CH_3)], 2.27 – 2.37 (m, 6H, H-4, H-4', H-6'), 2.39 – 2.45 (m, 2H, H-5), 4.73 (s, 2H, H-1'), 5.65 (*virt.* quint., $^3J \approx {}^4J$ = 1.7 Hz, 1H, H-3').

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.1 [q, C-3(*C*H_3)], 23.5 (t, C-5'), 27.4 (t, C-5), 32.6 (t, C-4*), 32.9 (t, C-6'*), 33.2 (t, C-4'*), 68.9 (t, C-1'), 128.6 (d, C-3'), 141.0 (s, C-2'), 151.9 (s, C-3), 155.2 (s, C-2), 203.5 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 192 (6) [M^+], 113 (42), 80 (100) [$C_6H_8^+$], 53 (9), 41 (16), [$C_3H_5^+$].

HRMS (EI, 70 eV): calc. for $C_{12}H_{16}O_2$ $[M]^+$: 192.1145; found: 192.1144,
calc. for $C_{11}{}^{13}C_1H_{16}O_2$ $[M]^+$: 193.1178; found: 193.1180.

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 248 nm (ε = 9632 $cm^{-1}M^{-1}$).

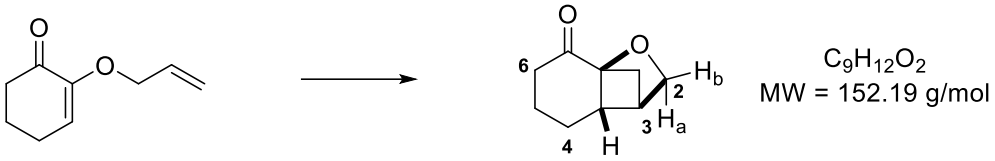
*Assignment is interconvertible.

4.3.3 Irradiation Products

General procedure 5:

Txt (**23**, 10 mol%) was dissolved in 1.0 mL dry degassed CH_2Cl_2 and transferred to a flame dried duran phototube. The respective 2-(2'-alkenyloxy)cycloalk-2-enone (1.0 equiv) dissolved in 1.0 mL dry degassed CH_2Cl_2 was then added, and the reaction mixture was diluted with dry degassed CH_2Cl_2 until a concentration of 10 mM (relative to the substrate) was reached. The reaction mixture was irradiated at λ = 420 nm at rt until full conversion was reached and the solvent was removed under reduced pressure. The crude product was purified using flash column chromatography (P/Et_2O).

(3*RS*,3a*SR*,7a*SR*)-Hexahydro-7*H*-3,7a-methanobenzofuran-7-one (*rac*-42)



39 *rac*-**42**

According to general procedure 5, compound *rac*-**42** was synthesized starting from enone **39** (15.6 mg, 103 µmol, 1.0 equiv) and txt (**23**) (2.21 mg, 10.4 µmol, 10 mol%) over 2.5 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 1/2, $KMnO_4$) afforded the product (11.2 mg, 73.6 µmol, 73%) as a colorless solid. The reaction on a 1 mmol scale was performed with 152 mg of **39** (1.00 mmol, 1.0 equiv) and 5.30 mg of txt (**23**) (25.0 µmol, 2.5 mol%) in 40 mL of CH_2Cl_2 (25 mM, irradiation time: 5 h). The yield was 138 mg (0.91 mmol, 91%).

TLC: R_f = 0.11 (P/Et_2O = 1/2) [$KMnO_4$].

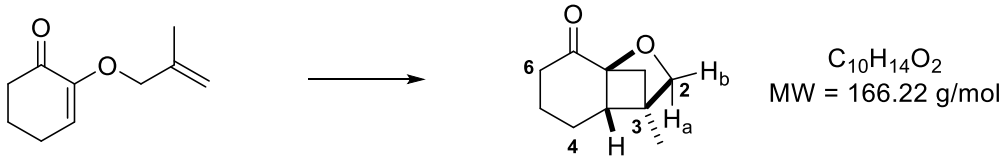
Mp: 59 – 65 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.64 – 1.78 (m, 1H, H-4), 1.81 – 1.96 (m, 2H, H-5, H-8), 2.03 – 2.18 (m, 2H, H-4, H-5), 2.30 (ddd, ^3J = 11.0, 7.8, 6.4 Hz, 1H, H-3a), 2.35 – 2.44 (m, 2H, H-6), 2.84 (dd, ^2J = 8.1 Hz, ^3J = 3.0 Hz, 1H, H-8), 2.88 (d, ^3J = 3.0 Hz, 1H, H-3), 3.85 (d, ^3J = 6.0 Hz, 1H, H_a-2), 3.94 (d, ^3J = 6.0 Hz, 1H, H_b-2).

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.4 (t, C-5), 27.3 (t, C-4), 40.1 (t, C-6), 41.6 (t, C-8), 42.0 (d, C-3), 55.4 (d, C-3a), 70.8 (t, C-2), 88.6 (s, C-7a), 203.6 (s, C-7).
Chiral GC: t_{R1} = 40.27 min, t_{R2} = 40.46 min, [60 °C (1 min), 220 °C (3 °C/min), 220 °C (10 min)], Cyclosil-B 30 m, 0.25 mm, 0.25 µm.

Data of this compound were in accordance with the literature.[60]

(3*RS*,3a*SR*,7a*SR*)-3-Methylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (*rac*-43)



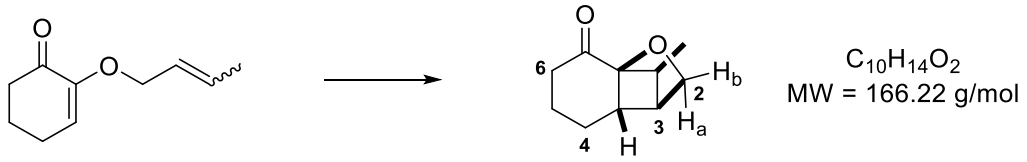
40 *rac*-**43**

According to general procedure 5, compound *rac*-**43** was synthesized starting from enone **40** (16.8 mg, 100 µmol, 1.0 equiv) and txt (**23**) (2.24 mg, 10.6 µmol, 10 mol%) over 3 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 1/2, $KMnO_4$) afforded the product (15.3 mg, 92.0 µmol, 91%) as a colorless oil.

TLC: R_f = 0.15 (P/Et_2O = 1/2) [$KMnO_4$].
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.25 (s, 3H, CH_3), 1.66 – 1.82 (m, 2H, H-4, H-5), 1.88 (*virt.* t, $^2J \approx {}^4J$ = 7.9 Hz, 1H, H-8), 1.95 – 2.04 (m, 1H, H-4), 2.14 (ddt, ^2J = 10.7 Hz, ^3J = 6.0, 2.9 Hz, 1H, H-5), 2.24 (*virt.* qd, $^3J \approx {}^3J$ = 7.7 Hz, ^4J = 3.7 Hz, 1H, H-3a), 2.31 – 2.44 (m, 2H, H-6), 2.59 (d, ^2J = 7.9 Hz, 1H, H-8), 3.64 (dd, ^2J = 5.9 Hz, ^4J = 1.2 Hz, 1H, H_a-2), 3.74 (d, ^2J = 5.9 Hz, 1H, H_b-2).
^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 12.8 (q, CH_3), 23.6 (t, C-4), 27.1 (t, C 5), 40.1 (t, C-6), 45.4 (t, C-8), 49.1 (s, C-3), 57.4 (d, C-3a), 75.4 (t, C-2), 87.2 (s, C-7a), 204.2 (s, C-7).
Chiral GC: t_{R1} = 13.08 min, t_{R2} = 14.49 min, [60 °C (1 min), 170 °C (15 °C/min), 200 °C (4 °C/min), 200 °C (5 min)], Lipodex E 25 m, 0.25 mm.

Data of this compound were in accordance with the literature.[60]

(3*RS*,3a*SR*,7a*SR*,8*SR*)-8-Methylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (*rac*-92)



E/Z-**52** *rac*-**92**

In analogy to general procedure 5, compound *rac*-**92** was synthesized starting from enone *E/Z*-**52** (16.6 mg, 100 µmol, 1.0 equiv) and txt (**23**) (2.15 mg, 10.1 µmol, 10 mol%) over 4.5 h. The solvent was removed under reduced pressure, the residue was redissolved in 1.0 mL of CH_2Cl_2 and dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (5.30 mg, 26.7 µmol, 0.27 equiv) was added. The reaction mixture was stirred at rt for 4.5 h and the solvent was removed under reduced pressure. Purification by flash column chromatography (SiO_2, P/Et_2O = 1/2, $KMnO_4$) afforded the product (13.0 mg, 78.2 µmol, 78%) as a colorless solid.

TLC: R_f = 0.21 (P/Et_2O = 1/2) [$KMnO_4$].

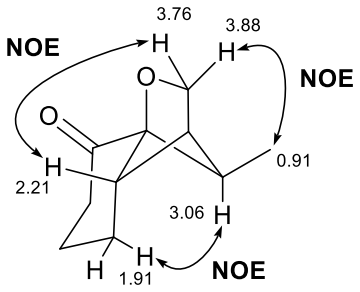
Mp: 48 – 53 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2946 (m, $C_{sp3}H$), 1710 (vs, C=O), 1451 (w, $C_{sp3}H$), 1320 (w), 1094 (m, C-O), 994 (m), 930 (m), 848 (m, $C_{sp3}H$).

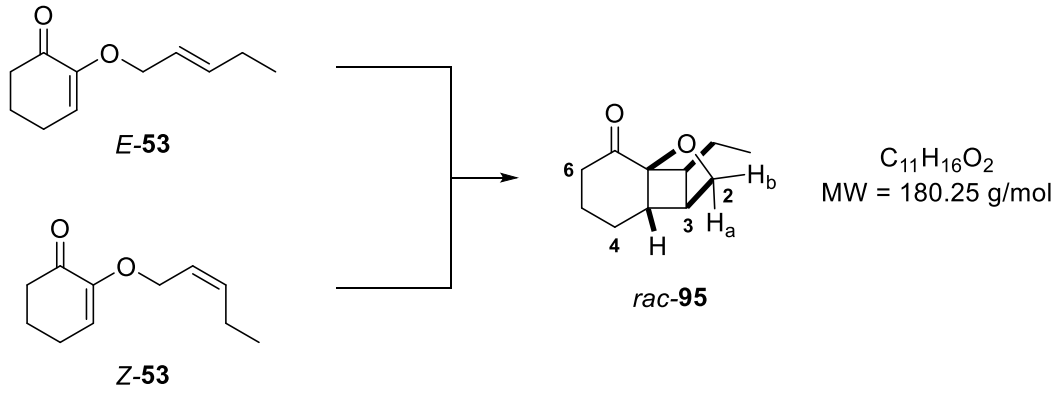
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.91 [d, ^3J = 6.4 Hz, 3H, C-8(CH_3)], 1.62 – 1.76 (m, 1H, H-5), 1.91 (*virt.* tdd, $^2J \approx {}^3J$ = 14.2 Hz, ^3J = 11.0 Hz, ^3J = 3.7 Hz, 1H, H_{ax}-4), 2.00 – 2.07 (m, 1H, H_{eq}-4), 2.11 (ddd, ^2J = 13.4 Hz, ^3J = 6.7, 3.6 Hz, 1H, H-5), 2.21 (dd, ^3J = 11.0, 6.7 Hz, 1H, H-3a), 2.28 – 2.41 (m, 2H, H-6), 2.65 (d, ^3J = 2.9 Hz, 1H, H-3), 3.06 (qd, ^3J = 6.4, 2.9 Hz, 1H, H-8), 3.76 (d, ^2J = 6.5 Hz, 1H, H_a-2), 3.88 (d, ^2J = 6.5 Hz, 1H, H_b-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 9.7 [q, C-8(*C*H_3)], 24.4 (t, C-4), 27.1 (t, C-5), 40.1 (t, C-6), 44.4 (d, C-3), 45.0 (d, C-8), 52.7 (d, C-3a), 67.5 (t, C-2), 89.1 (s, C-7a), 203.8 (s, C-7).

MS (EI, 70 eV): *m/z* (%) = 166 (20) [M^+], 151 (4) [$C_9H_{11}O_2^+$], 138 (5), 123 (5), 112 (100) [$C_6H_8O_2^+$], 109 (15), 95 (11) [$C_6H_7O^+$], 84 (41).
HRMS (EI, 70 eV): calc. for $C_{10}H_{14}O_2$ [$M]^+$: 166.0988; found: 166.0982.



(3*RS*,3a*SR*,7a*SR*,8*SR*)-8-Ethylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (*rac*-95)



According to general procedure 5, compound *rac*-**95** was synthesized starting from enone *E*-**53** (18.1 mg, 100 µmol, 1.0 equiv) and txt (**23**) (2.14 mg, 10.2 µmol, 10 mol%) over 2.5 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 2/1 → 1/1, $KMnO_4$) afforded a mixture of product *rac*-**95** and olefinic byproduct *rac*-**96** (18.1 mg, 100 µmol, quant., *rac*-**95**/*rac*-**96** = 82/18) as a colorless solid.

According to general procedure 5, compound *rac*-**95** was synthesized starting from enone *Z*-**53** (18.1 mg, 100 µmol, 1.0 equiv) and txt (**23**) (2.17 mg, 10.1 µmol, 10 mol%) over 2.5 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 1/1, $KMnO_4$) afforded

a mixture of product *rac*-**95** and olefinic byproduct *rac*-**96** (16.3 mg, 90.4 µmol, 90%, *rac*-**95**/*rac*-**96** = 83/17) as a colorless solid.

The product mixture (14.2 mg, 78.8 µmol) was dissolved in 500 µL DCE and 400 µL H_2O. Subsequently, $RuCl_3 \cdot xH_2O$ (1 small crystal, calc. 0.14 mg, 0.7 µmol, 3.5 mol% relative to byproduct) and $NaIO_4$ (18.6 mg, 87.0 µmol, 4.3 equiv) were added and the reaction mixture was stirred at rt for 20 h. The reaction was diluted by addition of 2.0 mL of H_2O and 2.0 mL Et_2O and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 5 mL). The combined organic layers were then washed with H_2O (1 × 10 mL) and brine (1 × 10 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Purification by flash column chromatography (SiO_2, P/Et_2O = 2/1, $KMnO_4$) afforded the product (9.80 mg, 54.4 µmol, 69%) as a colorless solid.

TLC: R_f = 0.16 (P/Et_2O = 1/2) [$KMnO_4$].

Mp: 58 – 61 °C

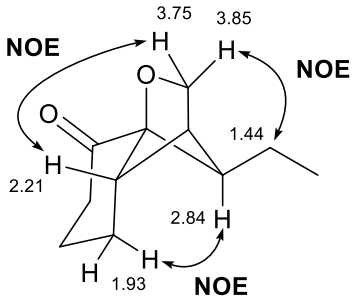
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2956 (m, $C_{sp3}H$), 1713 (vs, C=O), 1462 (w, $C_{sp3}H$), 1327 (w), 1095 (m, C-O), 1013 (w), 947 (m), 851 (m, $C_{sp3}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.79 (t, ^3J = 7.5 Hz, 3H, CH_2CH_3), 1.21 – 1.33 (m, 1H, CH_2CH_3), 1.37 – 1.51 (m, 1H, CH_2CH_3), 1.63 – 1.78 (m, 1H, H-5), 1.93 (*virt.* tdd, $^2J \approx {}^3J$ = 14.2 Hz, ^3J = 11.0, 3.8 Hz, 1H, H_{ax}-4), 1.99 – 2.09 (m, 1H, H_{eq}-4), 2.09 – 2.16 (m, 1H, H-5), 2.21 (dd, ^3J = 11.0, 6.7 Hz, 1H, H-3a), 2.31 – 2.43 (m, 2H, H-6), 2.71 (d, ^3J = 2.9 Hz, 1H, H-3), 2.84 (ddd, ^3J = 8.6, 6.0, 2.9 Hz, 1H, H-8), 3.75 (d, ^2J = 6.5 Hz, 1H, H_a-2), 3.85 (d, ^2J = 6.5 Hz, 1H, H_b-2).

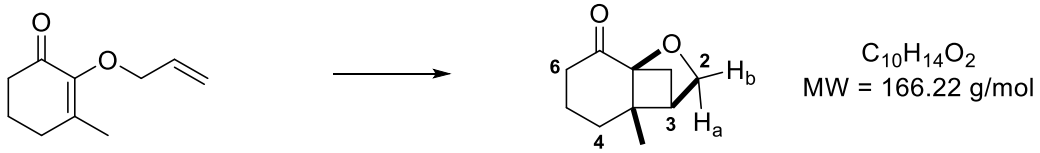
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 11.4 (q, CH_2CH_3), 17.9 (t, CH_2CH_3), 24.4 (t, C-4), 27.3 (t, C-5), 40.2 (t, C-6), 43.4 (d, C-3), 52.4 (d, C-8), 52.8 (d, C-3a), 67.8 (t, C-2), 88.9 (s, C-7a), 204.2 (s, C-7).

MS (EI, 70 eV): *m/z* (%) = 180 (8) [M^+], 151 (6) [$C_9H_{11}O_2^+$], 123 (7), 113 (100), 109 (9), 95 (12) [$C_6H_7O^+$], 84 (22) [$C_5H_8O^+$].

HRMS (EI, 70 eV): calc. for $C_{10}H_{14}O_2$ [$M]^+$: 180.1145; found: 180.1148.



(3*RS*,3a*SR*,7a*SR*)-3a-Methylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (*rac*-87)



55 *rac*-**87**

According to general procedure 5, compound *rac*-**87** was synthesized starting from enone **55** (16.8 mg, 101 µmol, 1.0 equiv) and txt (**23**) (2.19 mg, 10.3 µmol, 10 mol%) over 2 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 1/2, $KMnO_4$) afforded the product (15.2 mg, 91.2 µmol, 91%) as a colorless solid.

TLC: R_f = 0.04 (P/Et_2O = 1/2) [$KMnO_4$].

Mp: 38 – 47 °C.

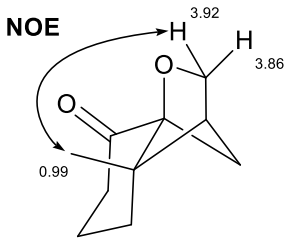
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2925 (m, $C_{sp3}H$), 1713 (s, C=O), 1458 (w, $C_{sp3}H$), 1123 (w, C-O), 1043 (w, C-O), 945 (w), 862 (w, $C_{sp3}H$).

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.99 (s, 3H, CH_3), 1.76 (d, ^2J = 8.2 Hz, H-8), 1.84 (ddt, ^2J = 14.1 Hz, ^3J = 4.2 Hz, ^4J = 1.9 Hz, 1H, H_{eq}-4), 2.00 (*virt.* qt, $^2J \approx {}^3J$ = 13.9 Hz, ^3J = 4.2 Hz, 1H, H_{ax}-5), 2.08 – 2.18 (m, 1H, H_{eq}-5), 2.28 (*virt.* td, $^2J \approx {}^3J$ = 14.1 Hz, ^3J = 4.3 Hz, 1H, H_{ax}-4), 2.36 (ddt, ^2J = 14.5 Hz, ^3J = 4.1 Hz, ^4J = 1.9 Hz, 1H, H-6), 2.49 td, ^2J = 14.5 Hz, ^3J = 5.8 Hz, 1H, H-6), 2.72 (d, ^3J = 3.0 Hz, 1H, H-3), 2.84 (dd, ^2J = 8.2 Hz, ^3J = 3.0 Hz, 1H, H-8), 3.86 (d, ^2J = 6.7 Hz, 1H, H_a-2), 3.92 (d, ^2J = 6.7 Hz, 1H, H_b-2).

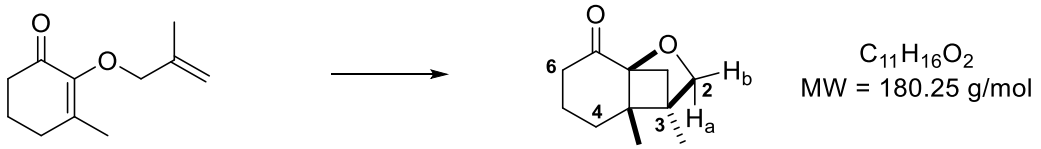
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.8 (q, CH_3), 25.7 (t, C-5), 31.8 (t, C-4), 40.1 (t, C-6), 40.8 (t, C-8), 44.6 (d, C-3), 56.0 (s, C-3a), 68.5 (t, C-2), 89.9 (s, C-7a), 204.0 (s, C-1).

MS (EI, 70 eV): *m/z* (%) =166 (100) [M^+], 163 (21), 149 (39), 123 (35), 109 (62) [$C_7H_9O^+$], 95 (44) [$C_6H_7O^+$], 81 (100) [$C_5H_5O^+$].

HRMS (EI, 70 eV): calc. for $C_{10}H_{14}O_2$ [$M]^+$: 166.0988; found: 166.0982.



(3*RS*,3a*SR*,7a*SR*)-3,3a-Dimethylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (*rac*-88)



56 *rac*-**88**

According to general procedure 5, compound *rac*-**88** was synthesized starting from enone **56** (18.2 mg, 101 µmol, 1.0 equiv) and txt (**23**) (2.14 mg, 10.1 µmol, 10 mol%) over 5 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 1/2, $KMnO_4$) afforded the product (15.9 mg, 88.3 µmol, 88%) as a colorless solid. The reaction on a 1 mmol scale was performed with 180 mg of **56** and 5.40 mg of txt (**23**) (25.0 µmol, 2.5 mol%) in 40 mL of CH_2Cl_2 (25 mM, irradiation time: 9 h). The yield was 169 mg (0.94 mmol, 94%).

