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Diastereoselectivity in Photochemistry

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Abstract

Diastereoselective photochemical reactions play an important role for asymmetric synthesis, for example for the synthesis of natural or biologically active compounds. Chirality is either induced by a chiral auxiliary or by a chiral centers already present in the substrates. In the first case, the source of chirality is removed during the ongoing multistep synthesis. In the second case, the chirality source is conserved in the target compound. In the present chapter examples of the [2+2] photocycloaddition of carbonyl compounds with alkenes (Paternò-Büchi reaction), between α,β -unsaturated carbonyl compounds and alkenes as well as between two alkenes are discussed. Typical diastereoselective photocycloaddition reaction with aromatic compounds are reported. Currently, photoinduced radical reactions are intensively investigated and photoredox or more generally photocatalysis play a key role. In such reactions neutral radicals and radical ions are typical intermediates. Under photochemical conditions, tautomeric equilibria significantly change. Due to this fact, interesting diastereoselective reactions have been reported. Electrocyclization has often been applied to the synthesis of heterocyclic compounds. Photochemical rearrangements provide convenient accesses to complex polycyclic compounds. The diastereoselectivity is significantly increased when the corresponding reactions are carried out under confinement conditions, for example with inclusion complexes. Photooxygenation with singlet oxygen is a very convenient oxidation method. Generally, such reactions are highly regio stereo and chemoselective.

Keywords

Chiral auxiliary, Chiral induction, Diastereoselectivity, Double induction, Electrocyclization, Electronic excitation, Hydrogen atom transfer, Inclusion complexes, Natural products, Photochemical sensitization, Photochemistry, Photocycloadditions, Photooxygenation, Photo-tautomerization, Radical reactions.

Key points/objectives box

- The chiral information is covalently bound to the reacting part of the molecule either as chiral auxiliary or as part of the target compound.
- The molecular structure at the electronically excited state and its influence on the stereoselectivity in photochemical reactions.
- Phenomena such as double induction or the influence of supramolecular structures such as inclusion complexes or crystal structure in diastereoselective photochemical reactions are discussed.
- Application to asymmetric organic synthesis.

1 Introduction

Photochemical reactions are an essential part of the methodology of organic synthesis.^{1,2,3} Using such reactions, compounds or compound families become easily available that cannot or hardly be obtained by conventional methods of organic synthesis. This can be explained by the fact that in photochemical reactions the electronic configuration of a chemical compound changes and the chemical reactivity is significantly modified.^{4,5} Since several years now, photochemical reactions are particularly appreciated in chemical and pharmaceutical industry, especially when novel biologically active compounds are looked for.⁶ This interest was further reinforced by recent research on different photocatalytic reactions.^{7,8,9} It should further be mentioned that many of these reactions fulfill requirements of sustainable chemistry. In many of the herein discussed photochemical reaction, the photon is considered as a traceless reagent.^{10,11,12}

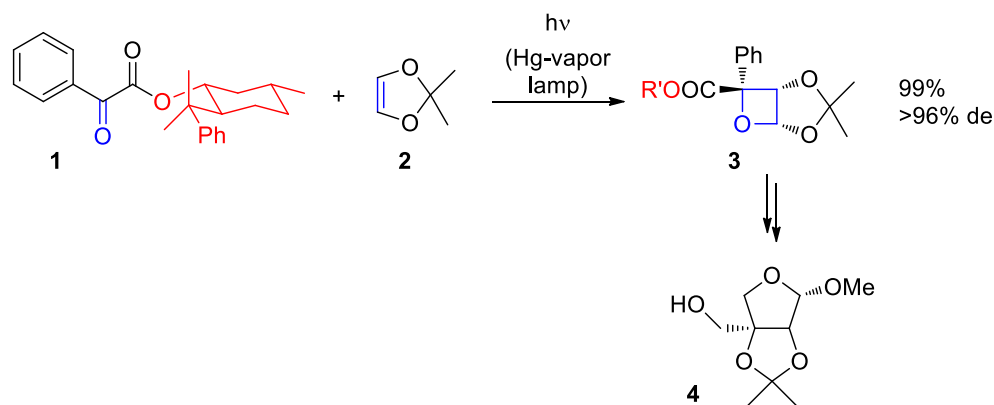
In this context, tridimensional structure play an important role which explains the high interest in stereoselective chemical reactions.^{13,14,15} Due to the high energy uptake in photochemical reactions, these transformations were often considered as inherently unselective. However, the dispersion of the energy excess can occur under controlled conditions¹⁶ so that these reactions becomes selective, even highly stereoselective. In fact, numerous stereoselective photochemical reactions have been reported.^{17,18,19,20,21,22,23,24,25} Several reports deal particularly with diastereoselective photochemical reactions.^{26,27}