TLC: R_f = 0.08 (P/Et_2O = 1/2) [$KMnO_4$].

Mp: 67 – 70 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2922 (s, $C_{sp3}H$), 1714 (vs, C=O), 1456 (w, $C_{sp3}H$), 1385 (w, $C_{sp3}H$), 1245 (w, C-O), 949 (w).

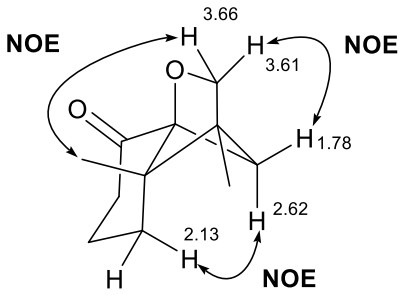
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.90 [s, 3H, C-3a(CH_3)], 1.14 [s, 3H, C-3(CH_3)], 1.65 (ddt, ^{2}J = 13.5 Hz, ^{3}J = 3.9 Hz, ^{4}J = 1.8 Hz, 1H, H_{eq}-4), 1.78 (d, ^{2}J = 8.2 Hz, 1H, H-8), 1.92 – 2.06 (m, 1H, H-5), 2.07 – 2.20 (m, 2H, H_{ax}-4, H-5), 2.28 – 2.36 (m, 1H, H-6), 2.38 – 2.51 (m, 1H, H-6), 2.62 (d, ^{2}J = 8.2 Hz, 1H, H-8), 3.61 (d, ^{2}J = 6.5 Hz, 1H, H_b-2), 3.66 (dd, ^{2}J = 6.5 Hz, ^{4}J = 1.4 Hz, 1H, H_a-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 10.5 [q, C-3(*C*H_3)], 13.8 [q, C-3a(*C*H_3)], 25.6 (t, C-5), 29.9 (t, C-4), 40.0 (t, C-6), 45.4 (t, C-8), 50.6 (s, C-3*), 57.0 (s, C-3a*), 72.9 (t, C-2), 89.4 (s, C-7a), 204.5 (s, C-7).

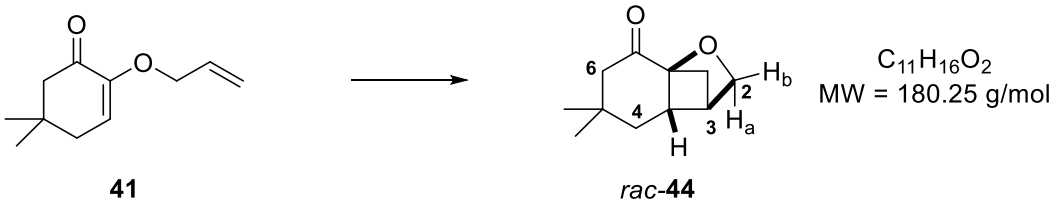
MS (EI, 70 eV): *m/z* (%) = 180 (6) [M^+], 165 (48) [$C_{10}H_{13}O_2^+$], 135 (54), 125 (78), 110 (49) [$C_7H_{10}O^+$], 97 (100), 83 (71).

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O_2$ [M^+]: 180.1145; found: 180.1145.

*Assignment is interconvertible.



(3*RS*,3a*SR*,7a*SR*)-5,5-Dimethylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (*rac*-44)



41 *rac*-**44**

According to general procedure 5, compound *rac*-**44** was synthesized starting from enone **41** (36.2 mg, 201 µmol, 1.0 equiv) and txt (**23**) (4.34 mg, 20.4 µmol, 10 mol%) over 2.5 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1 → 1/1, $KMnO_4$) afforded the product (36.2 mg, 201 µmol, 100%) as a colorless solid.

TLC: R_f = 0.14 (P/Et_2O = 1/1) [$KMnO_4$].

Mp: 73 – 74 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2955 (m, $C_{sp3}H$), 1716 (vs, C=O), 1468 (w, $C_{sp3}H$), 1058 (m, C-O), 967 (w), 921 (w).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.89 [s, 3H, C-5(CH_3)], 1.11 [s, 3H, C-5(CH_3)], 1.76 – 1.91 (m, 3H, H-4, H-8), 2.06 (dd, ^2J = 14.2 Hz, ^4J = 2.3 Hz, 1H, H-6), 2.34 – 2.45 (m, 2H, H-3a, H-6), 2.81 (ddd, ^2J = 8.2 Hz, ^3J = 3.1 Hz, ^4J = 1.1 Hz, 1H, H-8), 2.84 (d, ^3J = 3.1 Hz, 1H, H-3), 3.90 (d, ^2J = 6.0 Hz, 1H, H_a-2), 3.97 (d, ^2J = 6.0 Hz, 1H, H_b-2).

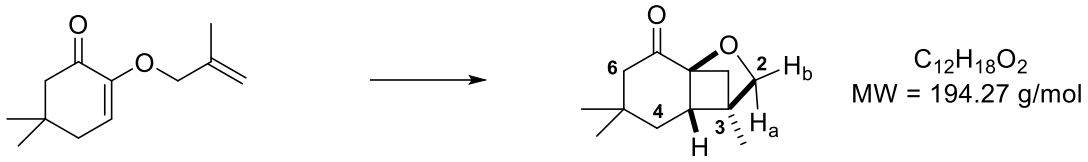
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.5 [q, C-5(*C*H_3)], 31.4 [q, C-5(*C*H_3)], 38.2 (t, C-4), 39.9 (s, C-5), 41.0 (t, C-8), 41.3 (d, C-3), 52.8 (d, C-3a), 53.1 (t, C-6), 71.6 (t, C-2), 88.5 (s, C-7a), 203.4 (s, C-7).

MS (EI, 70 eV): *m/z* (%) = 180 (100) [M^+], 165 (7) [$C_{10}H_{13}O_2^+$], 137 (17), 124 (63) [$C_8H_{12}O^+$], 109 (35) [$C_7H_9O^+$], 95 (72), 83 (16).

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O_2$ [$M]^+$: 180.1145; found: 180.1146.

Data of this compound were in accordance with the literature.[60]

(3*RS*,3a*SR*,7a*SR*)-3,5,5-Trimethylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (*rac*-89)



58 *rac*-**89**

According to general procedure 5, compound *rac*-**89** was synthesized starting from enone **58** (38.9 mg, 200 µmol, 1.0 equiv) and txt (**23**) (4.36 mg, 20.5 µmol, 10 mol%) over 2.5 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 1/1, $KMnO_4$) afforded the product (35.1 mg, 181 µmol, 90%) as a colorless solid. The reaction on a 1 mmol scale was performed with 194 mg of **58** and 5.30 mg of txt (**23**) (25.0 µmol, 2.5 mol%) in 40 mL of CH_2Cl_2 (25mM, irradiation time: 4.5 h). The yield was 178 mg (0.92 mmol, 92%).

TLC: R_f = 0.19 (P/Et_2O = 1/1) [$KMnO_4$].

Mp: 65 – 67 °C.

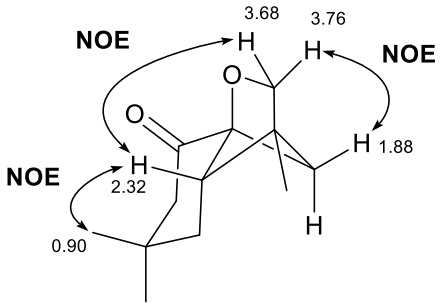
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2954 (m, $C_{sp3}H$), 1714 (vs, C=O), 1468 (w, $C_{sp3}H$), 1245 (w, C-O), 1163 (w, C-O), 1082 (w, C-O), 964 (s).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.90 [s, 3H, C-5(CH_3)$_{ax}$], 1.12 [s, 3H, C-5(CH_3)$_{eq}$], 1.23 [s, 3H, C-3(CH_3)], 1.68 (ddd, ^2J = 14.0 Hz, ^3J = 7.0 Hz, ^4J = 2.3 Hz, 1H, H-4), 1.75 (dd, ^2J = 14.0 Hz, ^3J = 11.1 Hz, 1H, H-4), 1.88 (*virt.* t, $^2J \approx {}^4J$ = 7.9 Hz, 1H, H-8), 2.05 (dd, ^2J = 14.2 Hz, ^4J = 2.3 Hz, 1H, H-6), 2.28 – 2.41 (m, 2H, H-3a, H-6), 2.56 (dd, ^2J = 8.0 Hz, ^4J = 1.2 Hz, 1H, H-8), 3.68 (dd, ^2J = 5.9 Hz, ^4J = 1.2 Hz, 1H, H_a-2), 3.76 (d, ^2J = 5.9 Hz, 1H, H_b-2).

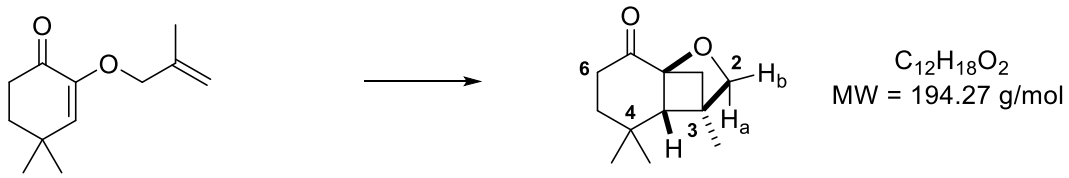
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 12.8 [q, C-3(*C*H_3)], 25.7 [q, C-5(*C*H_3)$_{ax}$], 31.4 [q, C-5(*C*H_3)$_{eq}$], 36.4 (t, C-4), 39.9 (s, C-5), 44.7 (t, C-8), 48.4 (s, C-3), 53.0 (t, C-6), 54.7 (d, C-3a), 76.1 (t, C-2), 87.1 (s, C-7a), 204.0 (s, C-7).

MS (EI, 70 eV): *m/z* (%) = 194 (25) [M^+], 179 (9), 151 (16), 124 (10) [$C_8H_{12}O^+$], 109 (100) [$C_7H_9O^+$], 95 (16), 83 (15).

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O_2$ [$M]^+$: 194.1301; found: 194.1301.



(3*RS*,3a*SR*,7a*SR*)-3,4,4-Trimethylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (*rac*-90)



According to general procedure 5, compound *rac*-**90** was synthesized starting from enone **61** (11.0 mg, 56.6 µmol, 1.0 equiv) and txt (**23**) (1.20 mg, 5.66 µmol, 10 mol%) over 7.5 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1 → 1/1, $KMnO_4$) afforded the product (4.20 mg, 21.6 µmol, 38%) as a colorless oil.

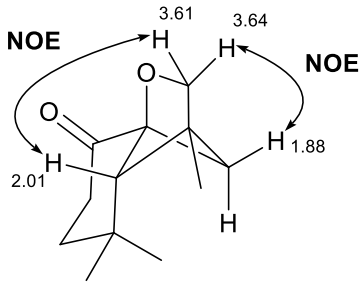
TLC: R_f = 0.14 (P/Et_2O = 1/1) [$KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2954 (m, $C_{sp3}H$), 1719 (vs, C=O), 1458 (w, $C_{sp3}H$), 1062 (m, C-O), 948 (w).

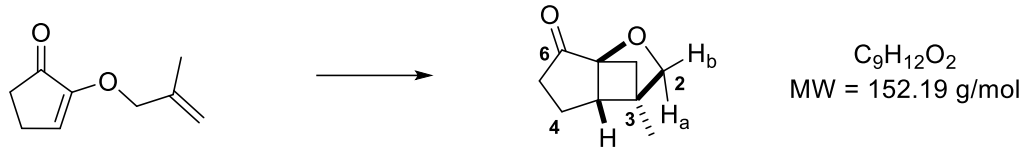
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.17 [s, 3H, C-3(CH_3)], 1.32 – 1.41 [m, 6H, C-4(CH_3)$_2$], 1.66 – 1.75 (m, 2H, H-5), 1.88 (*virt.* t, $^2J \approx {}^4J$ = 8.4 Hz, 1H, H-8), 2.01 (d, ^4J = 8.5 Hz, 1H, H-3a), 2.31 (dt, ^2J = 16.2 Hz, ^3J = 4.2 Hz, 1H, H-6), 2.50 (ddd, ^2J = 16.2 Hz, ^3J = 10.2, 7.4 Hz, 1H, H-6), 2.76 (dd, ^2J = 8.1 Hz, ^4J = 1.2 Hz, 1H, H-8), 3.61 (dd, ^2J = 5.9 Hz, ^4J = 1.2 Hz, 1H, H_a-2), 3.64 (d, ^2J = 5.9 Hz, 1H, H_b-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 13.6 [q, C-4(*C*H_3)], 24.0 [q, C-4(*C*H)$_3$], 32.9 (s, C-4), 33.7 [q, C-3(*C*H_3)], 37.0 (t, C-6), 41.4 (t, C-5), 45.9 (t, C-8), 49.7 (s, C-3), 65.0 (d, C-3a), 76.8 (t, C-2), 86.3 (s, C-7a), 205.1 (s, C-7).

MS (EI, 70 eV): *m/z* (%) = 194 (8) [M^+], 179 (33) [$C_{11}H_{15}O_2^+$], 164 (19), 149 (34), 138 (100) [$C_8H_{10}O_2^+$], 125 (38) [$C_7H_9O_2^+$], 109 (36) [$C_7H_9O^+$], 97 (34), 81 (43).
HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O_2$ [$M]^+$: 194.1301; found: 194.1298.



(3*RS*,3a*SR*,6a*SR*)-3-Methyltetrahydro-3,6a-methanocyclopenta[*b*]furan-6(2*H*)-one (*rac*-91)

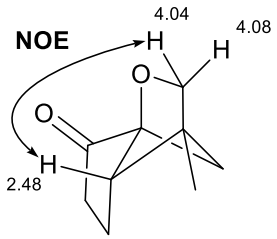


63 *rac*-**91**

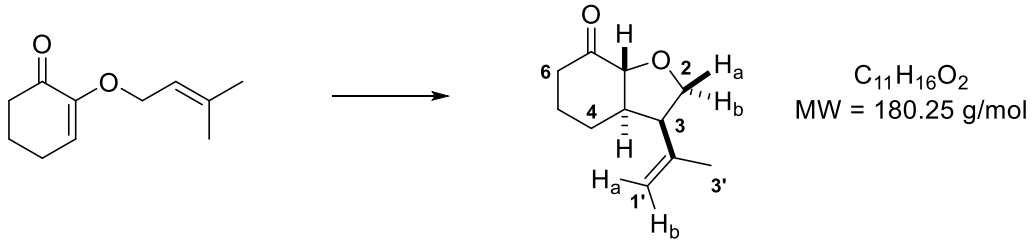
According to general procedure 5, compound *rac*-**91** was synthesized starting from enone **63** (30.7 mg, 202 µmol, 1.0 equiv) and txt (**23**) (4.26 mg, 20.1 µmol, 10 mol%) over 19 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, $KMnO_4$) afforded the product (10.4 mg, 68.3 µmol, 34%) as a colorless oil.

TLC: R_f = 0.07 (P/Et_2O = 3/1) [$KMnO_4$].
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2956 (w, $C_{sp3}H$), 1737 (vs, C=O), 1451 (w, $C_{sp3}H$), 1238 (w, C-O), 1038 (m), 1006 (m), 975 (s), 919 (m), 894 (m).
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.29 [s, 3H, C-3(CH_3)], 1.95 (*virt.* t, $^2J \approx {}^4J$ = 8.2 Hz, 1H, H-7), 2.02 (ddd, ^3J = 9.2, 7.7, 5.8 Hz, 2H, H-4), 2.48 (*virt.* q, $^3J \approx {}^3J$ = 8.3 Hz, 1H, H-3a), 2.57 (dt, ^2J = 19.2 Hz, ^3J = 9.2 Hz, 1H, H-5), 2.62 – 2.73 (m, 2H, H-5, H-7), 4.04 (dd, ^2J = 6.2 Hz, ^4J = 1.3 Hz, 1H, H_a-2), 4.08 (d, ^2J = 6.2 Hz, 1H, H_b-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 13.8 [q, C-3(*C*H_3)], 16.9 (t, C-4), 41.3 (t, C-5), 44.2 (t, C-7), 49.0 (s, C-3), 51.3 (d, C-3a), 83.1 (t, C-2), 93.0 (s, C-6a), 206.3 (s, C-6).
MS (EI, 70 eV): *m/z* (%) = 151 (6) [M-H$^+$], 137 (36) [$C_8H_9O_2^+$], 123 (13) [$C_7H_7O_2^+$], 110 (100), 96 (70) [$C_5H_4O_2^+$], 81 (92).
HRMS (EI, 70 eV): calc. for $C_9H_{12}O_2$ [M]$^+$: 152.0832; found: 152.0828.



(3*RS*,3a*RS*,7a*RS*)-3-(Prop-1-en-2-yl)hexahydrobenzofuran-7(4*H*)-one (*rac*-97)



51 *rac*-**97**

According to general procedure 5, compound *rac*-**97** was synthesized starting from enone **51** (18.4 mg, 102 µmol, 1.0 equiv) and txt (**23**) (2.21 mg, 10.4 µmol, 10 mol%) over 4.5 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 1/2, $KMnO_4$) afforded the product (11.9 mg, 66.0 µmol, 65%, d.r. > 95/5) as a colorless oil.

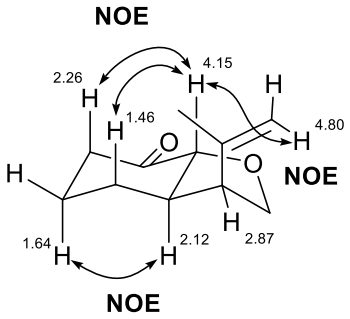
TLC: R_f = 0.05 (P/Et_2O = 1/2) [$KMnO_4$].
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2929 (m, $C_{sp3}H$), 1730 (vs, C=O), 1449 (w, $C_{sp3}H$), 1105 (m, C-O), 1045 (m, C-O), 900 (m).
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.46 (*virt.* qd, $^2J \approx {}^3J$ = 12.4 Hz, ^3J = 3.8 Hz, 1H, H_{ax}-4), 1.64 (*virt.* qdd, $^2J \approx {}^3J$ = 12.6 Hz, ^3J = 5.4, 3.8 Hz, 1H, H_{ax}-5), 1.81 (s, 3H, H-3'), 1.99 – 2.06 (m, 1H, H_{eq}-4), 2.08 – 2.17 (m, 2H, H_{eq}-5, H-3a), 2.26 (*virt.* tdd,

$^2J \approx {}^3J$ = 14 Hz, ^3J = 5.4 Hz, ^4J = 1.7 Hz, 1H, H_{ax}-6), 2.36 (*virt.* ddt, ^2J = 14.1 Hz, ^3J = 5.1 Hz, $^3J \approx {}^4J$ = 1.8 Hz, 1H, H_{eq}-6), 2.80 – 2.93 (m, 1H, H-3), 4.00 (dd, ^2J = 9.1 Hz, ^3J = 1.7 Hz, 1H, H_a-2), 4.10 (dd, ^2J = 9.1 Hz, ^3J = 6.3 Hz, 1H, H_b-2), 4.15 (dd, ^3J = 12.4 Hz, ^4J = 1.7 Hz, 1H, H-7a), 4.79 – 4.81 (m,1H, H_a-1'), 5.03 (*virt.* quint., $^2J \approx {}^4J$ = 1.3 Hz, 1H, H_b-1').

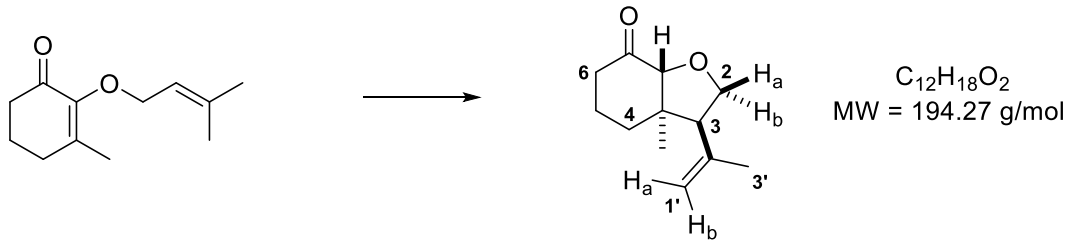
^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.7 (q, C-3'), 25.9 (t, C-4), 27.3 (t, C-5), 39.8 (t, C-6), 47.5 (d, C-3), 50.7 (d, C-3a), 73.7 (t, C-2), 84.0 (d, C-7a), 112.7 (t, C-1'), 144.3 (s, C-2'), 207.8 (s, C-7).

MS (EI, 70 eV): *m/z* (%) = 180 (73) [M^+], 165 (8) [$C_{10}H_{13}O_2^+$], 136 (21), 123 (17), 107 (100), 93 (46), 81 (29).

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O_2$ [$M]^+$: 180.1145; found:180.1145,
calc. for $C_{10}{}^{13}C_1H_{16}O_2$ [$M]^+$: 181.1178; found:181.1183.



(3*SR*,3a*RS*,7a*RS*)-3a-Methyl-3-(prop-1-en-2-yl)hexahydrobenzofuran-7(4*H*)-one (*rac*-98)



57 *rac*-**98**

According to general procedure 5, compound *rac*-**98** was synthesized starting from enone **57** (19.6 mg, 101 µmol, 1.0 equiv) and txt (**23**) (2.16 mg, 10.2 µmol, 10 mol%) over 5 h.

Purification by flash column chromatography (SiO_2, P/Et_2O = 1/2, $KMnO_4$) afforded the product (15.4 mg, 79.1 µmol, 79%, d.r. > 95/5) as a colorless solid.

TLC: R_f = 0.08 (P/Et_2O = 1/2) [$KMnO_4$].

Mp: 87 – 92 °C.

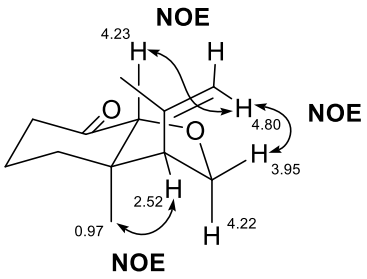
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2924 (s, $C_{sp3}H$), 1732 (vs, C=O), 1455 (w, $C_{sp3}H$), 1377 (w, $C_{sp3}H$), 1260 (w, C-O), 1104 (w, C-O), 1054 (m, C-O), 907 (w).

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.97 [s, 3H, C-3a(CH_3)], 1.66 (*virt.* td, $^2J \approx {}^3J$ = 13.0 Hz, ^3J = 5.4 Hz, 1H, H_{ax}-4), 1.73 – 1.79 (m, 1H, H_{eq}-4), 1.81 (s, 3H, H-3'), 1.87 – 1.98 (m, 1H, H_{ax}-5), 1.98 – 2.06 (m, 1H, H_{eq}-5), 2.20 – 2.34 (m, 2H, H-6), 2.52 (ddd, ^3J = 7.0, 2.1 Hz, ^4J = 0.9 Hz, 1H, H-3), 3.95 (dd, ^2J = 9.6 Hz, ^3J = 2.1 Hz, 1H, H_a-2), 4.19 – 4.26 (m, 2H, H_b-2, H-7a), 4.79 – 4.81 (m, 1H, H_a-1'), 5.07 (*virt.* quint., $^2J \approx {}^4J$ = 1.4 Hz, 1H, H_b-1').

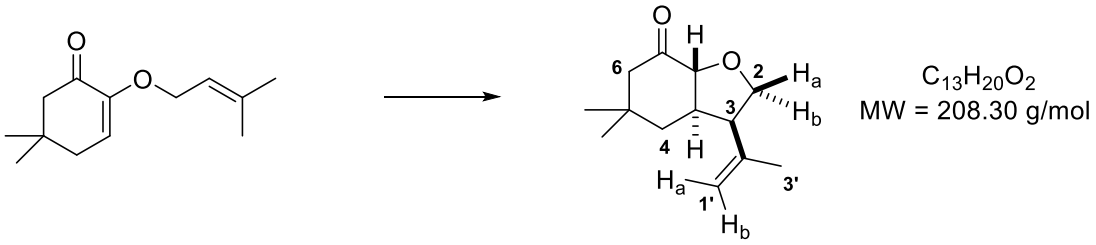
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 20.2 [q, C-3a(*C*H_3)], 23.4 (t, C-5), 25.5 (q, C-3'), 30.8 (t, C-4), 38.8 (t, C-6), 50.6 (s, C-3a), 55.3 (d, C-3), 72.6 (t, C-2), 85.3 (d, C-7a), 112.3 (t, C-1'), 145.5 (s, C-2'), 207.8 (s, C-7).

MS (EI, 70 eV): *m/z* (%) = 176 (6), 149 (7), 126 (97) [$C_7H_{10}O_2^+$], 111 (100) [$C_7H_{11}O^+$], 97 (67), 93 (45).

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O_2$ $[M]^+$: 194.1301; found: 194.1299.



(3*RS*,3a*RS*,7a*RS*)-5,5-Dimethyl-3-(prop-1-en-2-yl)hexahydrobenzofuran-7(4*H*)-one (*rac*-99)



59 *rac*-**99**

According to general procedure 5, compound *rac*-**99** was synthesized starting from enone **59** (24.8 mg, 120 µmol, 1.0 equiv) and txt (**23**) (2.57 mg, 12.1 µmol, 10 mol%) over 1.5 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, $KMnO_4$) afforded the product (21.2 mg, 102 µmol, 86%, d.r. > 95/5) as a colorless solid.

TLC: R_f = 0.09 (P/Et_2O = 3/1) [$KMnO_4$].

Mp: 95 – 101 °C.

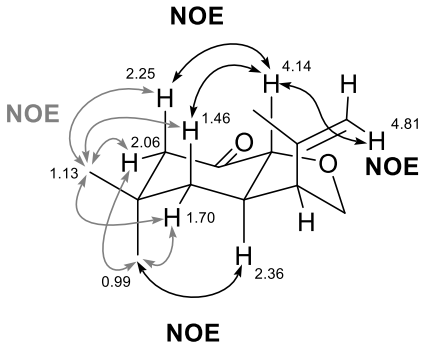
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2957 (m, $C_{sp3}H$), 1733 (vs, C=O), 1459 (w, $C_{sp3}H$), 1370 (w, $C_{sp3}H$), 1126 (w, C-O), 1060 (m, C-O), 919 (w).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.99 [s, 3H, C-5$(CH_3)_{ax}$], 1.13 [s, 3H, C-5$(CH_3)_{eq}$], 1.46 (*virt.* t, $^2J \approx {}^3J$ = 13.0 Hz, 1H, H_{ax}-4), 1.70 (ddd, ^2J = 13.0 Hz, ^3J = 3.2 Hz, ^4J = 2.3 Hz, 1H, H_{eq}-4), 1.81 (dd, ^4J = 1.4, 0.8 Hz, 3H, H-3'), 2.06 (dd, ^2J = 13.5 Hz, ^4J = 2.3 Hz, 1H, H_{eq}-6), 2.25 (ddd, ^2J = 13.5 Hz, ^4J = 1.7, 0.9 Hz, H_{ax}-6), 2.36 (*virt.* tdd, $^3J \approx {}^3J$ = 12.7 Hz, ^3J = 6.8, 3.2 Hz, 1H, H-3a), 2.84 (*virt.* t, $^3J \approx {}^3J$ = 6.6 Hz, 1H, H-3), 4.03 (dd, ^2J = 9.2 Hz, ^3J = 1.6 Hz, 1H, H_a-2), 4.10 – 4.21 (m, 2H, H_b-2, H-7a), 4.79 – 4.81 (m, 1H, H_a-1'), 5.06 (*virt.* quint., $^2J \approx {}^4J$ = 1.3 Hz, 1H, H_b-1').

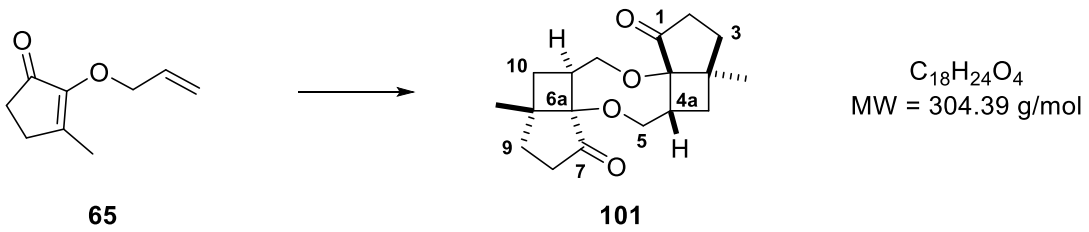
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.9 (q, C-3'), 27.2 [q, C-5($C_aH_3)_{ax}$], 32.1 [q, C-5($C_bH_3)_{eq}$], 38.5 (s, C-5), 39.0 (t, C-4), 46.3 (d, C-3a), 47.4 (d, C-3), 52.9 (t, C-6), 74.4 (t, C-2), 83.7 (d, C-7a), 112.7 (t, C-1'), 144.4 (s, C-2'), 207.2 (s, C-7).

MS (EI, 70 eV): *m/z* (%) = 208 (100) [M^+], 193 (8) [$C_{12}H_{17}O_2^+$], 164 (28), 152 (6) [$C_9H_{12}O_2^+$], 135 (44), 123 (87) [$C_8H_{11}O^+$], 105 (26), 95 (56) [$C_6H_7O^+$], 81 (10).

HRMS (EI, 70 eV): calc. for $C_{13}H_{20}O_2$ [$M]^+$: 208.1458; found: 208.1458.



(3a*RS*,4a*SR*,6a*SR*,9a*SR*,10a*RS*,12a*RS*)-3a,9a-Dimethyldodecahydro-1*H*,7*H*-cyclopenta[1,4]cyclobuta[1,2-*b*]cyclopenta[1,4]cyclobuta[1,2-*f*][1,5]dioxocine-1,7-dione (101)



65 **101**

According to general procedure 5, compound **101** was synthesized starting from enone **65** (61.7 mg, 405 µmol, 1.0 equiv) and txt (**23**) (8.50 mg, 40.0 µmol, 10 mol%) over 14 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, $KMnO_4$) afforded the product (11.1 mg, 36.5 µmol, 18%) as a colorless solid.

TLC: R_f = 0.30 (P/Et_2O = 3/1) [$KMnO_4$].

Mp: >220 °C

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2927 (m, $C_{sp3}H$), 1735 (vs, C=O), 1456 (w, $C_{sp3}H$), 1266 (w, C-O), 1114 (w, C-O), 1068 (s), 802 (w).

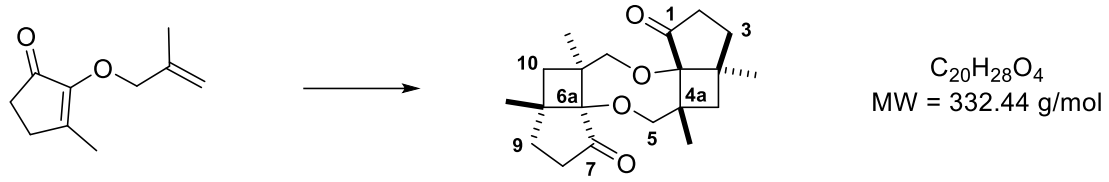
^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.15 [s, 6H, C-3a(CH_3), C-9a(CH_3)], 1.31 (dd, ^2J = 12.9 Hz, ^3J = 4.6 Hz, 2H, H-4, H-10), 1.58 – 1.70 (m, 2H, H-3, H-9), 1.72 – 1.89 (m, 4H, H-3, H-4, H-9, H-10), 2.27 – 2.47 (m, 4H, H-2, H-4a, H-8, H-10a), 2.67 (ddd, ^2J = 17.8 Hz, ^3J = 13.1, 8.8 Hz, 2H, H-2, H-8), 3.74 (dd, ^2J = 12.8 Hz, ^3J = 3.0 Hz, 2H, H-5, H-11), 4.46 – 4.53 (m, 2H, H-5, H-11).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 22.7 [q, C-3a(CH_3), C-9a(CH_3)], 28.9 (t, C-4, C-10), 34.0 (t, C-3, C-9), 35.8 (t, C-2, C-8), 36.0 (d, C-4a, C-10a), 44.5 (s, C-3a, C-9a), 66.8 (t, C-5, C-11), 81.3 (s, C-6a, C-12a), 220.2 (s, C-1, C-7).

MS (EI, 70 eV): *m/z* (%) = 304 (33) [M^+], 263 (25), 248 (53) [$C_{15}H_{20}O_3^+$], 230 (20), 208 (49) [$C_{12}H_{16}O_3^+$], 191 (15), 175 (10), 161 (13), 152 (72) [$C_9H_{12}O_2^+$], 137 (100) [$C_8H_9O_2^+$], 113 (54), 97 (74), 84 (67), 67 (63), 55 (85) [$C_3H_3O^+$], 41 (95).

HRMS (EI, 70 eV): calc. for $C_{18}H_{24}O_4$ [$M]^+$: 304.1669; found: 304.1674,
calc. for $C_{17}{}^{13}C_1H_{24}O_4$ [$M]^+$: 305.1703; found: 305.1723.

(3a*RS*,4a*SR*,6a*RS*,9a*SR*,10a*RS*,12a*SR*)-3a,4a,9a,10a-Tetramethyldodecahydro-1*H*,7*H*-cyclopenta[1,4]cyclobuta[1,2-*b*]cyclopenta[1,4]cyclobuta[1,2-*f*][1,5]dioxocine-1,7-dione (103)



66 **103**

According to general procedure 5, compound **103** was synthesized starting from enone **66** (66.9 mg, 402 µmol, 1.0 equiv) and txt (**23**) (8.50 mg, 40.0 µmol, 10 mol%) over 3 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1 → 3/1 → 1/1, $KMnO_4$) afforded the product (17.3 mg, 52.0 µmol, 26%) as a colorless solid.

TLC: R_f = 0.12 (P/Et_2O = 3/1) [$KMnO_4$].

Mp: 25 – 30 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2957 (m, $C_{sp3}H$), 1742 (vs, C=O), 1450 (w, $C_{sp3}H$), 1043 (w), 976 (w), 902 (w).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.99 [s, 6H, C-3a(CH_3), C-9a(CH_3)], 1.18 [s, 6H, C-4a(CH_3), C-10a(CH_3)], 1.65 (dddd, ^2J = 14.1 Hz, ^3J = 9.2, 4.0 Hz, ^4J = 0.9 Hz, 2H, H-3, H-9), 1.84 (d, ^2J = 8.3 Hz, 2H, H_b-4, H_b-10), 2.27 (dt, ^2J = 14.1 Hz, ^3J = 8.7 Hz,

2H, H-3, H-9), 2.49 – 2.68 (m, 6H, H-2, H_a-4, H-8, H_a-10), 3.95 (d, ^2J = 6.7 Hz, 2H, H-5, H-11), 4.11 (dd, ^2J = 6.7 Hz, ^4J = 1.7 Hz, 2H, H-5, H-11).

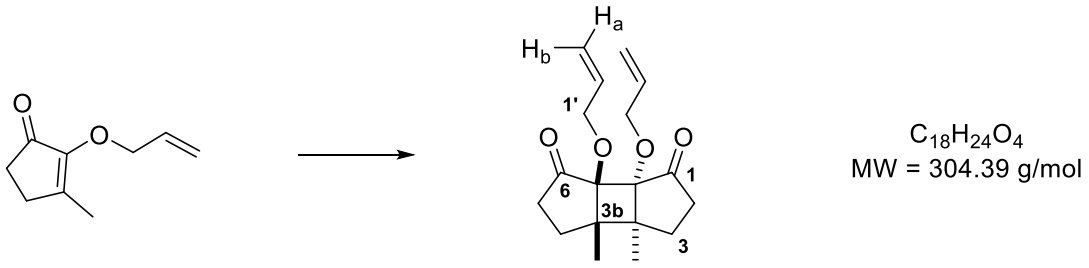
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 11.6 [q, C-4a(*C*H_3), C-10a(*C*H_3)], 15.0 [q, C-3a(*C*H_3), C-9a(*C*H_3)], 25.0 (t, C-3, C-9), 39.6 (t, C-2, C-8), 44.7 (t, C-4, C-10), 51.1 (s, C-3a*, C-9a*), 52.2 (s, C-4a*, C-10a*), 81.0 (t, C-5, C-11), 95.4 (s, C-6a, C-12a), 205.5 (s, C-1, C-7).

MS (EI, 70 eV): *m/z* (%) = 151 (37) [$C_9H_{11}O_2^+$], 137 (9) [$C_8H_9O_2^+$], 123 (58), 110 (43) [$C_7H_{10}O^+$], 95 (100) [$C_7H_{10}O^+$], 81 (64), 67 (92), 55 (79), 41 (47).

HRMS (EI, 70 eV): calc. for $C_{20}H_{28}O_4$ $[M]^+$: 332.1982; found: 332.1983.

* Assignment is interconvertible.

(3a*SR*,3b*SR*,6a*RS*,6b*RS*)-6a,6b-bis(allyloxy)-3a,3b-Dimethyloctahydrocyclobuta[1,2:3,4]-di[5]annulene-1,6-dione (*rac*-100)



According to general procedure 5, compound *rac*-**100** was synthesized starting from enone **65** (61.7 mg, 405 µmol, 1.0 equiv) and txt (**23**) (8.50 mg, 40.0 µmol, 10 mol%) over 14 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, $KMnO_4$) afforded the product (7.10 mg, 23.3 µmol, 12%) as a colorless solid.

TLC: R_f = 0.47 (P/Et_2O = 3/1) [$KMnO_4$].

Mp: > 220 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2964 (w, $C_{sp3}H$), 1748 (vs, C=O), 1451 (w, $C_{sp3}H$), 1413 (w), 1186 (w, C-O), 1089 (m), 1060 (w), 988 (w), 923 (w).

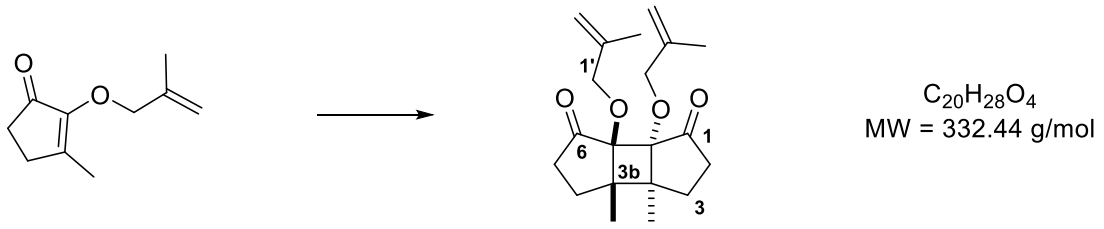
^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.25 [s, 6H, C-3a(CH_3), C-3b(CH_3)], 1.70 (ddd, ^2J = 14.9 Hz, ^3J = 13.1, 8.8 Hz, 2H, H-3, H-4), 2.24 – 2.41 (m, 4H, H-2, H-3, H-4, H-5), 2.54 – 2.73 (m, 2H, H-2, H-5), 4.08 (*virt.* ddt, ^2J = 12.8 Hz, ^3J = 5.4 Hz, $^4J \approx {}^4J$ = 1.5 Hz, 2H, H-1'), 4.18 (*virt.* ddt, ^2J = 12.8 Hz, ^3J = 5.0 Hz, $^4J \approx {}^4J$ = 1.6 Hz, 2H, H-1'), 5.07 (*virt.* dq, ^3J = 10.5 Hz, $^2J \approx {}^4J$ = 1.6 Hz, 2H, H_a-3'), 5.18 (*virt.* dq, ^3J = 17.2 Hz, $^2J \approx {}^4J$ = 1.6 Hz, 2H, H_b-3'), 5.71 – 5.89 (m, 2H, H-2').

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 19.1 [q, C-3a(*C*H_3), C-3b(*C*H_3)], 32.7 (t, C-3, C-4), 37.2 (t, C-2, C-5), 44.2 (s, C-3a, C-3b), 68.4 (t, C-1'), 86.1 (s, C-6a, C-6b), 116.1 (t, C-3'), 134.8 (d, C-2'), 214.2 (s, C-1, C-6).

MS (EI, 70 eV): *m/z* (%) = 152 (66) [$C_9H_{12}O_2^+$], 137 (100) [$C_8H_9O_2^+$], 123 (31), 96 (25) [$C_6H_8O^+$], 81 (19), 69 (31), 57 (34) [$C_3H_5O^+$], 41 (95) [$C_3H_5^+$].

HRMS (EI, 70 eV): calc. for $C_{18}H_{24}O_4$ $[M]^+$: 304.1669; found: 304.1660.

(3a*SR*,3b*SR*,6a*RS*,6b*RS*)-3a,3b-Dimethyl-6a,6b-bis((2-methylallyl)oxy)octahydro-cyclobuta[1,2:3,4]di[5]annulene-1,6-dione (*rac*-102)



66 *rac*-**102**

According to general procedure 5, compound *rac*-**102** was synthesized starting from enone **66** (66.9 mg, 402 µmol, 1.0 equiv) and txt (**23**) (8.50 mg, 40.0 µmol, 10 mol%) over 3 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1 → 3/1 → 1/1, $KMnO_4$) afforded the product (11.3 mg, 34.0 µmol, 17%) as a colorless solid.

TLC: R_f = 0.44 (P/Et_2O = 3/1) [$KMnO_4$].

Mp: 50 – 65 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2967 (m, $C_{sp3}H$), 1749 (vs, C=O), 1450 (w, $C_{sp3}H$), 1186 (w, C-O), 1097 (m), 1060 (w), 897 (w).

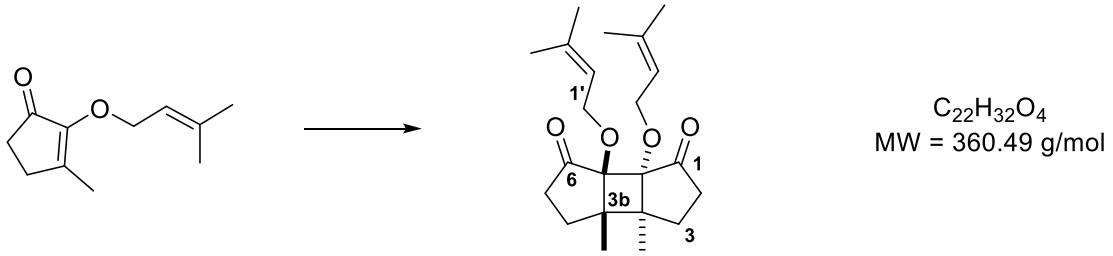
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.26 [s, 6H, C-3a(CH_3), C-3b(CH_3)], 1.66 [s, 6H, C-2'(CH_3)], 1.69 – 1.78 (m, 2H, H-3, H-4), 2.21 – 2.42 (m, 4H, H-2, H-3, H-4, H-5), 2.63 (ddd, ^2J = 17.6 Hz, ^3J = 13.7, 9.4 Hz, 2H, H-2, H-5), 3.99 (d, ^2J = 12.7 Hz, 2H, H-1'), 4.10 (d, ^2J = 12.7 Hz, 2H, H-1'), 4.78 (*virt.* dt, ^4J = 3.0 Hz, $^2J \approx {}^4J$ = 1.6 Hz, 2H, H-3'), 4.83 – 4.94 (m, 2H, H-3').