The present chapter deals with diastereoselectivity in photochemical reactions as far as they can be considered for application or potential application to asymmetric synthesis; that means the production of more or less enantiopure compounds. Therefore, the aim is not to report on reactions which lead to racemic compounds although such investigations are very helpful for a profound understanding of reaction mechanisms and stereoselection processes. In this context, it should be pointed out that, in many photochemical reactions in which each substrate molecule reacts individually, the racemic diastereoselectivity is the same as in the corresponding enantiopure diastereoselectivity.^{28,29} In the first case, a racemic mixture of the substrate is transformed leading, for example, to two diastereoisomers, both as racemates. In the second case, the same substrate as an enantiopure compound is transformed leading to the same diastereoisomers, both in enantiopure form. In the first case or when both cases are discussed concomitantly, the *like*, *unlike* descriptors are used.³⁰ Furthermore reactions of substrates are considered in which the chiral information is covalently bounded to the reacting molecule's part. Either the chiral information is present as chiral auxiliary or it is part of the substrate and the target compound.

2 Photocycloadditions

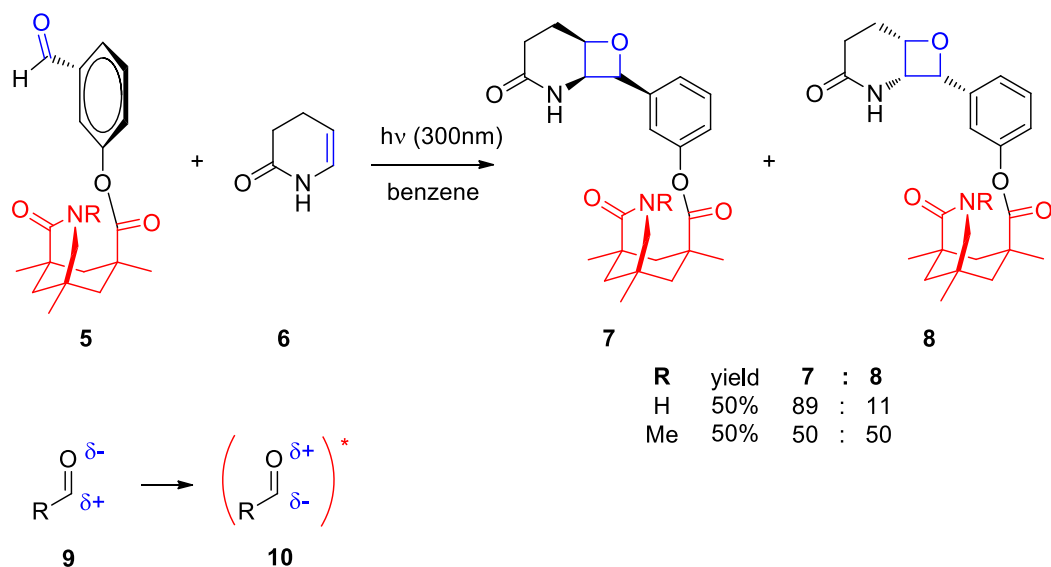
2.1 Paternò-Büchi Reaction

The Paternò-Büchi reaction is the [2+2] photocycloaddition of a carbonyl compound with an alkene leading to oxetanes.^{31,32} In the first highly diastereoselective reaction of this kind, α -ketoesters such as **1** carrying a chiral auxiliary react with electron rich alkenes **2**. The corresponding oxetans (**3**) are obtained in almost quantitative yield and complete diastereoselectivity (Scheme 1).³³ In this case, the cycloadduct was transformed into the enantiopure apiose derivative **4**. The Paternò-Büchi reaction with dienolethers can be considered as a photo-aldol reaction. The chiral information is present in the chiral alcohol of the ester function. Best diastereoselectivities have been observed with chiral α -alkyl cyclohexanol based alcohols as chiral auxiliaries. An extensive mechanistic study was carried out in order to characterize the stereoselection process with respect to the enthalpy and entropy influence.^{34,35}