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 19.1 [q, C-3a(*C*H_3), C-3b(*C*H_3)], 19.6 [q, C-2'(*C*H_3)], 32.7 (t, C-3, C-4), 37.2 (t, C-2, C-5), 44.4 (s, C-3a, C-3b), 70.3 (t, C-1'), 85.8 (s, C-6a, C-6b), 110.5 (t, C-3'), 142.3 (s, C-2'), 214.0 (s, C-1, C-6).

MS (EI, 70 eV): *m/z* (%) = 213 (13), 182 (25), 166 (65) [$C_{10}H_{14}O_2^+$], 151 (44) [$C_9H_{11}O_2^+$], 123 (23), 110 (41) [$C_7H_{10}O^+$], 97 (23), 84 (46), 69 (27), 55 (100) [$C_4H_7^+$].

HRMS (EI, 70 eV): calc. for $C_{20}H_{28}O_4$ $[M]^+$: 332.1982; found: 332.1998.

(3a*SR*,3b*SR*,6a*RS*,6b*RS*)-3a,3b-Dimethyl-6a,6b-bis((3-methylbut-2-en-1-yl)oxy)octahydrocyclobuta[1,2:3,4]di[5]annulene-1,6-dione (*rac*-104)



67 *rac*-**104**

According to general procedure 5, compound *rac*-**104** was synthesized starting from enone **67** (72.3 mg, 401 µmol, 1.0 equiv) and txt (**23**) (8.50 mg, 40.0 µmol, 10 mol%) over 4 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 9/1 → 3/1 → 1/1, $KMnO_4$) afforded the product (24.3 mg, 67.4 µmol, 34%) as a colorless solid.

TLC: R_f = 0.44 (P/Et_2O = 3/1) [$KMnO_4$].

Mp: 85 – 98 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2967 (m, $C_{sp3}H$), 1748 (vs, C=O), 1448 (w, $C_{sp3}H$), 1381 (w, $C_{sp3}H$), 1185 (w, C-O), 1090 (m), 1060 (w), 982 (w).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.24 [s, 6H, C-3a(CH_3), C-3b(CH_3)], 1.58 [s, 6H, C-3'(CH_3)*], 1.64 – 1.72 (m, 8H, H-4'*, H-3, H-4), 2.23 – 2.39 (m, 4H, H-2, H-3, H-4, H-5), 2.62 (ddd, ^{2}J = 17.6 Hz, ^{3}J = 13.8, 9.3 Hz, 2H, H-2, H-5), 4.05 (dd, ^{2}J = 11.6 Hz, ^{3}J = 6.9 Hz, 2H, H-1'), 4.14 (dd, ^{2}J = 11.6 Hz, ^{3}J = 6.5 Hz, 2H, H-1'), 5.08 – 5.26 (m, 2H, H-2').

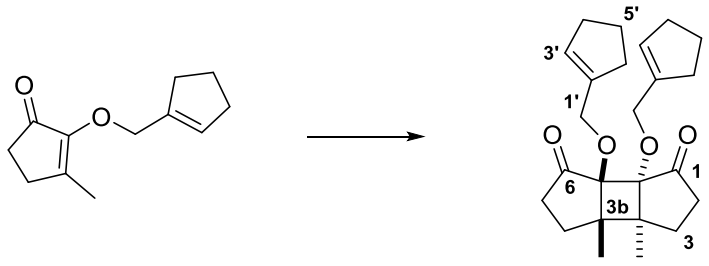
^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 18.3 [q, C-3'(CH_3)*], 19.3 [q, C-3a(CH_3), C-3b(CH_3)], 25.9 (q, C-4'*), 32.8 (t, C-3, C-4), 37.1 (t, C-2, C-5), 44.0 (s, C-3a, C-3b), 64.7 (t, C-1'), 86.3 (s, C-6a, C-6b), 121.6 (d, C-2'), 135.7 (s, C-3'), 214.4 (s, C-1, C-6).

MS (EI, 70 eV): *m/z* (%) = 224 (13), 160 (14) [$C_{10}H_8O_2^+$], 124 (11) [$C_8H_{12}O^+$], 113 (43), 97 (21), 83 (29), 69 (100) [$C_5H_9^+$], 55 (39) [$C_4H_7^+$], 41 (64).

HRMS (EI, 70 eV): calc. for $C_{22}H_{32}O_4$ $[M]^+$: 360.2295; found: 360.2296.

* Assignment is interconvertible.

(3a*SR*,3b*SR*,6a*RS*,6b*RS*)-6a,6b-Bis(cyclopent-1-en-1-ylmethoxy)-3a,3b-dimethylocta-hydrocyclobuta[1,2:3,4]di[5]annulene-1,6-dione (*rac*-105)



68 *rac*-**105**

$C_{24}H_{32}O_4$
MW = 384.52 g/mol

$^{F}Ir_{pic}$ (1.80 mg, 2.59 μmol, 2.5 mol%) was dissolved in 1.0 mL dry degassed CH_2Cl_2 and transferred to a flame dried duran phototube. Substrate **68** (19.4 mg, 101 μmol, 1.0 equiv) dissolved in 1.0 mL dry degassed CH_2Cl_2 was then added, and the reaction mixture was diluted with dry degassed CH_2Cl_2 until a concentration of 10 mM (relative to the substrate) was reached. The reaction mixture was irradiated at λ = 420 nm at rt until full conversion was achieved. The solvent was removed under reduced pressure. After purification by flash

column chromatography (SiO_2, P/Et_2O = 9/1, $KMnO_4$) the product *rac*-**105** (3.8 mg, 9.88 μmol, 10%) was obtained as a colorless oil.

TLC: R_f = 0.45 (P/Et_2O = 3/1) [UV, $KMnO_4$].

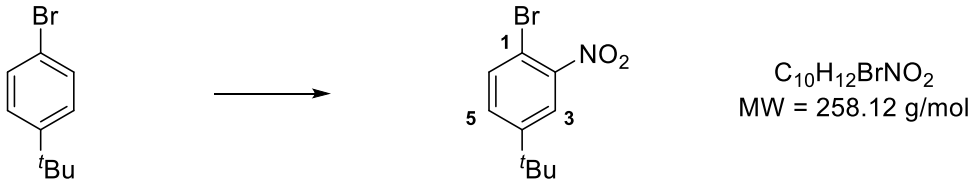
^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.25 [s, 6H, C-3a(CH_3), C-3b(CH_3)], 1.70 (*virt.* td, $^2J \approx {}^3J$ = 14.0 Hz, ^3J = 9.1 Hz, 2H, H-3, H-4), 1.86 (*virt.* dquint., ^2J = 14.8 Hz, $^3J \approx {}^3J$ = 7.6 Hz, 4H, H-5'), 2.16 – 2.42 (m, 12H, H-2, H-3, H-4, H-5, H-4', H-6'), 2.63 (ddd, ^2J = 17.8 Hz, ^3J = 13.6, 9.4 Hz, 2H, H-2, H-5), 4.07 – 4.16 (m, 2H, H-1'), 4.20 – 4.30 (m, 2H, H-1'), 5.47 – 5.59 (m, 2H, H-3').

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 19.1 [q, C-3a(*C*H_3), C-3b(*C*H_3], 23.3 (t, C-5'), 32.4 (t, C-4'*), 32.8 (t, C-3, C-4), 32.9 (t, C-6'*), 37.2 (t, C-2, C-5), 44.3 (s, C-3a, C-3b), 66.4 (t, C-1'), 85.8 (s, C-6a, C-6b), 126.0 (d, C-3'), 141.4 (s, C-2'), 214.0 (s, C-1, C-6).

* Assignment is interconvertible.

4.3.4 Chiral-at-metal Rh Catalyst

1-Bromo-4-(*tert*-butyl)-2-nitrobenzene (107)



106 **107**

A round bottom flask charged with nitric acid (65 wt%, 2.58 mL, 3.59 g, 57.0 mmol, 1.4 equiv) was cooled to 0 °C and sulfuric acid (96 wt%, 3.60 mL, 6.62 g, 67.5mmol, 1.7 equiv) was added dropwise. Subsequently, 1-bromo-4-*tert*-butylbenzene (**106**) (6.92 mL, 8.50 g, 40.0 mmol, 1.0 equiv) was added dropwise and the two-phase reaction mixture was stirred at rt for 23 h. At this time it was poured onto 200 mL of ice-water, the product was taken up in 20 mL of Et_2O and the aqueous layer was extracted with Et_2O

(3 × 50 mL). The combined organic layers were washed with brine (1 × 50 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, CyH/EtOAc = 98/2, UV) the product **107** (5.97 g, 23.1 mmol, 58%) was obtained as a yellow oil.

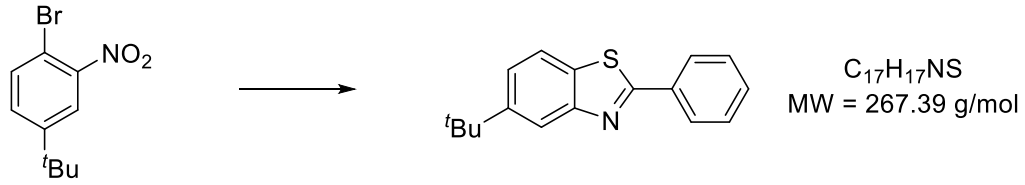
TLC: R_f = 0.49 (P) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.34 [s, 9H, $C(CH_3)_3$], 7.44 (dd, ^3J = 8.5 Hz, ^4J = 2.3 Hz, 1H, H-5), 7.64 (d, ^3J = 8.5 Hz, 1H, H-6), 7.83 (d, ^4J = 2.3 Hz, 1H, H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 31.1 [q, $C(CH_3)_3$], 35.1 [s, $C(CH_3)_3$], 111.2 (s, C-1), 122.9 (d, C-3), 130.8 (d, C-5), 134.7 (d, C-6), 149.7 (s, C-4), 152.6 (s, C-2).

Data of this compound were in accordance with the literature.[38]

5-(*tert*-Butyl)-2-phenylbenzo[*d*]thiazole (108)



107 **108**

To compound **107** (2.20 g, 8.52 mmol, 1.0 equiv) were added S_8 (0.41 g, 12.8 mmol, 1.5equiv) and benzylamine (2.33 mL, 2.29 g, 21.3 mmol, 2.5 equiv) and the system was evacuated. Subsequently, the reagents were dissolved in 1.7 mL of dry pyridine and the reaction mixture was stirred at 100 °C for 23 h. The reaction mixture was allowed to cool to rt and the reaction was quenched by the addition of 25 mL 2 M HCl. The aqueous layer was extracted with EtOAc (3 × 15 mL), the combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, CyH/EtOAc = 95/5, UV) the product **108** (2.02g, 7.54 mmol, 89%) was obtained as a yellow solid.

TLC: R_f = 0.15 (CyH/EtOAc = 95/5) [UV, $KMnO_4$].

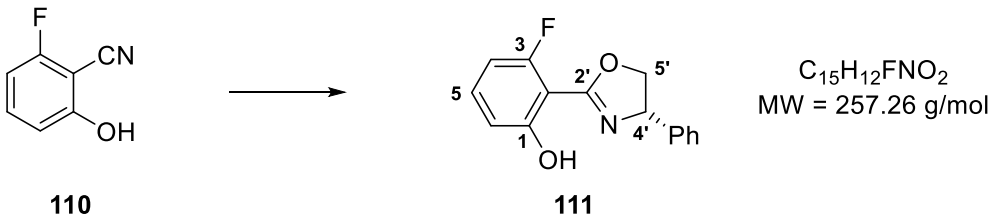
Mp: 79 – 83 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.42 [s, 9H, $C(CH_3)_3$], 7.44 – 7.54 (m, 4H, H_{ar}), 7.83 (d, ^3J = 8.5 Hz, 1H, H_{ar}), 8.08 – 8.11 (m, 2H, H_{ar}), 8.12 (d, ^4J = 1.9 Hz, 1H, H_{ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 31.7 [q, $C(CH_3)_3$], 35.1 [s, $C(CH_3)_3$], 119.8 (d, C_{ar}), 121.1 (d, C_{ar}), 123.6 (d, C_{ar}), 127.6 (d, C_{ar}), 129.2 (d, C_{ar}), 131.0 (d, C_{ar}), 132.1 (s, C_{ar}), 133.9 (s, C_{ar}), 150.2 (s, C_{ar}), 168.3 (s, NCS).

Data of this compound were in accordance with the literature.[38]

(*S*)-3-Fluoro-2-(4-phenyl-4,5-dihydrooxazol-2-yl)phenol (111)



To a solution of 2-fluoro-6-hydroxybenzonitrile (**110**) (3.56 g, 26.0 mmol, 1.3 equiv) and L-phenylglycinol (**109**) (2.74 g, 20.0 mmol, 1.0 equiv) in 20 mL of dry tol was added $ZnCl_2$ (1.0 M in Et_2O, 0.5 mL, 0.5 mmol, 2.5 mol%) and the reaction mixture was refluxed for 15 h. Subsequently, it was allowed to cool to rt, extracted with EtOAc (1 × 30 mL) and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 10/1, UV) product **111** (2.83 g, 11.0 mmol, 55%) was obtained as a colorless solid.

TLC: R_f = 0.53 (P/Et_2O = 2/1) [UV, $KMnO_4$].

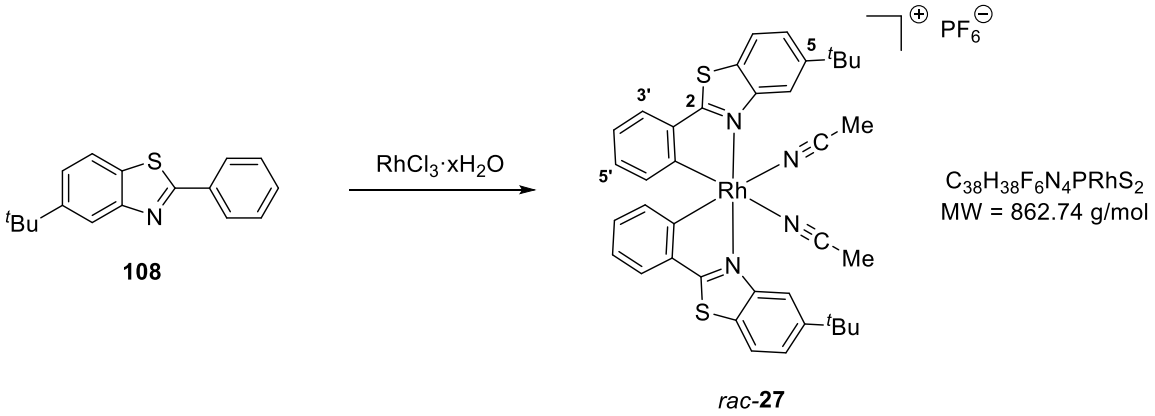
Mp: 64 – 67 °C.

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 4.32 (*virt.* t, $^2J \approx {}^3J$ = 8.5 Hz, 1H, H-5'), 4.87 (dd, ^2J = 8.6 Hz, ^3J = 10.3 Hz, 1H, H-5'), 5.42 (dd, ^3J = 10.3, 8.4 Hz, 1H, H-4'), 6.63 (ddd, ^3J = 11.1, 8.3 Hz, ^4J = 1.1 Hz, 1H, H_{ar}), 6.84 (dt, ^3J = 8.5 Hz, ^4J = 1.0 Hz, 1H, H_{ar}), 7.41 – 7.27 (m, 6H, H_{ar}).

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 67.4 (d, C-4'), 74.7 (t, C-5'), 106.3 (d, *J* = 22.2 Hz, C-3), 113.1 (d, *J* = 3.3 Hz, C_{ar}), 126.7 (d, C_{ar}), 128.2 (d, C_{ar}), 129.1 (d, C_{ar}), 133.7 (d, *J* = 11.6 Hz, C_{ar}), 141.3 (s, C_{ar}), 160.4 (s, C_{ar}), 163.0 (d, C_{ar}), 165.6 (s, C-2').

Data of this compound were in accordance with the literature.[38]

***rac*-RhS (*rac*-27)**



To a solution of $RhCl_3 \cdot xH_2O$ (40 wt% Rh, 1.01 g, 3.74 mmol, 1.0 equiv) and thiazol ligand **108** (2.00 g, 7.48 mmol, 2.0 equiv) in 56 mL 2-ethoxyethanol were added 18.7 mL of H_2O under inert gas, and the reaction mixture was stirred at 125 °C for 4 h. The reaction mixture was allowed to cool to rt, the solvent was removed under reduced pressure, and the flask was evacuated and backfilled with Ar. The residue was dissolved in 75 mL of dry MeCN, $AgPF_6$ (189 mg, 7.48 mmol, 2.0 equiv) was added and the reaction mixture was stirred at rt for 14 h. The formed precipitate was filtered off and the solvent was removed under reduced pressure. After purification by flash column chromatography (CH_2Cl_2 → CH_2Cl_2/MeCN = 99/1 →99/5, UV) product *rac*-RhS (*rac*-**27**) (1.02 g, 1.19 mmol, 32%) was obtained as a pale yellow solid.

TLC: R_f = 0.64 (CH_2Cl_2/MeCN = 4/1) [UV].

Mp: > 230 °C.

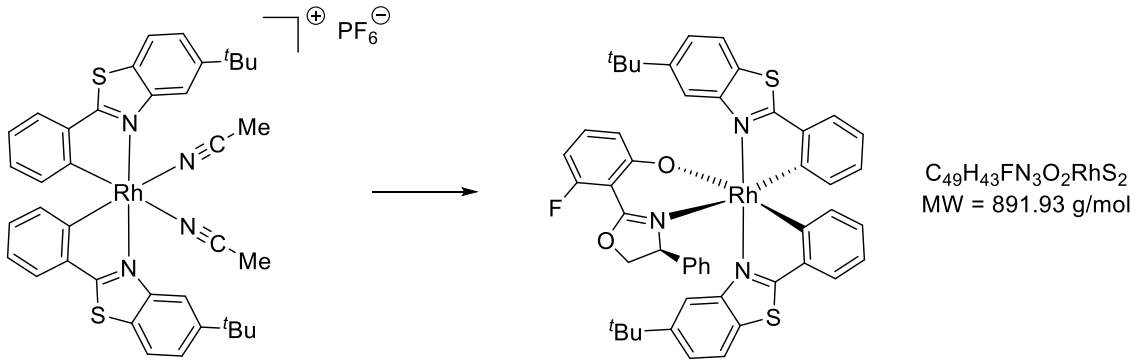
^{1}H NMR (500 MHz, CD_2Cl_2, 300 K): δ [ppm] = 1.45 [s, 18H, $C(CH_3)_3$], 2.18 [s, 6H, $NC(CH_3)$], 6.19 (d, ^3J = 7.9 Hz, 2H, H-6'), 6.83 (td, ^3J = 7.6 Hz, ^4J = 1.4 Hz, 2H, H-5'),

7.03 (td, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 2H, H-4'), 7.66 (dd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 2H, H-3'), 7.72 (dd, ^3J = 8.6 Hz, ^4J = 1.8 Hz, 2H, H-6), 8.02 (d, ^4J = 8.6 Hz, 2H, H-7), 8.48 (s, 2H, H-4).

^{13}C NMR (126 MHz, CD_2Cl_2, 300 K): δ [ppm] = 3.9 [q, NC(*C*H$_3$)], 31.8 [q, C(*C*H$_3$)$_3$], 35.7 [s, *C*(CH$_3$)$_3$)], 117.0 [s, N*C*(CH$_3$)], 122.3 (d, C-4), 123.1 (d, C$_{Ar}$), 124.6 (d, C$_{Ar}$), 125.6 (d, C$_{Ar}$), 126.4 (s, C$_{Ar}$), 129.2 (d, C$_{Ar}$), 131.4 (d, C$_{Ar}$), 133.5 (s, C$_{Ar}$), 140.5 (s, C$_{Ar}$), 150.1 (s, C$_{Ar}$), 152.9 (s, C$_{Ar}$), 160.8 (s, C$_{Ar}$), 161.0 (s, C$_{Ar}$), 177.0 (s, NCS).

Data of this compound were in accordance with the literature.[38]

Δ-RhS-aux (113)



rac-**27** **113**

Under inert gas, *rac*-RhS (*rac*-**27**) (863 mg, 1.00 mmol, 1.0 equiv), K_2CO_3 (414 mg, 3.00 mmol, 3.0 equiv) and auxiliary **111** (284 mg, 1.10 mmol, 1.1 equiv) were dissolved in 40 mL of dry EtOH. The reaction mixture was stirred at 70 °C for 5 h and the solvent was removed under reduced pressure. After separation of the diastereoisomers by flash column chromatography (SiO_2, P/Et_2O = 20/1 → 10/1 → 5/1 → 1/1 → EtOAc, UV) Δ-RhS-aux (**113**) (297 mg, 333 µmol, 33%) was obtained as a yellow solid.

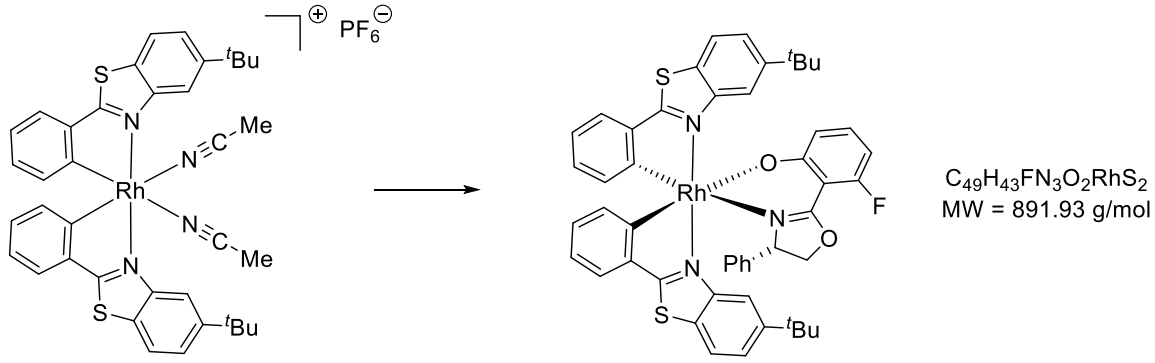
TLC: R_f = 0.37 (P/Et_2O = 1/1) [UV].
Mp: 145 – 155 °C.

^{1}H NMR (400 MHz, CD_2Cl_2, 300 K): δ [ppm] = 1.22 [s, 3H, $C(CH_3)_3$], 1.36 [s, 3H, $C(CH_3)_3$], 3.91 (dd, ^{2}J = 8.3 Hz, ^{3}J = 12.0 Hz, C*H*H), 4.02 (dd, ^{3}J = 12.0, 9.1 Hz, 1H, CH), 4.30 (*virt*. t, $^{2}J \approx {}^{3}J$ = 8.7 Hz, 1H, CH*H*), 5.80 (dd, ^{3}J = 11.6, 7.9 Hz, 1H, H_{Ar}), 6.13 (d, ^{3}J = 7.8 Hz, 1H, H_{Ar}), 6.23 (d, ^{3}J = 8.7 Hz, 1H, H_{Ar}), 6.28 (d, ^{3}J = 7.8 Hz, 1H, H_{Ar}), 6.35 – 6.49 (m, 1H, H_{Ar}), 6.56 (t, ^{3}J = 7.4 Hz, 1H, H_{Ar}), 6.70 – 6.89 (m, 7H, H_{Ar}), 6.89 – 6.98 (m, 1H, H_{Ar}), 7.18 (d, ^{3}J = 7.6 Hz, H_{Ar}), 7.50 (dd, ^{3}J = 8.7 Hz, ^{4}J = 1.8 Hz, 1H, H_{Ar}), 7.56 – 7.67 (m, 2H, H_{Ar}), 7.79 (d, ^{3}J = 8.6 Hz, 1H, H_{Ar}), 7.93 (d, ^{3}J = 8.5 Hz, 1H, H_{Ar}), 8.36 (d, ^{4}J = 1.8 Hz, 1H, H_{Ar}), 9.05 (d, ^{4}J = 1.9 Hz, 1H, H_{Ar}).

^{13}C NMR (126 MHz, CD_2Cl_2, 300 K): δ [ppm] = 31.6 [q, $C(CH_3)_3$], 31.7 [q, $C(CH_3)_3$], 35.5 [s, $C(CH_3)_3$], 35.7 [s, $C(CH_3)_3$], 70.4 (d, CH), 75.1 (t, CH_2), 98.7 (d, *J* = 22.8 Hz, C_{Ar}), 103.9 (d, *J* = 7.7 Hz, C_{Ar}), 117.4 (d, C_{Ar}), 119.0 (d, C_{Ar}), 122.1 (d, C_{Ar}), 122.2 (d, C_{Ar}), 122.4 (d, C_{Ar}), 123.2 (d, C_{Ar}), 124.6 (d, C_{Ar}), 124.7 (d, C_{Ar}), 125.8 (d, C_{Ar}), 126.1 (d, C_{Ar}), 127.5 (d, C_{Ar}), 127.8 (d, C_{Ar}), 128.3 (d, C_{Ar}), 128.7 (d, C_{Ar}), 128.9 (d, C_{Ar}), 129.7 (d, C_{Ar}), 130.3 (d, C_{Ar}), 132.9 (d, C_{Ar}), 133.0 (d, C_{Ar}), 133.6 (d, C_{Ar}), 135.3 (d, C_{Ar}), 138.8 (s, C_{Ar}), 140.7 (s, C_{Ar}), 141.2 (s, C_{Ar}), 151.2 (s, C_{Ar}), 151.4 (s, C_{Ar}), 152.7 (s, C_{Ar}), 163.9 (d, C_{Ar}), 167.2 (s, NCS), 168.6 (s, NCS), 169.0 (s, C_{Ar}), 169.2 (s, C_{Ar}), 169.5 (s, C_{Ar}), 175.0 (s, C_{Ar}), 176.7 (s, C_{Ar}, NCO).

Data of this compound were in accordance with the literature.[38]

Λ-RhS-aux (112)



rac-**27** **112**

Under inert gas, *rac*-RhS (*rac*-**27**) (863 mg, 1.00 mmol, 1.0 equiv), K_2CO_3 (414 mg, 3.00 mmol, 3.0 equiv) and auxiliary **111** (284 mg, 1.10 mmol, 1.1 equiv) were dissolved in

40 mL of dry EtOH. The reaction mixture was stirred at 70 °C for 5 h and the solvent was removed under reduced pressure. After separation of the diastereoisomers by flash column chromatography (SiO_2, P/Et_2O = 20/1 → 10/1 → 5/1 → 1/1 → EtOAc, UV) Λ-RhS-aux (**112**) (280 mg, 314 μmol, 31%) was obtained as a yellow solid.

TLC: R_f = 0.51 (P/Et_2O = 1/1) [UV].

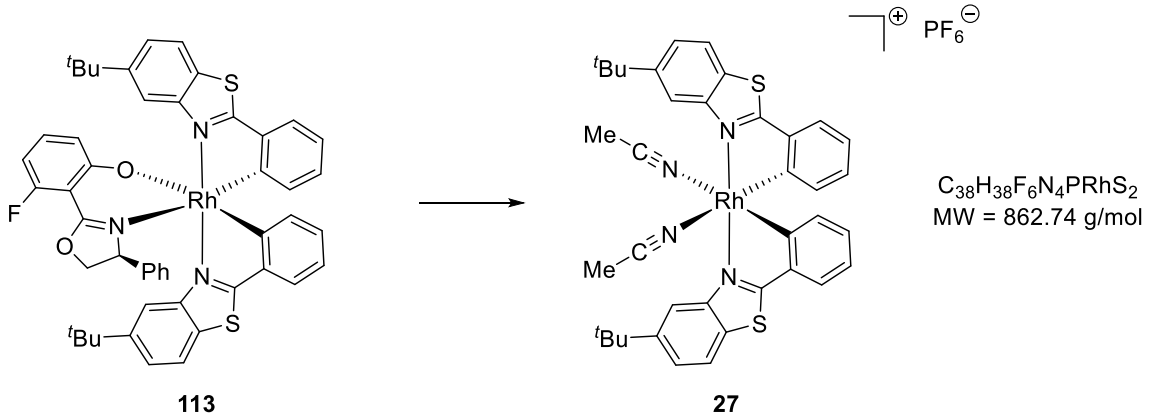
Mp: > 230 °C.

^{1}H NMR (500 MHz, CD_2Cl_2, 300 K): δ [ppm] = 1.27 [s, 9H, $C(CH_3)_3$], 1.44 [s, 9H, $C(CH_3)_3$], 3.96 – 4.04 (m,1H, C*H*H), 4.82 – 4.90 (m, 2H, CH, CH*H*), 5.80 (ddd, ^3J = 12.7, 7.9 Hz, ^4J = 1.2 Hz, 1H, H_{Ar}), 5.87 (dt, ^3J = 8.0 Hz, ^4J = 1.0 Hz, 1H, H_{Ar}), 6.27 – 6.34 (m, 3H, H_{Ar}), 6.37 (*virt.* dt, ^3J = 8.8 Hz, $^4J \approx {}^4J$ = 0.9 Hz, 1H, H_{Ar}), 6.69 – 6.86 (m, 6H, H_{Ar}), 6.93 (td, ^3J = 7.4 Hz, ^4J = 1.1 Hz, 1H, H_{Ar}), 6.97 (td, ^3J = 7.4 Hz, ^4J = 1.2 Hz, 1H, H_{Ar}), 7.40 (ddd, ^3J = 7.6 Hz, ^4J = 1.4, 0.9 Hz, 1H, H_{Ar}), 7.46 (dd, ^3J = 8.6 Hz, ^4J = 1.9 Hz, 1H, H_{Ar}), 7.53 (dd, ^3J = 8.6 Hz, ^4J = 1.8 Hz, 1H, H_{Ar}), 7.57 – 7.63 (m, 2H, H_{Ar}), 7.80 (dd, ^3J = 8.6 Hz, ^4J = 0.5 Hz, 1H, H_{Ar}), 7.97 (dd, ^3J = 1.7 Hz, ^4J = 0.5 Hz, 1H, H_{Ar}), 8.89 (dd, ^3J = 1.9 Hz, ^4J = 0.5 Hz, 1H, H_{Ar}).

^{13}C NMR (126 MHz, CD_2Cl_2, 300 K): δ [ppm] = 31.8 [q, $C(CH_3)_3$], 35.4 [s, $C(CH_3)_3$], 35.5 [s, $C(CH_3)_3$], 69.6 (d, CH), 75.9 (t, CH_2), 98.8 (d, J = 24.2 Hz, C_{Ar}), 101.5 (d, C_{Ar}), 116.7, (d, C_{Ar}), 119.8 (d, C_{Ar}), 120.6 (d, C_{Ar}), 121.5 (d, C_{Ar}), 122.5 (d, C_{Ar}), 122.6 (d, C_{Ar}), 123.2 (d, C_{Ar}), 124.1 (d, C_{Ar}), 126.0 (d, C_{Ar}), 126.1 (d, C_{Ar}), 127.7 (d, C_{Ar}), 128.1 (d, C_{Ar}), 129.5 (d, C_{Ar}), 129.7 (d, C_{Ar}), 130.0 (d, C_{Ar}), 133.1 (d, C_{Ar}), 133.4 (d, C_{Ar}), 135.5 (d, C_{Ar}), 141.4 (s, C_{Ar}), 141.6 (s, C_{Ar}), 141.9 (s, C_{Ar}), 151.5 (s, C_{Ar}), 151.6 (s, C_{Ar}), 151.7 (s, C_{Ar}), 163.5 (d, C_{Ar}), 165.9 (s, NCS), 168.1 (s, C_{Ar}), 168.2 (s, C_{Ar}), 170.4 (s, C_{Ar}), 175.3 (s, C_{Ar}), 175.9 (s, C_{Ar}), 177.5 (s, NCO).

Data of this compound were in accordance with the literature.[38]

Δ-RhS (27)



113 **27**

To a suspension of Δ-RhS-aux (**113**) (150 mg, 168 µmol, 1.0 equiv) in 5.0 mL of dry MeCN was added TFA (90.0 µL, 134 mg, 1.14 mmol, 6.8 equiv) and the reaction mixture was stirred at rt under the exclusion of light for 30 min. The solvent was removed under reduced pressure, the residue was dissolved in a minimum of CH_2Cl_2 and transferred onto a column (SiO_2). After elution of the cleaved auxiliary (CH_2Cl_2 → CH_2Cl_2/MeCN = 99/1, 2 vol% TFA → 95/5), NH_4PF_6 (331 mg, 2.03 mmol. 12 equiv) was added on top of the column and **27** was eluted (CH_2Cl_2/MeCN = 1/1). The solvent was removed under reduced pressure and after purification by flash column chromatography (SiO_2, CH_2Cl_2/MeCN = 99/1, UV) product **27** (138 mg, 160 µmol, 95%) was obtained as a pale yellow solid.

TLC: R_f = 0.64 (CH_2Cl_2/MeCN = 4/1) [UV].

Mp: > 230 °C.

^{1}H NMR (400 MHz, CD_2Cl_2, 300 K): δ [ppm] = 1.45 [s, 18H, $C(CH_3)_3$], 2.18 [s, 6H, $NC(CH_3)$], 6.19 (d, ^3J = 7.9 Hz, 2H, H-6'), 6.83 (td, ^3J = 7.6 Hz, ^4J = 1.4 Hz, 2H, H-5'), 7.03 (td, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 2H, H-4'), 7.66 (dd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 2H, H-3'), 7.72 (dd, ^3J = 8.6 Hz, ^4J = 1.8 Hz, 2H, H-6), 8.02 (d, ^4J = 8.6 Hz, 2H, H-7), 8.48 (s, 2H, H-4).

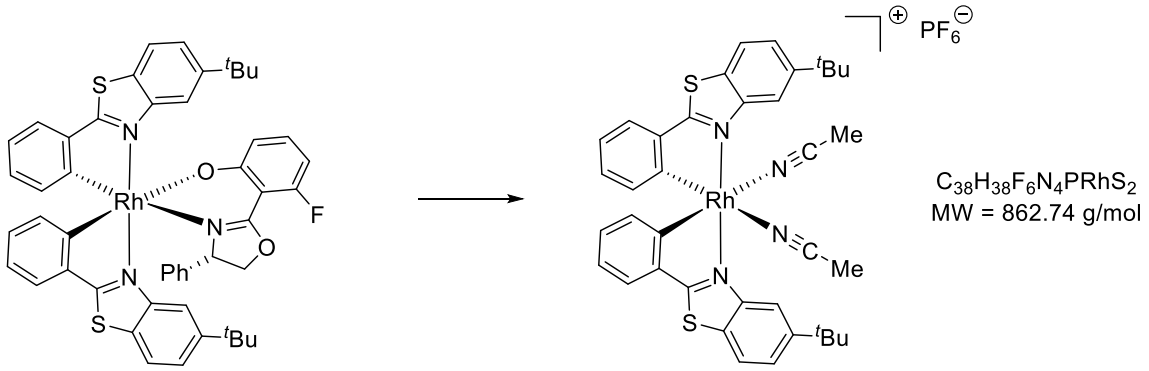
^{13}C NMR (126 MHz, CD_2Cl_2, 300 K): δ [ppm] = 3.9 [q, NC(CH_3)], 31.8 [q, C(CH_3)$_3$], 35.7 [s, $C(CH_3)_3$)], 117.0 [s, N$C(CH_3)$], 122.3 (d, C-4), 123.1 (d, C_{Ar}), 124.6 (d, C_{Ar}), 125.6 (d, C_{Ar}), 126.4 (s, C_{Ar}), 129.2 (d, C_{Ar}), 131.4 (d, C_{Ar}), 133.5 (s, C_{Ar}), 140.5 (s, C_{Ar}), 150.1 (s, C_{Ar}), 152.9 (s, C_{Ar}), 160.8 (s, C_{Ar}), 161.0 (s, C_{Ar}), 177.0 (s, NCS).

Rotation angle $[\alpha]_D^{25}$ = -230 (*c* = 0.104, CH_2Cl_2).

EA: calc. for $C_{38}H_{38}F_6N_4PRhS_2$: C 52.90, H 4.44, N 6.49, S 7.43; found: C 53.11, H 4.78, N 5.61, S 7.26.

Data of this compound were in accordance with the literature.[38]

Λ-RhS (*ent*-27)



112 *ent*-**27**

To a suspension of Λ-RhS-aux (**112**) (158 mg, 176 µmol, 1.0 equiv) in 5.0 mL of dry MeCN was added TFA (90.0 µL, 134 mg, 1.14 mmol, 6.8 equiv) and the reaction mixture was stirred at rt under the exclusion of light for 30 min. The solvent was removed under reduced pressure, the residue was dissolved in a minimum of CH_2Cl_2 and transferred onto a column (SiO_2). After elution of the cleaved auxiliary (CH_2Cl_2 → CH_2Cl_2/MeCN = 99/1, 2 vol% TFA → 95/5), NH_4PF_6 (327 mg, 2.01 mmol. 11 equiv) was added on top of the column and *ent*-**27** was eluted (CH_2Cl_2/MeCN = 1/1). The solvent was removed under reduced pressure and after purification by flash column chromatography (SiO_2, CH_2Cl_2/MeCN = 99/1, UV) product *ent*-**27** (109 mg, 126 µmol, 72%) was obtained as a pale yellow solid.

TLC: R_f = 0.64 (CH_2Cl_2/MeCN = 4/1) [UV].

Mp: > 230 °C.

^{1}H NMR (500 MHz, CD_2Cl_2, 300 K): δ [ppm] = 1.45 [s, 18H, $C(CH_3)_3$], 2.18 [s, 6H, $NC(CH_3)$], 6.19 (d, ^3J = 7.9 Hz, 2H, H-6'), 6.83 (td, ^3J = 7.6 Hz, ^4J = 1.4 Hz, 2H, H-5'), 7.03 (td, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 2H, H-4'), 7.66 (dd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 2H, H-3'),

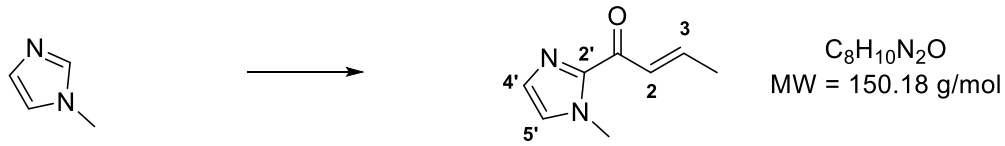
7.72 (dd, ^{3}J = 8.6 Hz, ^{4}J = 1.8 Hz, 2H, H-6), 8.02 (d, ^{4}J = 8.6 Hz, 2H, H-7), 8.48 (s, 2H, H-4).

^{13}C NMR (126 MHz, CD_2Cl_2, 300 K): δ [ppm] = 3.9 [q, NC(*C*H_3)], 31.8 [q, C(*C*H_3)$_3$], 35.7 [s, *C*(CH$_3$)$_3$)], 117.0 [s, N*C*(CH$_3$)], 122.3 (d, C-4), 123.1 (d, C_{Ar}), 124.6 (d, C_{Ar}), 125.6 (d, C_{Ar}), 126.4 (s, C_{Ar}), 129.2 (d, C_{Ar}), 131.4 (d, C_{Ar}), 133.5 (s, C_{Ar}), 140.5 (s, C_{Ar}), 150.1 (s, C_{Ar}), 152.9 (s, C_{Ar}), 160.8 (s, C_{Ar}), 161.0 (s, C_{Ar}), 177.0 (s, NCS).

Rotation angle $[\alpha]_D^{25}$ = 212 (*c* = 0.113, CH_2Cl_2).

Data of this compound were in accordance with the literature.[38]

(*E*)-1-(1-Methyl-1*H*-imidazol-2-yl)but-2-en-1-one (114)



115 **114**

A solution of 1-methylimidazole (**115**) (2.00 g, 24.4 mmol, 2.1 equiv) in 50 mL of dry THF was cooled to –78 °C and *n*-BuLi (2.5 m in H, 11.0 mL, 1.76 g, 27.5 mmol, 2.4 equiv) was added dropwise and the reaction mixture was stirred for 45 min. Subsequently, a solution of crotonic acid (1.00 g, 11.6 mmol, 1.0 equiv) in 8.0 mL of dry THF was added dropwise. The reaction mixture was allowed to warm to rt and stirred for 2 h. The reaction was quenched by the addition of 50 mL of $NaHCO_{3(aq)}$ and the aqueous layer was extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with brine (1 × 80 mL), filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 1/1, UV) product **114** (450 mg, 2.99 mmol, 27%) was obtained as a colorless solid.

TLC: R_f = 0.43 (Et_2O) [UV, $KMnO_4$].

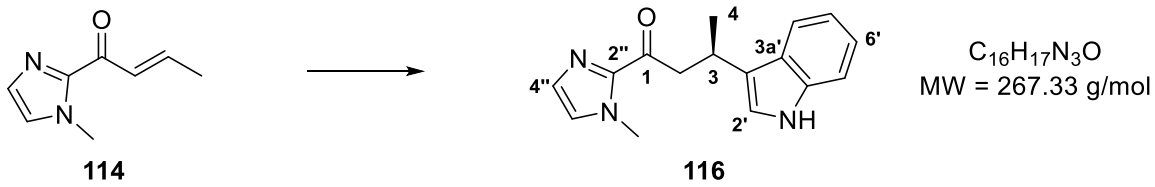
Mp: 29 – 32 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.99 (dd, ^{3}J = 6.9 Hz, ^{4}J = 1.7 Hz, 3H, H-4), 4.04 [s, 3H, $N(CH_3)$], 7.03 (s, 1H, H-4'*), 7.12 (dq, ^{3}J = 15.6, 6.9 Hz, 1H, H-3), 7.16 (s, 1H, H-5'*), 7.41 (dq, ^{3}J = 15.6 Hz, ^{4}J = 1.7 Hz, 1H, H-2).
^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 18.6 (q, C-4), 36.4 [q, $N(CH_3)$], 127.2 (d, C-4'*), 128.0 (d, C-2), 129.3 (d, C-5'*), 143.8 (s, C-2'), 144.0 (d, C-3), 180.8 (s, C-1).