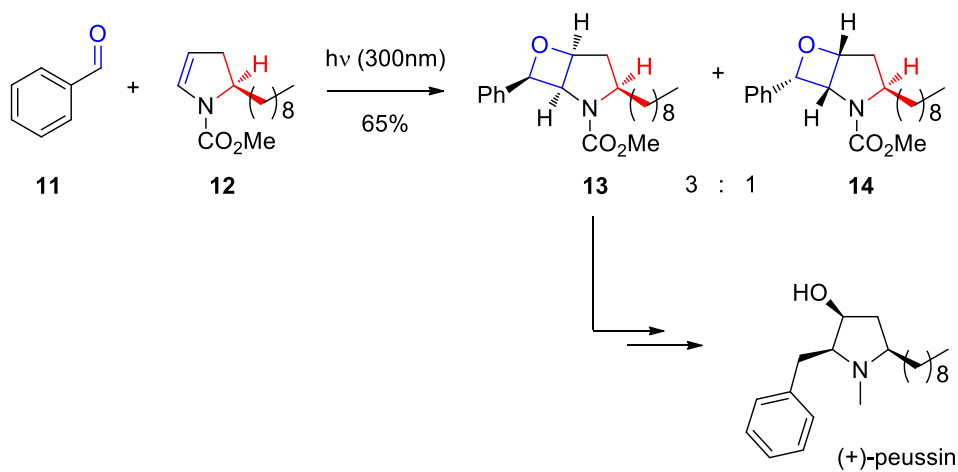
Scheme 1. Diastereoselective Paternò-Büchi reaction and its application to asymmetric synthesis.

The benzaldehyde derivative **5** reacts with the dihydropyridinone **6** leading to the diastereomeric oxetanes **7** and **8** (Scheme 2).³⁶ In this transformation a Kemp acid derivative is used as chiral auxiliary. Both the carbonyl and the olefin reaction partner possess lactam functions. Thus, a complexation of both is facilitated by the formation of two hydrogen bonds. In this way, the approach in diastereotopic half spaces is controlled. When the lactam function of the carbonyl reaction partner **5** is N-methylated (R=Me), no diastereoselectivity is observed as no complexation is possible. Such hydrogen bonds play a key role in many photocatalytic reactions applied to asymmetric catalysis.³⁷ It should further be pointed out that only one regioisomer is formed in both cases (R=H and R=Me). Compared to corresponding ground state reactions of carbonyl compounds with enol or enamine derivatives, the regioselectivity in this photochemical reaction is reversed. This umpolung is explained by the fact that the polarity of a carbonyl function is reversed when this function is electronically excited as shown in structures **9** and **10**.



Scheme 2. Diastereoselective Paternò-Büchi of an aromatic aldehyde bounded to a Kemp acid derived chiral auxiliary.

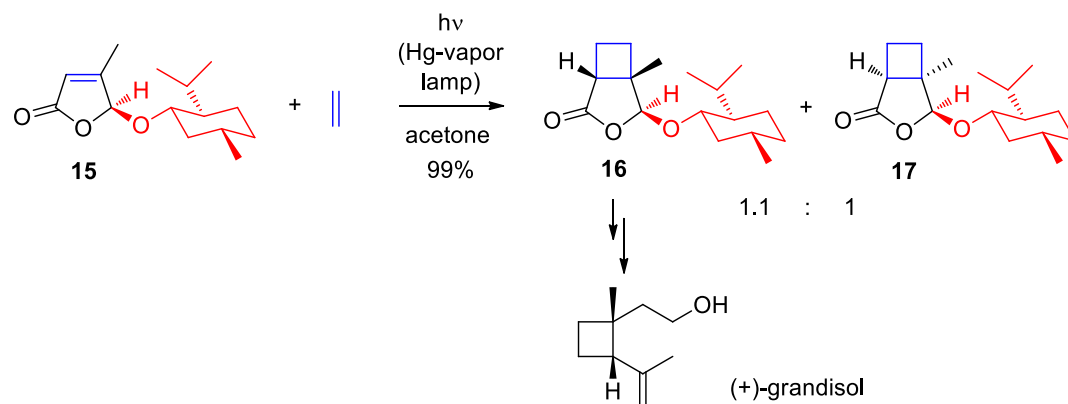
Many photochemical reactions are carried out with chiral, enantiopure substrates. Such reactions are of high interest in asymmetric synthesis. In such a reaction benzaldehyde **11** reacts with the dihydropyridine derivative **12** yielding the two diastereomeric oxetanes **13** and **14** (Scheme 3).³⁸ The major isomer **13** was transformed into (+)-preussine. With respect to the chiral center in the phenyl position, only one relative configuration is generated in which the phenyl substituent is *syn* orientated with respect to the pyrrolidine ring. Due to steric hindrance, this configuration is thermodynamically less stable. Detailed mechanistic studies have been performed on the kinetic control of this stereoselectivity.^{39,40}



Scheme 3. Application of the diastereoselective Paternò-Büchi to the synthesis of (+)-preussin.