* Assignment is interconvertible.

Data of this compound were in accordance with the literature.[33]

(*R*)-3-(1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (116)



114 116

Racemic Friedel-Crafts alkylation
To a solution of *rac*-**27** (1.80 mg, 0.21 μmol, 1.2 mol%) in 200 μL of dry THF was added substrate **114** (26.5mg, 180 μmol, 1.0 equiv) and the reaction mixture was stirred for 20 min at rt. Subsequently, indole (60.2 mg, 510 μmol, 2.8 equiv) was added, the reaction mixture was stirred for further 15 h and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 2/3, UV) product *rac*-**116** (42.2 mg, 158 μmol, 79%) was obtained as a colorless oil.

Enantioselective Friedel-Crafts alkylation
To a solution of **27** (1.72 mg, 0.20 μmol, 1.0 mol%) in 200 μL of dry THF was added substrate **114** (30.6 mg, 204 μmol, 1.0 equiv) and the reaction mixture was stirred for 20 min at rt. Subsequently, indole (58.3 mg, 498 μmol, 2.5 equiv) was added, the reaction mixture was stirred for further 17 h and the solvent was removed under reduced pressure. After

purification by flash column chromatography (SiO_2, P/Et_2O = 2/3 → 1/3, UV) product **116** (41.2 mg, 154 µmol, 77%, 95% *ee*) was obtained as a colorless oil.

TLC: R_f = 0.09 (P/Et_2O = 2/3) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] =1.43 (d, ^3J = 6.9 Hz, 3H, H-4), 3.46 (dd, ^2J = 15.8 Hz, ^3J = 8.1 Hz, 1H, H-2), 3.58 (dd, ^2J = 15.8 Hz, ^3J = 6.5 Hz, 1H, H-2), 3.85 (*virt.* sept., $^3J \approx {}^3J$ = 7.1 Hz, 1H, H-3), 3.93 [s, 3H, N(CH_3)], 6.99 (s, 1H, H-5''), 7.07 (s, 1H, H-2'), 7.08 – 7.12 (m, 1H, H-5'), 7.15 (s, 1H, H-4''), 7.15 – 7.19 (m, 1H, H-6'), 7.33 (d, ^3J = 8.1 Hz, 1H, H-7'), 7.67 (d, ^3J = 7.9 Hz, 1H, H-4'), 7.96 (s, 1H, NH).

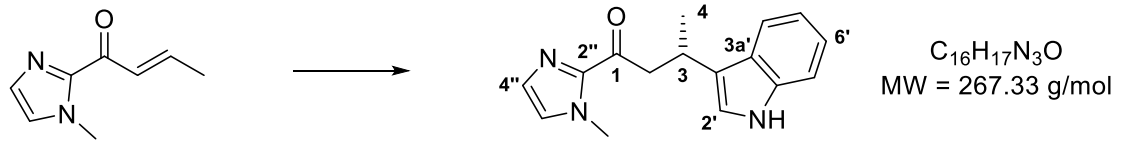
^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.9 (q, C-4), 27.4 (d, C-3), 36.3 [q, N(CH_3)], 46.9 (t, C-2), 111.2 (d, C-7'), 119.3 (d, C-5'), 119.5 (d, C-4'), 120.3 (d, C-2'), 121.7 (s, C-3'), 122.0 (d, C-6'), 126.8 (s, C-3a'*), 127.0 (d, C-5''), 129.0 (d, C-4''), 136.5 (s, C-7a'*), 143.5 (s, C-2''), 192.5 (s, C-1).

Chiral HPLC: t_{R1} = 9.00 min, t_{R2} = 13.15 min, [AD-H, 250 × 4.6 mm, *n*-heptane/*i*-PrOH = 70/30, 1 mL/min, λ = 210 nm]

* Assignment is interconvertible.

Data of this compound were in accordance with the literature.[33]

(*S*)-3-(1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (*ent*-116)



114 *ent*-**116**

Enantioselective Friedel-Crafts alkylation

To a solution of *ent*-**27** (1.73 mg, 0.20 µmol, 1.1 mol%) in 200 µL of dry THF was added substrate **114** (28.6 mg, 190 µmol, 1.0 equiv) and the reaction mixture was stirred for 20 min at rt. Subsequently, indole (58.4 mg, 499 µmol, 2.6 equiv) was added, the reaction mixture was stirred for further 17 h and the solvent was removed under reduced pressure.

After purification by flash column chromatography (SiO_2, P/Et_2O = 2/3 → 1/3, UV) product *ent*-**116** (34.8 mg, 130 µmol, 69%, 97% *ee*) was obtained as a colorless oil.

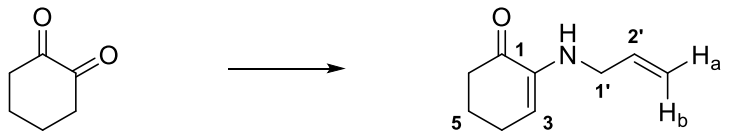
TLC: R_f = 0.09 (P/Et_2O = 2/3) [UV, $KMnO_4$].
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] =1.43 (d, ^3J = 6.9 Hz, 3H, H-4), 3.46 (dd, ^2J = 15.8 Hz, ^3J = 8.1 Hz, 1H, H-2), 3.58 (dd, ^2J = 15.8 Hz, ^3J = 6.5 Hz, 1H, H-2), 3.85 (*virt.* sept., $^3J \approx {}^3J$ = 7.1 Hz, 1H, H-3), 3.93 [s, 3H, N(CH_3)], 6.99 (s, 1H, H-5''), 7.07 (s, 1H, H-2'), 7.08 – 7.12 (m, 1H, H-5'), 7.15 (s, 1H, H-4''), 7.15 – 7.19 (m, 1H, H-6'), 7.33 (d, ^3J = 8.1 Hz, 1H, H-7'), 7.67 (d, ^3J = 7.9 Hz, 1H, H-4'), 7.96 (s, 1H, NH).
^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.9 (q, C-4), 27.4 (d, C-3), 36.3 [q, N(CH_3)], 46.9 (t, C-2), 111.2 (d, C-7'), 119.3 (d, C-5'), 119.5 (d, C-4'), 120.3 (d, C-2'), 121.7 (s, C-3'), 122.0 (d, C-6'), 126.8 (s, C-3a'*), 127.0 (d, C-5''), 129.0 (d, C-4''), 136.5 (s, C-7a'*), 143.5 (s, C-2''), 192.5 (s, C-1).
Chiral HPLC: t_{R1} = 9.00 min, t_{R2} = 13.15 min, [AD-H, 250 × 4.6 mm, *n*-heptane/*i*-PrOH = 70/30, 1 mL/min, λ = 210 nm]

* Assignment is interconvertible.

Data of this compound were in accordance with the literature.[33]

4.3.5 Further Substrates and Intermediates of Failed Synthetic Routes

2-(Allylamino)cyclohex-2-en-1-one (121)



45 **121**

$C_9H_{13}NO$
MW = 151.21 g/mol

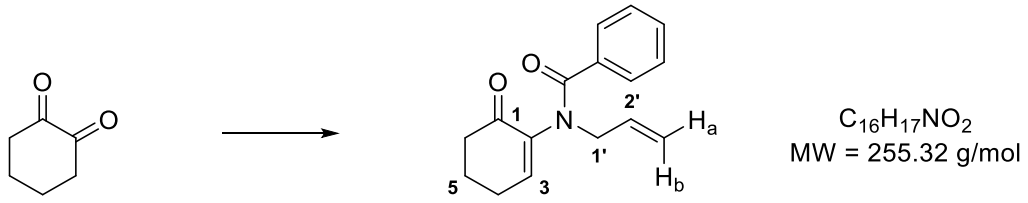
To a solution of cyclohexan-1,2-dione (**45**) (575 mg, 5.13 mmol, 1.0 equiv) in 25 mL of dry tol allylamine (460 µL, 351 mg, 6.15 mmol, 1.2 equiv) was added dropwise and the reaction mixture was heated at reflux in a *Dean-Stark* apparatus for 14 h. The solution was

allowed to cool to rt, washed with brine (2 × 25 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 3/1, UV) product **121** (412 mg, 2.73 mmol, 53%) was obtained as a yellow oil.

TLC: R_f = 0.47 (P/Et_2O = 3/1) [UV, $KMnO_4$].
^{1}H NMR (400 MHz, C_6D_6, 300 K): δ [ppm] = 1.46 (dt, ^2J = 12.4 Hz, ^3J = 7.0 Hz, 2H, H-5), 1.91 (*virt.* q, $^3J \approx {}^3J$ = 5.6 Hz, 2H, H-4), 2.18 (t, ^3J = 7.0 Hz, 2H, H-6), 3.14 – 3.23 (m, 2H, H-1'), 4.53 (s, 1H, NH), 4.94 (dq, ^3J = 10.4 Hz, ^4J = 1.7 Hz, H_a-3'), 5.04 – 5.10 (m, 2H, H-3, H_b-3'), 5.60 (dtt, ^3J = 17.2, 10.4, 5.3 Hz, 1H, H-2').
^{13}C NMR (101 MHz, C_6D_6, 300 K): δ [ppm] = 24.0 (t, C-5), 24.8 (t, C-4), 38.3 (t, C-6), 46.0 (t, C-1'), 109.8 (d, C-3), 115.7 (t, C-3'), 135.8 (d, C-2'), 140.8 (s, C-2), 194.7 (s, C-1).
UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 210 nm (ε = 3916 cm^{-1} M^{-1}), 311 nm (ε = 3966 cm^{-1} M^{-1}).

Data of this compound were in accordance with the literature.[119]

***N*-Allyl-*N*-(6-oxocyclohex-1-en-1-yl)benzamide (122)**



45 **122**

To a solution of cyclohexan-1,2-dione (**45**) (505 mg, 4.50 mmol, 1.0 equiv) in 15 mL of dry tol allylamine (380 µL, 291 mg, 5.09 mmol, 1.1 equiv) was added dropwise and the reaction mixture was heated at reflux in a *Dean-Stark* apparatus for 14 h. The solution was then cooled to 0 °C and NEt_3 (690 µL, 501 mg, 4.95 mmol, 1.1 equiv) as well as benzoyl chloride (570 µL, 696 mg, 4.95 mmol, 1.1 equiv) were added. The reaction mixture was allowed to warm to rt and stirred for further 20 h. The reaction was quenched by addition of 40 mL of H_2O and diluted with 40 mL of Et_2O. The organic layer was washed with water

(2 × 20 mL) and brine (1 × 30 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (Si_2O, P/Et_2O = 2/3, UV) product **122** (645 mg, 2.52 mmol, 56%) was obtained as a yellow oil.

TLC: R_f = 0.21 (P/Et_2O = 2/3) [UV, $KMnO_4$].

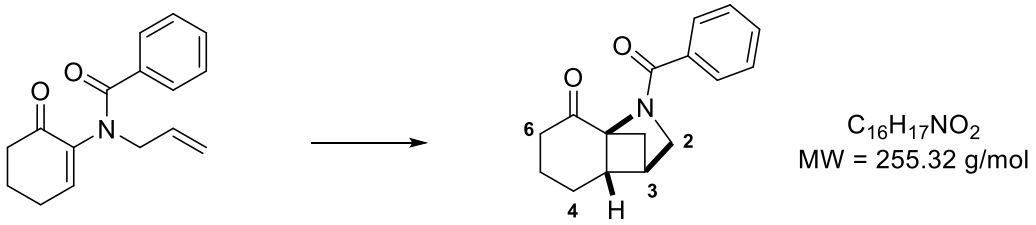
^{1}H NMR (400 MHz, C_6D_6, 300 K): δ [ppm] = 1.07 – 1.23 (m, 2H, H-5), 1.34 – 1.51 (m, 2H, H-4), 1.89 (t, ^3J = 6.8 Hz, 2H, H-6), 3.85 – 4.75 (m, 2H, H-1'), 4.93 – 5.06 (m, 2H, H-3'), 5.91 (dt, ^3J = 12.8, 6.5 Hz, 1H, H-2'), 6.00 (t, ^3J = 4.4 Hz, 1H, H-3), 6.87 – 7.05 (m, 3H, H_{ar}), 7.43 – 7.63 (m, 2H, H_{ar}).

^{13}C NMR (101 MHz, C_6D_6, 300 K): δ [ppm] = 22.3 (t, C-5), 25.6 (t, C-4), 38.4 (t, C-6), 51.3 (t, C-1'), 117.6 (t, C-3'), 127.9 (d, C_{ar}), 128.2 (d, C_{ar}), 129.6 (d, C_{ar}), 134.5 (d, C-2'), 137.7 (s, C_{ar}), 140.8 (s, C-2), 146.7 (d, C-3), 170.6 (s, NCO), 193.8 (s, C-1).

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 220 nm (ε = 12920 cm^{-1} M^{-1}).

Data of this compound were in accordance with the literature.[94,120]

(3*RS*,3a*SR*,7a*SR*)-1-Benzoylhexahydro-3,7a-methanoindol-7(1*H*)-one (*rac*-123)



122 *rac*-**123**

According to general procedure 5, compound *rac*-**123** was synthesized starting from enone **122** (25.5 mg, 99.9 µmol, 1.0 equiv) and txt (**23**) (2.13 mg, 10.0 µmol, 10 mol%) over 22.5 h. Purification by flash column chromatography (SiO_2, P/Et_2O = 2/3, $KMnO_4$) afforded the product (17.3 mg, 67.9 µmol, 68%) as a colorless solid.

TLC: R_f = 0.12 (P/Et_2O = 2/3) [UV, $KMnO_4$].

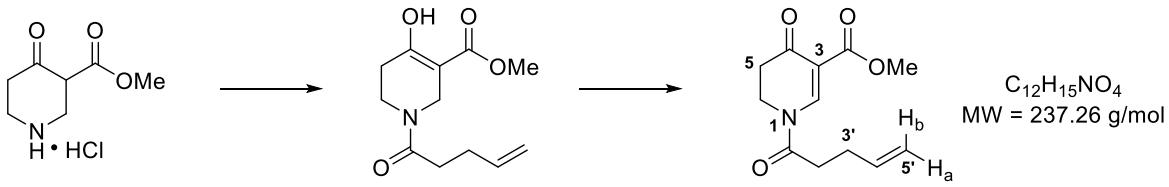
Mp: 68 – 74 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.78 – 1.95 (m, 2H, H-4, H-5), 1.98 – 2.03 (m, 2H, H-3a, H_a-8), 2.03 – 2.12 (m, 2H, H-4, H-5), 2.34 (ddd, ^{2}J = 17.8 Hz, ^{3}J = 13.0, 5.2 Hz, 1H, H_{ax}-6), 2.66 (*virt.* ddt, ^{2}J = 17.8 Hz, ^{3}J = 4.1 Hz, $^{3}J \approx {}^{4}J$ = 2.1 Hz, 1H, H_{eq}-6), 2.72 (d, ^{3}J = 3.2 Hz, 1H, H-3), 2.79 (dt, ^{3}J = 7.9, 2.7 Hz, 1H, H_b-8), 3.35 (d, ^{2}J = 8.1 Hz, 1H, H_a-2), 3.81 (d, ^{2}J = 8.1 Hz, 1H, H_b-2), 7.41 (dd, ^{3}J = 8.3, 7.0 Hz, 2H, H-3', H-5'), 7.45 – 7.52 (m, 1H, H-4'), 7.79 – 7.88 (m, 2H, H-2', H-6').

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 23.8 (t, C-5), 24.2 (t, C-4), 38.9 (t, C-6), 39.7 (d, C-3), 40.8 (t, C-8), 52.7 (d, C-3a), 57.6 (t, C-2), 71.8 (s, C-7a), 128.5 (d, C-3', C-5'), 129.3 (d, C-2', C-6'), 132.0 (d, C-4'), 134.3 (s, C-1'), 175.0 (s, NCO), 202.3 (s, C-7).

Data of this compound were in accordance with the literature.[94]

Methyl 4-oxo-1-(pent-4-enoyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (124)



125 **124**

Methyl 4-hydroxy-1-(pent-4-enoyl)-1,2,5,6-tetrahydropyridine-3-carboxylate

To a solution of 4-pentenoic acid (1.12 g, 11.2 mmol, 1.1 equiv) in 20 mL of dry CH_2Cl_2 were added 5 drops of DMF and oxalyl chloride (0.94 mL, 1.40 g, 11.0 mmol, 1.1 equiv). The reaction mixture was stirred at rt for 3 h. Simultaneously, NEt_3 (5.54 mL, 4.05 g, 40.0 mmol, 4.0 equiv) and 5 grains DMAP were added to a solution of hydrochloride **125** (1.95 g, 10.1 mmol, 1.0 equiv) in 40 mL of dry CH_2Cl_2. The reaction mixture was cooled to 0 °C and the *in situ* formed acid chloride was added dropwise. Subsequently, the reaction mixture was allowed to warm to rt and stirred overnight. The mixture was washed with $NH_4Cl_{(aq)}$ (3 × 50 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude product was used in the next step without further purification.

Methyl 4-oxo-1-(pent-4-enoyl)-1,4,5,6-tetrahydropyridine-3-carboxylate

To a solution of the crude product (2.39 g, 10.0 mmol, 1.0 equiv) in 70 mL of dry 1,4-dioxane was added DDQ (2.41 g, 10.5 mmol, 1.0 equiv) in small portions. The reaction mixture was stirred at rt for 4 h. The reaction was quenched by addition of 50 mL $NaHCO_{3(aq)}$ and the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with $NaHCO_{3(aq)}$ (1 × 100 mL) and brine (2 × 60 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/EtOAc = 1/1, UV) product **124** (742 mg, 3.13 mmol, 31%) was obtained as a colorless solid.

TLC: R_f = 0.14 (P/EtOAc = 1/1) [UV, $KMnO_4$].

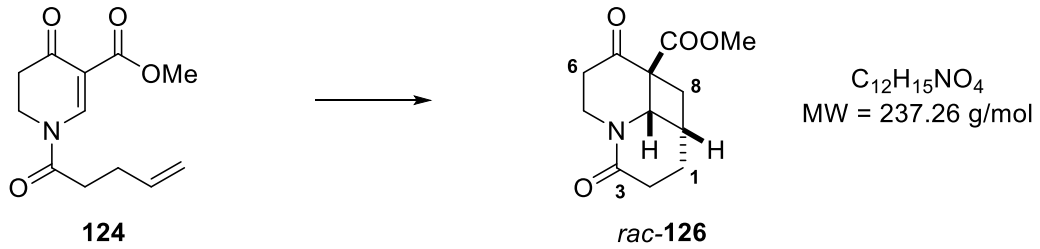
Mp: 95 – 98 °C.

^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 2.50 (*virt.* qtt, ^3J = 8.6, 7.2 Hz, $^4J \approx {}^4J$ = 1.5 Hz, 2H, H-3'), 2.57 – 2.71 (m, 2H, H-2'), 2.78 (t, ^3J = 7.3 Hz, 2H, H-5), 3.84 (s, 3H, $COOCH_3$), 4.03 (t, ^3J = 7.3 Hz, 2H, H-6), 5.01 – 5.22 (m, 2H, H-5'), 5.86 (ddt, ^3J = 16.9, 10.2, 6.6 Hz, 1H, H-4'), 8.73 (s, 1H, H-2).

^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 28.5 (t, C-3'), 32.8 (t, C-5), 36.3 (t, C-2'), 41.6 (t, C-6), 52.3 (q, $COOCH_3$), 109.5 (s, C-3), 116.8 (t, C-5'), 135.9 (d, C-4'), 149.9 (d, C-2), 164.8 (s, $COOCH_3$), 171.4 (s, C-1'), 188.4 (s, C-4).

Data of this compound were in accordance with the literature.[95]

Methyl(4^1*SR*,7a*SR*,8a*SR*)-3,7-dioxohexahydro-1*H*,5*H*-cyclobuta[*ij*]quinolizine-7a(4^1*H*)-carboxylate (*rac*-126)



Txt (**23**) (2.12 mg, 9.98 μmol, 10 mol%) was dissolved in 1.0 mL dry degassed CH_2Cl_2 and transferred to a flame dried duran phototube. The substrate **124** (23.7 mg, 100 μmol, 1.0 equiv) dissolved in 1.0 mL dry degassed CH_2Cl_2 was then added, and the reaction mixture was diluted with dry degassed CH_2Cl_2 until a concentration of 20 mM (relative to the substrate) was reached. The reaction mixture was irradiated at λ = 420 nm at rt until full conversion was achieved. The solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, EtOAc, $KMnO_4$) product *rac*-**126** (21.6 mg, 91.0 μmol, 91%) was obtained as a colorless oil.