2.2 [2+2] Photocycloaddition with α,β -unsaturated carbonyl compounds

The [2+2] photocycloaddition of α,β -unsaturated carbonyl, α,β -unsaturated carboxyl compounds or lactams with alkenes is one of the most frequently applied photochemical reaction to organic synthesis.⁴¹ Many asymmetric variants of this transformation have been published.^{42,43,44} The molecular structure is significantly affected by electronic excitation. Consequently, the diastereoselectivity of photochemical reactions is modified. Thus the chiral α,β -unsaturated lactone **15** reacts in photochemical [2+2] cycloaddition with ethylene yielding the cyclobutanes **16** and **17** (Scheme 4).⁴⁵ Compound **15** is electronically excited via photosensitization involving triplet energy transfer from acetone. One of the diastereoisomers (**16**) was transformed into (+)-grandisol. Chiral alkoxyfuranones like **15** have frequently been applied to asymmetric synthesis.^{46,47} A lot ground state reactions such as Michael addition or Diels-Alder reactions are carried out with high diastereoselectivity. In the herein reported photocycloaddition the furanone **15** reacts at its $\pi\pi^*$ triplet state. A detailed computational study was carried out on the structure of this excited state (Figure 1).⁴⁸ At the $\pi\pi^*$ triplet state, the C=C π -bond is partially suppressed by two motions, twisting and pyramidalization at the β -position. Furthermore, two energetically very close conformations **18** and **19** are found with opposite orientations of the hydroxyl group and the methyl group in β position. By these effects, the diastereodifferentiation is considerably reduced with respect to the ground state and corresponding cycloadditions at the excited state become diastereo-unselective.⁴⁹



Scheme 4. Triplet sensitized [2+2] photocycloaddition of a chiral α,β -unsaturated lactone.

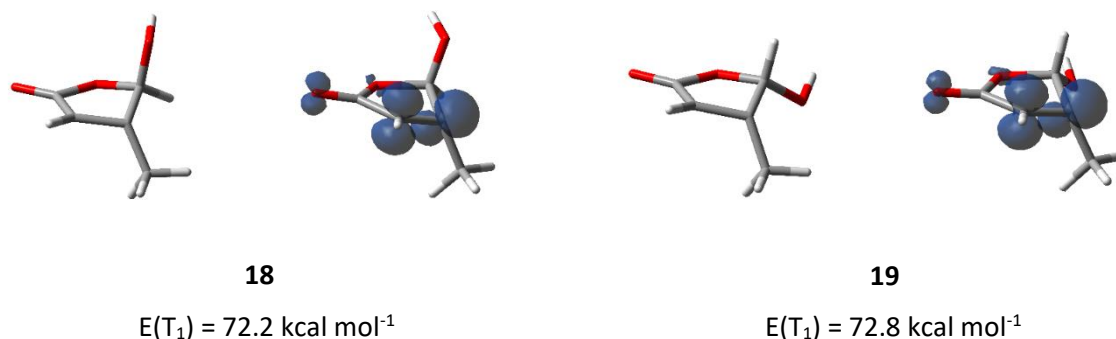
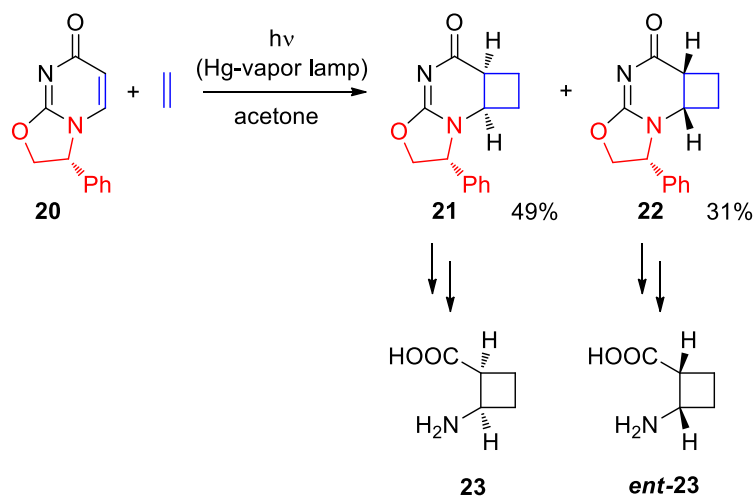