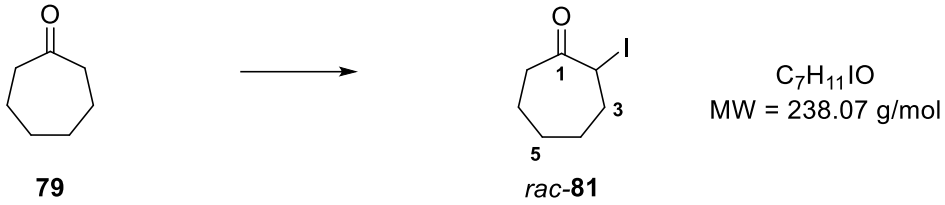
TLC: R_f = 0.19 (EtOAc) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.50 – 1.64 (m, 1H, H-1), 2.04 – 2.26 (m, 2H, H-1, H-2), 2.33 (dd, ^2J = 12.8 Hz, ^3J = 6.8 Hz, 1H, H-8), 2.40 (dt, ^2J = 15.6 Hz, ^3J = 3.7 Hz, 1H, H-2), 2.58 – 2.74 (m, 2H, H-6), 2.86 (*virt.* sext., $^3J \approx {}^3J$ = 8.6 Hz, 1H, H-8a), 2.98 (ddd, ^2J = 12.8 Hz, ^3J = 9.1 Hz, ^4J = 1.8 Hz, 1H, H-8), 3.10 (ddd, ^2J = 13.6 Hz, ^3J = 10.9, 5.9 Hz, 1H, H-5), 3.79 (s, 3H, $COOCH_3$), 4.44 (d, ^3J = 7.9 Hz, 1H, H-4^1), 4.79 (ddd, ^2J = 13.6 Hz, ^3J = 7.4, 2.4 Hz, 1H, H-5).

^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 26.8 (t, C-1), 28.9 (d, C-8a), 31.3 (t, C-2), 33.3 (t, C-8), 38.3 (t, C-5, C-6), 53.4 (q, $COOCH_3$), 54.6 (s, C-7a), 58.7 (d, C-4^1), 170.0 (s, $COOCH_3$), 170.6 (s, C-3), 204.8 (s, C-7).

Data of this compound were in accordance with the literature.[95]

2-Iodocycloheptan-1-one (*rac*-81)



79 *rac*-**81**

To a solution of cycloheptan-1-one (**79**) (530 µL, 503 mg,4.48 mmol, 1.0 equiv) in 15 mL of dry DMSO was added NIS (1.05 g, 4.67 mmol, 1.0 equiv) and the reaction mixture was stirred at rt for 40 min. Subsequently, the reaction mixture was washed with $NH_4Cl_{(aq)}$ (1 × 15 mL) and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine (1 × 40 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 9/1, $KMnO_4$) product *rac*-**81** (326 mg, 1.37 mmol, 31%) was obtained as a yellow oil.

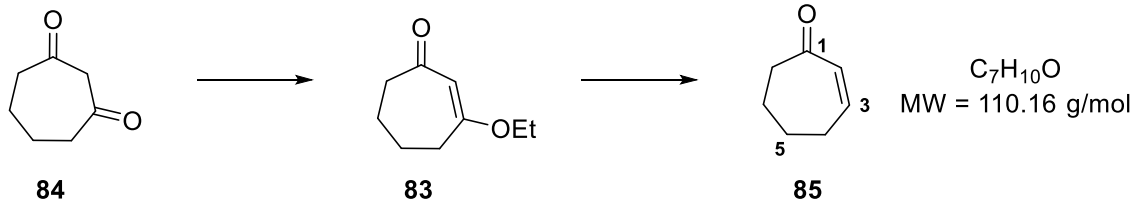
TLC: R_f = 0.23 (P/Et_2O = 3/1) [$KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.18 – 1.26 (m, 1H, H-4), 1.45 – 1.59 (m, 2H, H-5, H-6), 1.82 – 1.90 (m, 2H, H-4, H-6), 1.96 – 2.14 (m, 2H, H-5, H-7), 2.29 – 2.49 (m, 2H, H-3, H-7), 2.94 (td, ^2J = 12.0 Hz, ^3J = 2.9 Hz, 1H, H-3), 4.57 (dd, ^2J = 10.5 Hz, ^3J = 5.6 Hz, 1H, H-2).

^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.6 (t, C-5), 29.0 (t, C-4), 30.3 (t, C-6), 32.1 (d, C-2), 35.9 (t, C-7), 38.4 (t, C-3), 207.9 (s, C-1).

Data of this compound were in accordance with the literature.[77]

Cyclohept-2-en-1-one (85)



84 **83** **85**

3-Ethoxycyclohept-2-en-1-one

To a solution of cycloheptane-1,3-dione (**84**) (700 µL, 770 mg, 6.10 mmol, 1.0 equiv) in 12.3 mL of dry $CHCl_3$ were added dry EtOH (900 µL, 711 mg, 15.4 mmol, 2.5 equiv) and *p*-TsOH·H_2O (15.0 mg, 78.9 µmol, 1.3 mol%). The reaction mixture was heated at 100 °C for 2.5 h and the formed H_2O was removed by 4 Å MS placed in a dopping funnel on top of the flask. The reaction mixture was allowed to cool to rt and Na_2CO_3 (540 mg, 5.09 mmol, 0.8 equiv) was added. The reaction mixture was stirred for 10 min, filtered and the solvent was removed under reduced pressure. The crude product **83** was used in the next step without further purification.

Cyclohept-2-en-1-one

A round bottom flask charged with LAH (76.4 mg, 1.97 mmol, 0.4 equiv) was cooled to 0 °C and a solution of compound **83** (760 mg, 4.92 mmol, 1.0 equiv) in 5.0 mL of dry THF was added dropwise. The reaction mixture was allowed to warm to rt and stirred for 2 h. The reaction was then quenched by the addition of MeOH (approx. 6 mL) until no further gas evolution was observed. After addition of 13 mL 1M HCl the reaction was stirred for 30 min, the layers were separated and the aqueous layer was extracted wit Et_2O (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 6/1 → 3/1, UV) product **85** (260 mg, 2.36 mmol, 21% over 2 steps) was obtained as a colorless oil.

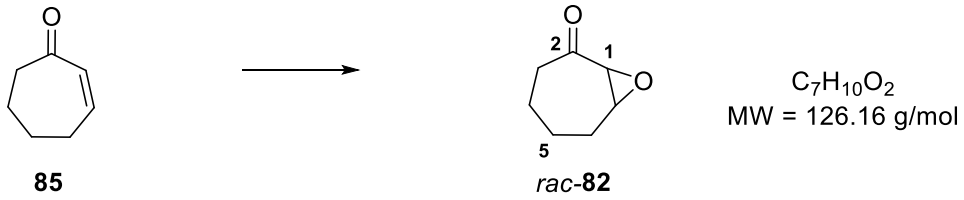
TLC: R_f = 0.35 (P/Et_2O = 1/1) [UV, $KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.71 – 1.98 (m, 4H, H-5, H-6), 2.45 (ddt, ^{3}J = 7.0, 5.4, 2.6 Hz, 2H, H-4), 2.61 (dd, ^{3}J = 7.1, 4.9 Hz, 2H, H-7), 6.01 (dt, ^{3}J = 12.3 Hz, ^{4}J = 1.7 Hz, 1H, H-2), 6.57 (dt, ^{3}J = 12.3, 5.4 Hz, 1H, H-3).

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.9 (t, C-6), 26.3 (t, C-5), 30.4 (t, C-4), 43.7 (t, C-7), 132.7 (d, C-2), 146.5 (d, C-3), 204.4 (s, C-1).

Data of this compound were in accordance with the literature.[121]

(1*SR*,7*SR*)-8-Oxabicyclo[5.1.0]octan-2-one (*rac*-82)



85 *rac*-**82**

To an ice-cooled solution of cyclohept-2-en-1-one (**85**) (250 mg, 2.27 mmol, 1.0 equiv) in 4.0 mL of MeOH were dropwise added H_2O_2 (30-wt%, 1.20 mL, 0.40 g, 11.6 mmol, 5.1 equiv) and 6M NaOH (190 µL, 45.2 mg, 1.13 mmol, 0.5 equiv). The reaction mixture was allowed to warm to rt and stirred for 3.5 h. Subsequently, the reaction mixture was diluted with 8 mL of CH_2Cl_2 and H_2O was added until proper phase separation was achieved. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (1 × 20 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 9/1, $KMnO_4$) product *rac*-**82** (165 mg, 1.31 mmol, 58%) was obtained as a colorless oil.

TLC: R_f = 0.45 (P/Et_2O = 3/1) [$KMnO_4$].

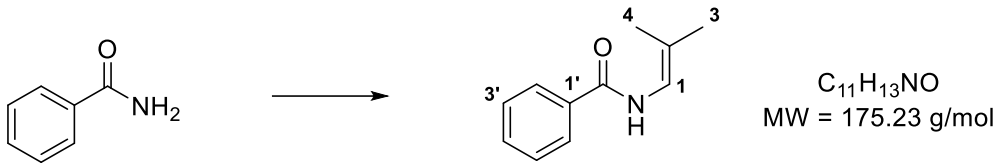
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] =1.02 (dddt, ^{2}J = 16.8 Hz, ^{3}J = 13.8, 11.1, 2.7 Hz, 1H, H-4), 1.67 – 1.76 (m, 2H, H-5), 1.76 – 1.89 (m, 2H, H-4, H-6), 2.25 – 2.36 (m, 1H, H-3), 2.47 (dtd, ^{2}J = 15.3 Hz, ^{3}J = 5.0, 2.9 Hz, 1H, H-6), 2.65 (ddd, ^{2}J = 13.6 Hz, ^{3}J = 11.1, 3.8 Hz, 1H, H-3), 3.38 (*virt.* t, $^{3}J \approx {}^{3}J$ = 5.1 Hz, 1H, H-7), 3.42 (dd, ^{3}J = 5.0 Hz, ^{4}J = 1.3 Hz, 1H, H-1).

^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 23.1 (t, C-5), 23.7 (t, C-4), 27.6 (t, C-6), 40.7 (t, C-3), 55.2 (d, C-7), 59.6 (d, C-1), 210.6 (s, C-2).

Data of this compound were in accordance with the literature.[122]

4.3.6 Thiocarbonyl Compounds

***N*-(2-Methylprop-1-en-1-yl)benzamide (135)**



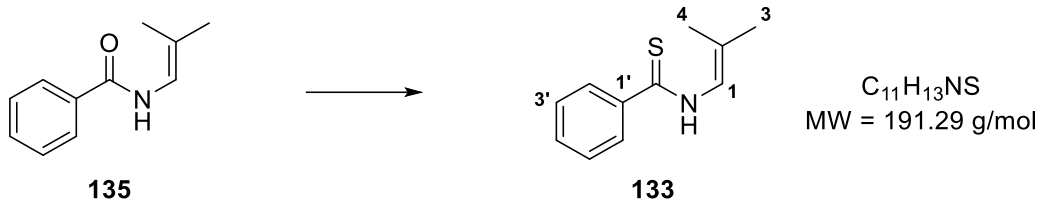
137 **135**

To a solution of benzamide (**137**) (2.12 g, 17.5 mmol, 1.0 equiv) and *i*-butyraldehyde (3.20 ml, 2.53 g, 35.1 mmol, 2.0 equiv) in 75 mL of dry tol was added *p*-TsOH·H_2O (65.1 mg, 342 µmol, 2.0 mol%). The reaction mixture was heated at reflux in a *Dean-Stark* apparatus for 21 h. The solution was allowed to cool to rt, filtered and the solvent was removed under reduced pressure. After recrystallization (H/EtOAc = 5/1) product **135** (2.19 g, 12.5 mmol, 72%) was obtained as a colorless solid.

TLC: R_f = 0.20 (P/Et_2O = 3/1) [UV, $KMnO_4$].
Mp: 78 – 79 °C.
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.74 (d, ^4J = 1.5 Hz, 3H, H-4), 1.81 (d, ^4J = 1.4 Hz, 3H, H-3), 6.78 (*virt.* dquint., ^3J = 10.3 Hz, $^4J \approx {}^4J$ = 1.5 Hz, 1H, H-1), 7.43 (*br* s, 1H, NH), 7.48 (ddd, ^3J = 8.30, 6.5 Hz, ^4J = 1.4 Hz, 2H, H-3', H-5') 7.52 – 7.58 (m, 1H, H-4'), 7.78 – 7.87 (m, 2H, H-2', H-6').
^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 16.8 (q, C-4), 22.7 (q, C-3), 116.4 (s, C-2), 117. 5 (d, C-1), 127.1 (d, C-2', C-6'), 128.9 (d, C-3', C-5'), 131.9 (d, C-4'), 134.5 (s, C-1'), 164.2 (s, C=O).

Data of this compound were in accordance with the literature.[111]

***N*-(2-Methylprop-1-en-1-yl)benzothioamide (133)**



135 **133**

To a solution of amide **135** (250 mg, 1.43 mmol, 1.0 equiv) in 5.0 mL of dry tol was added *Lawesson* reagent (380 mg. 940 µmol, 0.7 equiv) and the reaction mixture was heated at reflux for 5 h. It was then allowed to cool to rt and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 9/1, UV) product **133** (160 mg, 836 µmol, 58%) was obtained as a yellow solid.

TLC: R_f = 0.30 (P/Et_2O = 9/1) [UV, $KMnO_4$].

Mp: 36 – 38 °C.

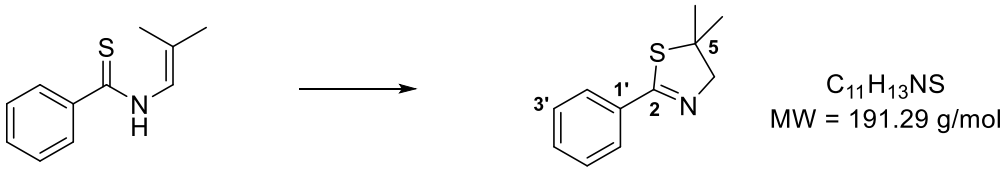
^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.79 (dd, ^4J = 1.4, 0.7 Hz, 3H, H-4), 1.86 (dd, ^4J = 1.5, 0.7 Hz, 3H, H-3), 7.26 – 7.31 (m, 1H, H-1), 7.42 (*virt.* ddt, ^3J = 8.2, 6.6 Hz, $^4J \approx {}^5J$ = 1.4 Hz, 2H, H-3', H-5'), 7.46 – 7.52 (m, 1H, H-4'), 7.76 – 7.81 (m, 2H, H-2', H-6'), 8.72 (*br* s, 1H, NH).

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 17.4 (q, C-4), 22.9 (q, C-3), 122.3 (d, C-1), 122.7 (s, C-2), 126.8 (d, C-2', C-6'), 128.8 (d, C-3', C-5'), 131.4 (d, C-4'), 142.2 (s, C-1'), 193.7 (s, C=S).

UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 272 nm (ε = 9134 cm^{-1} M^{-1}), 332 (ε = 8528 cm^{-1} M^{-1}).

Data of this compound were in accordance with the literature.[106]

5,5-Dimethyl-2-phenyl-4,5-dihydrothiazole (146)



133 **146**

UV irradiation

Substrate **133** (8.40 mg, 43.9 μmol, 1.0 equiv) was dissolved in 1.0 mL dry CyH and transferred to a flame dried duran phototube. The reaction mixture was diluted with dry CyH until a concentration of 5 mM (relative to the substrate) was reached and the reaction mixture was degassed by bubbling Ar through for 10 min. The reaction mixture was irradiated at λ = 300 nm at rt for 3 h. The solvent was removed under reduced pressure and product **146** (8.00 mg, 41.8 μmol, 95%) was obtained in pure form without further purification as a colorless solid.

Visible light irradiation

Substrate **133** (8.50 mg, 44.4 μmol, 1.0 equiv) was dissolved in 1.0 mL dry CyH and transferred to a flame dried duran phototube. The reaction mixture was diluted with dry CyH until a concentration of 5 mM (relative to the substrate) was reached and the reaction mixture was degassed by bubbling Ar through for 10 min. The reaction mixture was irradiated at λ = 420 nm at rt for 3 h. The solvent was removed under reduced pressure and product **146** (7.30 mg, 38.2 μmol, 86%) was obtained in pure form without further purification as a colorless solid.

TLC: R_f = 0.16 (P/Et_2O = 9/1) [UV, $KMnO_4$].

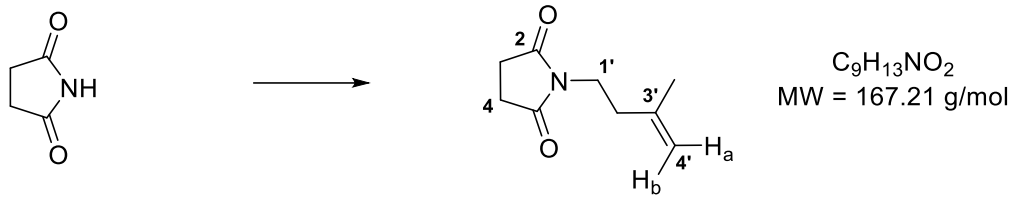
^{1}H NMR (400 MHz, C_6D_6, 300 K): δ [ppm] = 1.23 [s, 6H, C-5(CH_3)$_2$], 3.94 (s, 2H, H-4), 7.02 – 7.11 (m, 3H, H-3', H-4', H-5'), 8.01 – 8.15 (m, 2H, H-2', H-6').

^{13}C NMR (101 MHz, C_6D_6, 300 K): δ [ppm] = 28.8 [q, C-5(*C*H_3)$_2$], 58.9 (s, C-5), 78.2 (t, C-4), 128.7 (d, C-2', C-3'*, C-5'*, C-6'), 131.0 (d, C-4'*), 134.8 (s, C-1'), 167.4 (s, C-2).

* Assignment is interconvertible.

Data of this compound were in accordance with the literature.[106]

1-(3-Methylbut-3-en-1-yl)pyrrolidine-2,5-dione (136)



139 **136**

To a mixture of 3-methylbut-3-en-1-ol (**140**) (3.10 mL, 2.64 g, 30.7 mmol, 4.4 equiv), succinimide (**139**) (683 mg, 6.90 mmol, 1.0 equiv) and PPh_3 (1.83 g, 6.97 mmol, 1.0 equiv) in 11 mL of dry THF was added DEAD (40-wt% in Tol, 3.10 mL, 1.20 g, 6.90 mmol, 1.0 equiv) and the reaction mixture was stirred for 3 h. The solvent was removed under reduced pressure and the residue was taken up in 15 ml of a P/EtOAc (7/3) mixture, filtered and washed with another 10 mL of the same mixture. The solvent was removed under reduced pressure and the process was repeated. After purification by flash column chromatography (SiO_2, CH_2Cl_2, $KMnO_4$) product **136** (900 mg, 5.38 mmol, 78%) was obtained as a colorless oil.

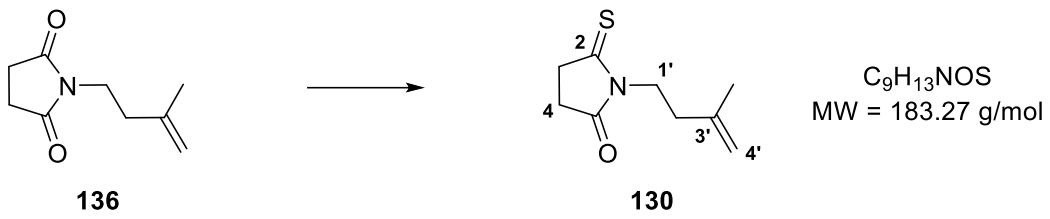
TLC: R_f = 0.15 (CH_2Cl_2) [$KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.94 [dd, ^4J = 1.6, 1.0 Hz, C-3'(CH_3)], 2.47 (*virt.* td, $^3J \approx {}^3J$ = 7.2 Hz, ^4J = 1.1 Hz, 2H, H-2'), 2.86 (s, 4H, H-3, H-4), 3.82 (t, ^3J = 7.2 Hz, 2H, H-1'), 4.83 (*virt.* dq, ^2J = 1.8 Hz, $^4J \approx {}^4J$ = 1.0 Hz, 1H, H_b-4'), 4.93 (*virt.*t, $^2J \approx {}^4J$ = 1.7 Hz, 1H, H_a-4').

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 22.1 [q, C-3'(*C*H_3)], 28.3 (t, C-3, C-4), 35.6 (t, C-2'), 37.2 (t, C-1'), 112.8 (d, C-4'), 142.3 (s, C-3'), 177.2 (s, C=O).

Data of this compound were in accordance with the literature.[110,123]

1-(3-Methylbut-3-en-1-yl)-5-thioxopyrrolidin-2-one (130)



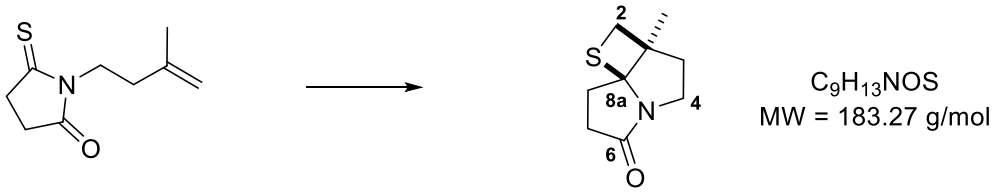
136 **130**

To a solution of imide **136** (900 mg, 5.38 mmol, 1.0 equiv) in 20 mL of dry tol was added *Lawesson* reagent (1.14 g.2.82 mmol, 0.5 equiv) and the reaction mixture was heated at reflux for 30 min. It was then allowed to cool to rt and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/CH_2Cl_2 = 1/1, P/CH_2Cl_2 =1/2 → CH_2Cl_2, P/CH_2Cl_2 =1/2, UV) product **130** (280 mg, 1.53 mmol, 28%) was obtained as a yellow oil.

TLC: R_f = 0.22 (P/CH_2Cl_2 = 1/1) [UV, $KMnO_4$].
^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.80 [s, 3H, C-3'(CH_3)], 2.22 – 2.44 (m, 2H, H-2'), 2.63 – 2.84 (m, 2H, H-4), 3.09 – 3.16 (m, 2H, H-3), 3.95 – 4.09 (m, 2H, H-1'), 4.69 (dq, ^2J = 1.8 Hz, ^4J = 1.1 Hz, 1H, H-4'), 4.77 (*virt.* q, $^2J \approx {}^4J$ = 1.6 Hz, 1h, H-4').
^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 22.4 [q, C-3'(CH_3)], 28.8 (t, C-4), 34.3 (t, C-2'), 38.9 (t, C-3), 40.8 (t, C-1'), 112.8 (t, C-4'), 142.3 (s, C-3'), 178.7 (s, C=O), 210.7 (s, C=S).
UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 277 nm (ε = 18968 cm^{-1} M^{-1}), 386 (ε = 44 cm^{-1} M^{-1}).

Data of this compound were in accordance with the literature.[108]

(2a*RS*,8a*SR*)-2a-Methylhexahydro-6*H*-thieto[3,2-*g*]pyrrolizin-6-one (*rac*-132)



130 *rac*-**132**

UV irradiation

Substrate **130** (16.2 mg, 88.4 µmol, 1.0 equiv) was dissolved in 1.0 mL dry CyH and transferred to a flame dried LED phototube. The reaction mixture was diluted with dry CyH until a concentration of 15 mM (relative to the substrate) was reached and the reaction mixture was degassed by three freeze-pump-thaw cycles. The reaction mixture was irradiated at λ = 368 nm at rt for 2.5 h and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, CH_2Cl_2/MeOH = 99/1, $KMnO_4$) product *rac*-**132** (16.2 mg, 88.4 µmol, 100%) was obtained as a colorless solid.

Visible light irradiation

Substrate **130** (21.7 mg, 118 µmol, 1.0 equiv) was dissolved in 1.0 mL dry CH_2Cl_2 and transferred to a flame dried LED phototube. The reaction mixture was diluted with dry CH_2Cl_2 until a concentration of 15 mM (relative to the substrate) was reached and the reaction mixture was degassed by three freeze-pump-thaw cycles. The reaction mixture was irradiated at λ = 424 nm at rt for 2.5 h and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, CH_2Cl_2/MeOH = 99/1, $KMnO_4$) product *rac*-**132** (21.0 mg, 115 µmol, 96%) was obtained as a colorless solid.

TLC: R_f = 0.02 (CH_2Cl_2/MeOH = 99/1) [$KMnO_4$].

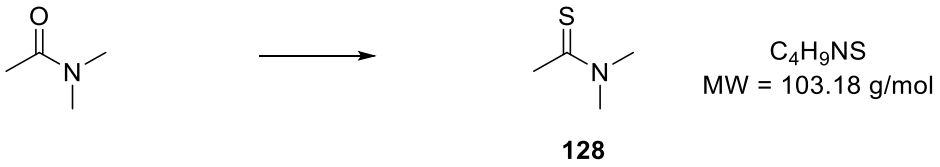
^{1}H NMR (400 MHz, C_6D_6, 300 K): δ [ppm] = 0.66 [s, 3H, C-2a(CH_3)], 0.75 – 0.86 (m, 1H, H-3), 1.11 (dt, ,^2J = 15.8 Hz, ^3J = 4.1 Hz, 1H, H-3), 1.69 – 1.84 (m, 2H, H-2), 1.88 (ddd, ^2J = 16.4 Hz, ^3J = 9.0, 3.7 Hz, 1H, H-7), 2.10 – 2.20 (m, 1H, H-7), 2.21 (dd, ^3J = 9.0 Hz, 2.9 Hz, 1H, H-8), 2.27 – 2.37 (m, 1H, H-8), 3.22 (dt, ^2J = 11.3 Hz, ^3J = 5.5 Hz, 1H, H-4), 3.92 (*virt.* td, $^2J \approx {}^3J$ = 8.5 Hz, ^3J = 3.1 Hz, 1H, H-4).

^{13}C NMR (101 MHz, C_6D_6, 300 K): δ [ppm] = 22.4 [q, C-2a(CH_3)], 30.1 (t, C-8), 31.1 (t, C-2), 32.3 (t, C-7), 40.3 (t, C-4), 40.7 (t, C-3), 56.5 (s, C-2a*), 82.1 (s, C-8a*), 171.7 (s, C=O).

* Assignment is interconvertible.

Data of this compound were in accordance with the literature.[108]

***N*,*N*-Dimethylethanethioamide (128)**



128

To a solution of *N*,*N*-dimethylacetamide (270 µL, 250 mg, 2.87 mmol, 1.0 equiv) in 10 mL of dry tol was added *Lawesson* reagent (690 mg. 1.71 mmol, 0.6 equiv) and the reaction mixture was heated at reflux for 6 h. It was then allowed to cool to rt and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO_2, P/Et_2O = 1/1, UV) product **128** (122 mg, 1.18 mmol, 41%) was obtained as a colorless solid.

TLC: R_f = 0.28 (P/Et_2O = 1/1) [UV, $KMnO_4$].
Mp: 154 – 159 °C.
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 2.66 [s, 3H, (C=S)CH_3], 3.30 [s, 3H, N(CH_3)$_2$], 3.50 [s, 3H, N(CH_3)$_2$].
^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 32.9 [q, (C=S)*C*H_3], 42.3 [q, N(CH_3)$_2$], 44.5 [q, N(CH_3)$_2$], 199.9 (s, C=S).
UV/vis (CH_2Cl_2, *c* = 0.5 mM): λ = 273 nm (ε = 14674 cm^{-1} M^{-1}).

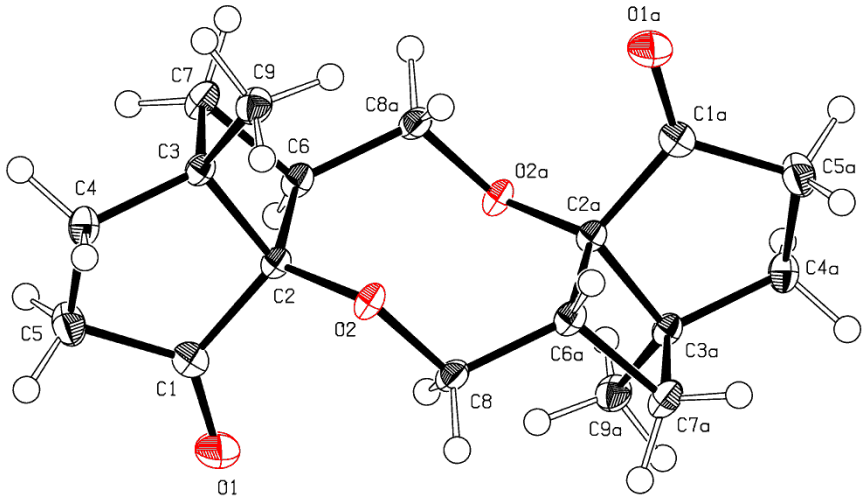
Data of this compound were in accordance with the literature.[124]

4.3.7 Crystal Data[63]

Data were collected on a Bruker D8 Venture single crystal X-ray diffractometer equipped with a CPAD detector (Bruker Photon II) (compounds **101**, *rac*-**78**) or a CMOS detector (Bruker Photon-100) (compound *rac*-**104**), an IMS micro source (compounds **101**, *rac*-**78**) or a TXS rotating anode (compound *rac*-**104**) with MoK_α radiation (λ = 0.71073 Å) and a Helios optic using the APEX3 software package.[125] Measurements were performed on single crystals coated with perfluorinated ether. The crystals were fixed on top of a kapton micro sampler and frozen under a stream of cold nitrogen. A matrix scan was used to determine the initial lattice parameters. Reflections were corrected for Lorentz and polarization effects, scan speed, and background using SAINT.[126] Absorption correction, including odd and even ordered spherical harmonics was performed using SADABS.[126] Space group assignments were based upon systematic absences, E statistics, and successful refinement of the structures. The structures were solved using SHELXT with the aid of successive difference Fourier maps, and were refined against all data using SHELXL in conjunction with SHELXLE.[127,128] Hydrogen atoms were calculated in ideal positions as follows: Methyl hydrogen atoms were refined as part of rigid rotating groups, with a C–H distance of 0.98 Å and $U_{iso(H)} = 1.5 \cdot U_{eqI}$. Other H atoms were placed in calculated positions and refined using a riding model, with methylene and aromatic C–H distances of 0.99 Å and 0.95 Å, respectively, other C–H distances of 1.00 Å, all with $U_{iso(H)} = 1.2 \cdot U_{eqI}$. Non-hydrogen atoms were refined with anisotropic displacement parameters. Full-matrix least-squares refinements were carried out by minimizing $\Sigma w(F_o^2 - F_c^2)^2$ with the SHELXL weighting scheme.[127] Neutral atom scattering factors for all atoms and anomalous dispersion corrections for the non-hydrogen atoms were taken from *International Tables for Crystallography*.[129] Images of the crystal structures were generated with Mercury and PLATON.[130] CCDC 2010591-2010593 contain the supplementary crystallographic data for this thesis. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

Compound 101 (CCDC 2010593)

Single crystals were obtained by solvent evaporation from a saturated solution of **101** in Et_2O. Ellipsoids in the ORTEP structure are displayed at the 50% probability level.



Diffractometer operator C. Jandl
scanspeed 1-10 s per frame
dx 37 mm
3415 frames measured in 13 data sets
phi-scans with delta_phi = 0.5
omega-scans with delta_omega = 0.5
shutterless mode

Crystal data

$C_{18}H_{24}O_4$

M_r = 304.37	D_x = 1.320 Mg m^{-3}
Monoclinic, *C*2/*c*	Melting point: > 493 K
Hall symbol: -C 2yc	Mo *K*α radiation, λ = 0.71073 Å
a = 18.1075 (17) Å	Cell parameters from 9504 reflections
b = 11.052 (1) Å	θ = 2.2–28.3°
c = 8.2387 (8) Å	μ = 0.09 mm^{-1}
β = 111.686 (3)°	*T* = 100 K
V = 1532.1 (3) Å^3	Fragment, colorless
Z = 4	0.26 × 0.16 × 0.13 mm

$F(000)$ = 656

Data collection

Bruker D8 Venture diffractometer

Radiation source: IMS microsource

Helios optic monochromator

Detector resolution: 7.5 pixels mm^{-1}

phi– and ω–rotation scans

Absorption correction: multi-scan *SADABS* 2016/2, Bruker

T_{min} = 0.725, T_{max} = 0.746

49708 measured reflections

1827 independent reflections

1720 reflections with $I > 2\sigma(I)$

R_{int} = 0.029

θ_{max} = 27.9°, θ_{min} = 2.2°

h = −23 23

k = −14 14

l = −10 10

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)]$ = 0.034

$wR(F^2)$ = 0.093

S = 1.09

1827 reflections

101 parameters

0 restraints

0 constraints

Primary atom site location: intrinsic phasing

Secondary atom site location: difference Fourier map

Hydrogen site location: inferred from neighbouring sites

H-atom parameters constrained

$W = 1/[\Sigma^2(FO^2) + (0.0421P)^2 + 1.3923P]$
WHERE $P = (FO^2 + 2FC^2)/3$

$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max}$ = 0.39 e $Å^{-3}$

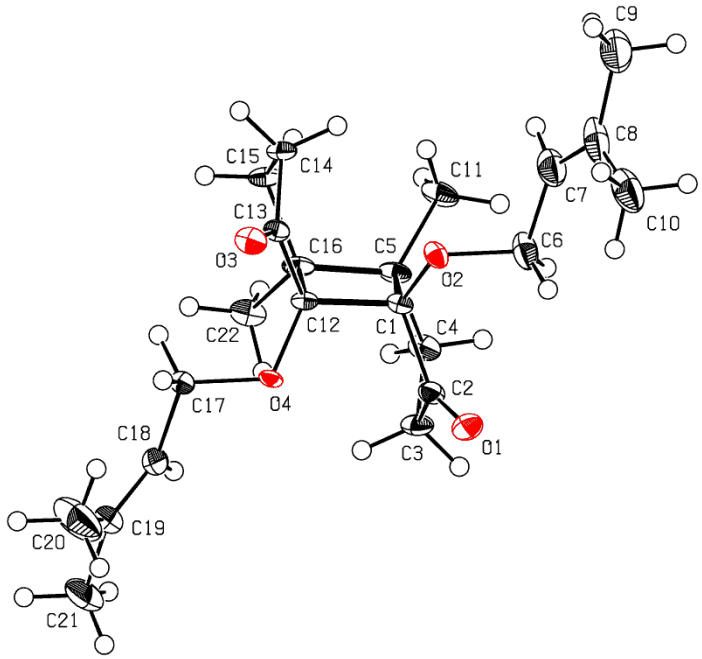
$\Delta\rho_{min}$ = −0.21 e $Å^{-3}$

Extinction correction: none

Extinction coefficient: -

Compound *rac*-104 (CCDC 2010591)

Single crystals were obtained by diffusion of P into a saturated solution of *rac*-**104** in CH_2Cl_2. Ellipsoids in the ORTEP structure are displayed at the 50% probability level.



Diffractometer operator C. Jandl
scanspeed 10-60 s per frame
dx 50 mm
1488 frames measured in 6 data sets
phi-scans with delta_phi = 0.5
omega-scans with delta_omega = 0.5
shutterless mode

Crystal data

$C_{22}H_{32}O_4$

M_r = 360.47

Monoclinic, $P2_1/n$

Hall symbol: -P 2yn

a = 11.8018 (14) Å

b = 6.7440 (8) Å

c = 25.405 (3) Å

β = 100.493 (4)°

D_x = 1.204 Mg m^{-3}

Melting point: 358–371 K

Mo $K\alpha$ radiation, λ = 0.71073 Å

Cell parameters from 8914 reflections

θ = 3.1–25.5°

μ = 0.08 mm^{-1}

T = 100 K

V = 1988.2 (4) Å^3

Z = 4

F(000) = 784

Fragment, colorless

0.15 × 0.12 × 0.04 mm

Data collection

Bruker D8 Venture diffractometer

Radiation source: TXS rotating anode

Helios optic monochromator

Detector resolution: 7.5 pixels mm^{-1}

phi– and ω–rotation scans

Absorption correction: multi-scan *SADABS* 2016/2, Bruker

T_{min} = 0.647, T_{max} = 0.745

28402 measured reflections

3647 independent reflections

2817 reflections with $I > 2\sigma(I)$

R_{int} = 0.066

θ_{max} = 25.4°, θ_{min} = 2.7°

h = −14 14

k = −8 7

l = −28 30

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)]$ = 0.065

$wR(F^2)$ = 0.188

S = 1.10

3647 reflections

489 parameters

602 restraints

0 constraints

Primary atom site location: intrinsic phasing

Secondary atom site location: difference Fourier map

Hydrogen site location: inferred from neighbouring sites

H-atom parameters constrained

$W = 1/[\Sigma^2(FO^2) + (0.0982P)^2 + 1.8965P]$ WHERE $P = (FO^2 + 2FC^2)/3$

$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max}$ = 0.47 e Å^{-3}

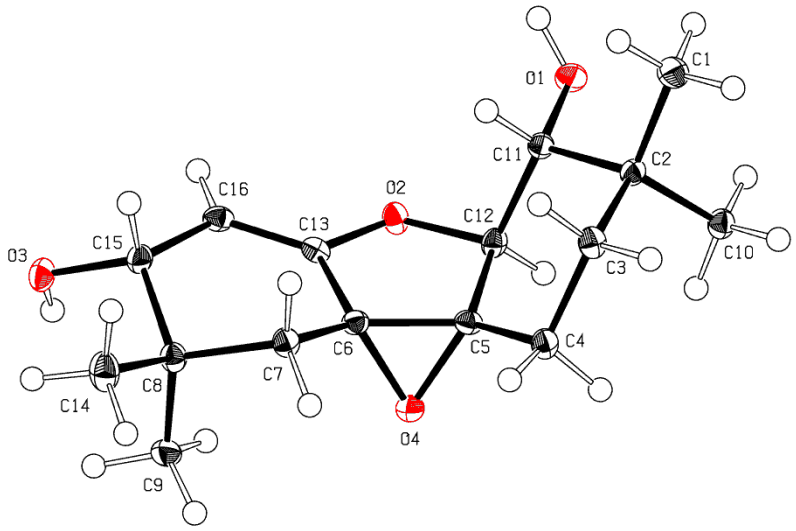
$\Delta\rho_{min}$ = −0.46 e Å^{-3}

Extinction correction: none

Extinction coefficient: -

Compound *rac*-78 (CCDC 2010592)

Single crystals were obtained by solvent evaporation from a saturated solution of *rac*-**78** in CH_2Cl_2. Ellipsoids in the ORTEP structure are displayed at the 50% probability level.



Diffractometer operator T. Pickl & A. Poethig
phi-scans with delta_phi = 0.5
omega-scans with delta_omega = 0.5
shutterless mode

Crystal data

$C_{16}H_{24}O_4$

M_r = 280.35

D_x = 1.291 Mg m^{-3}

Monoclinic, $P2_1/n$

Hall symbol: -P 2yn

Mo $K\alpha$ radiation, λ = 0.71073 Å

a = 6.1182 (3) Å

Cell parameters from 6447 reflections

b = 10.6025 (5) Å

θ = 2.7–26.4°

c = 22.3764 (12) Å

μ = 0.09 mm^{-1}

β = 96.280 (3)°

T = 100 K

V = 1442.81 (13) Å^3

Needle, clear colorless

Z = 4

0.74 × 0.09 × 0.06 mm

F(000) = 608

Data collection

Bruker D8 Venture diffractometer

Radiation source: IMS microsource

HELIOS optic monochromator

Detector resolution: 7.5 pixels mm^{-1}

phi– and ω–rotation scans

Absorption correction: multi-scan *SADABS* 2016/2, Bruker

T_{min} = 0.655, T_{max} = 0.745

28565 measured reflections

2960 independent reflections

2598 reflections with $I > 2\sigma(I)$

R_{int} = 0.065

θ_{max} = 26.4°, θ_{min} = 2.1°

h = −7 7

k = −13 13

l = −27 27

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)]$ = 0.053

$wR(F^2)$ = 0.128

S = 1.14

2960 reflections

193 parameters

0 restraints

0 constraints

Primary atom site location: intrinsic phasing

Secondary atom site location: difference Fourier map

Hydrogen site location: mixed

H atoms treated by a mixture of independent and constrained refinement

$W = 1/[\Sigma^2(FO^2) + (0.0351P)^2 + 1.9676P]$ WHERE $P = (FO^2 + 2FC^2)/3$

$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max}$ = 0.30 e $Å^{-3}$

$\Delta\rho_{min}$ = −0.24 e $Å^{-3}$

Extinction correction: none

Extinction coefficient: -

5. Abbreviations

A	additive
Å	Ångaström
ac	acetone
add	additive
aq	aqueous
Ar	aryl
A_{surf}	surface area
ATR	attenuated total reflexion
aux	auxiliary
BA	*Brønsted* acid
bath	bathochromic
binol	1,1'-bi-2-naphtol
BOX	bisoxazoline
bpy	2,2'-bipyridine
br	broad
Bu	butyl
c	concentration
c	speed of light
calcd	calculated
CAN	ceric ammonium nitrate
cat	catalyst
CD	circular dichroism
CFL	compact fluorescent lamp
CyH	cyclohexane
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	dichloroethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEAD	diethyl diazenedicarboxylate
DFT	density functional theory
DIPEA	*N*,*N*-di-*iso*-propylethylamine
DMAP	*N*,*N*-dimethylaminopyridine

DMF	*N*,*N*-dimethylformamide
d.r.	diastereomeric ratio
dtbbpy	4,4′-di-*tert*-butyl-2,2′-dipyridyl
E	energy
EA	elemental analysis
EDG	electron donating group
ee	enantiomeric excess
equiv	equivalent
Et	ethyl
E_T	triplet energy
EWG	electron withdrawing group
FLT	fluorescent light tube
FTIR	fourier-transform infrared
GC	gas chromatography
GRG	Generalized Reduced Gradient
H	hexane
h	*Planck*'s constant
HD	halogen bond donor
HFX	hexafluoro-*m*-xylene
HH	head-to-head
HPML	high pressure mercury lamp
HT	head-to-tail
I	intensity
i	*iso*
IC	internal conversion
IM	intermediate
ISC	intersystem crossing
LA	*Lewis* acid
LAH	lithium aluminum hydride
LED	light emitting diode
M	metal
Me	methyl

MS	mass spectromerty
MS	molecular sieves
m-xyl	*meta*-xylene
N_A	*Avogadro* constant
NIS	*N*-Iodosuccinimide
NMR	nulear magnetic resonance
NOE	nuclear *Overhauser* effect
NOESY	two-dimensional NOE experiment
o	*ortho*
Oac	acetate
ORTEP	Oak Ridge Thermal Ellipsoid Plot
P	pentane
P	power
p	*para*
*p*Fppy	*para*-fluoro-(2-pyridyl)phenyl
Ph	phenyl
pic	picolinato
ppm	parts per million
ppy	(2-pyridyl)phenyl
Pr	propyl
prod	product
py	pyridine
pyBOX	pyridine-2,6-bis(oxazoline)
quant.	quantitative
rac	racemic
R_f	retention factor
rsm	recovered starting material
rt	room temperature
SC-XRD	single crystal X-ray diffraction
sens	sensitizer
SET	single electron transfer
sm	starting material

t	time
t	*tert*
T	temperature
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
tol	toluene
Ts	*para*-toluenesulfonyl
txt	thioxanthone
UV	ultraviolet
vis	visible
v	volume
W	work
wt	weight
ε	extinction coefficient
Φ	quantum yield
λ	wavelength
ν	photon frequency

6. References

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