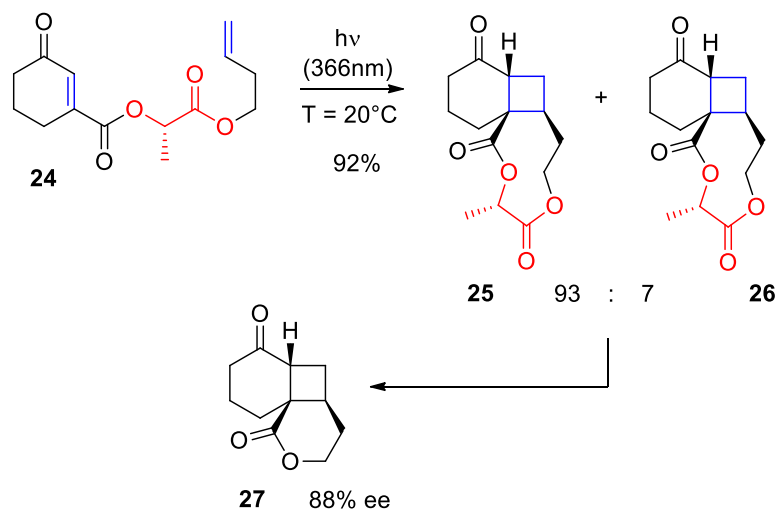
Figure 1. Computational study on the structure of vibrational relaxed $\pi\pi^*$ triplet state of a model compounds for 5-alkoxyfuranones.

The fact that the diastereodifferentiation at the excited state of α,β -unsaturated carbonyl and related compounds is diminished has also had an impact on [2+2] photocycloadditions with heterocyclic compounds. The [2+2] photocycloaddition of chiral pyrimidone compound **20**, an uracil derivative, with ethylene yields the diastereoisomeric cyclobutanes **21** and **22** (Scheme 5).⁵⁰ (*R*)-2-Amino-2-phenylethanol is used as chiral auxiliary. The reaction is sensitized by acetone. The cycloadducts were transformed into the β -aminoacids **23** and *ent*-**23**. In the further developed synthesis strategy, an epimerization step was involved so that all four stereoisomers of the amino acid derivative became available. Although the photochemical key step is not highly diastereoselective, the reaction is very useful for comprehensive studies and applications where a large number of stereoisomers are needed. In the present case, the compounds are involved in studies of peptidomimetics and foldamers.^{51,52,53} Similar studies have been performed with corresponding oxetan β -amino acids.⁵⁴ [2+2] Photocycloadditions with nucleic bases play also an important role in investigations of DNA damage and repair mechanism.^{55,56,57}

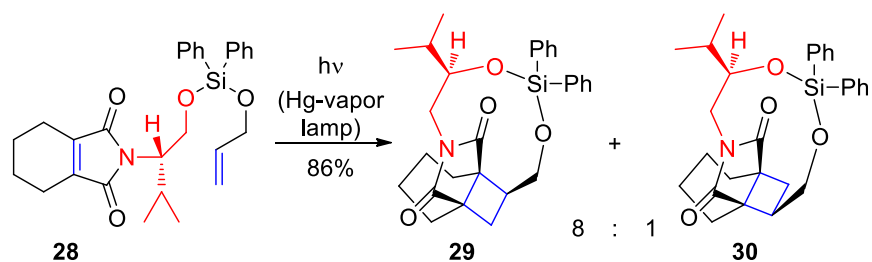


Scheme 5. [2+2] Photocycloaddition with a chiral uracil derivative and the application to the synthesis of cyclobutane β -aminoacids.

In an intramolecular [2+2] photocycloaddition of an alkene to a α,β -unsaturated ketone moiety, chiral induction is efficiently induced by a chiral auxiliary that is inserted in the tether bounding the two reaction partners together. When compound **24** was irradiated at room temperature, two diastereoisomeric cyclobutanes **25** and **26** were formed in high yield and in the high stereoisomer ratio of 93:7 which corresponds to 86% de (Scheme 6).⁵⁸ In this case, lactic acid was inserted into the tether. The product mixture was easily transformed into the δ -lactone derivative **27** which was isolated with 88% ee. The diastereomeric excess could be increased up to 94% when the reaction was carried out at lower temperature such as -40°C . However, under these conditions the yield diminished and oligomers were also formed. At lower temperatures and increased viscosity, the conformation selection necessary for the approach of two reaction partners is inhibited which favors competing intermolecular reactions. The diastereoselectivity could be increased by replacing lactic acid by mandelic acid as chiral auxiliary. The strategy to use a chiral tether can be extended to various functional groups. Thus the silyldioxy tether was used in the transformation of **28** into the diastereoisomeric cyclobutanes **29** and **30** (Scheme 7).⁵⁹ In this reaction, chirality is induced by a L-(+)-valinol moiety which is also inserted in the tether.

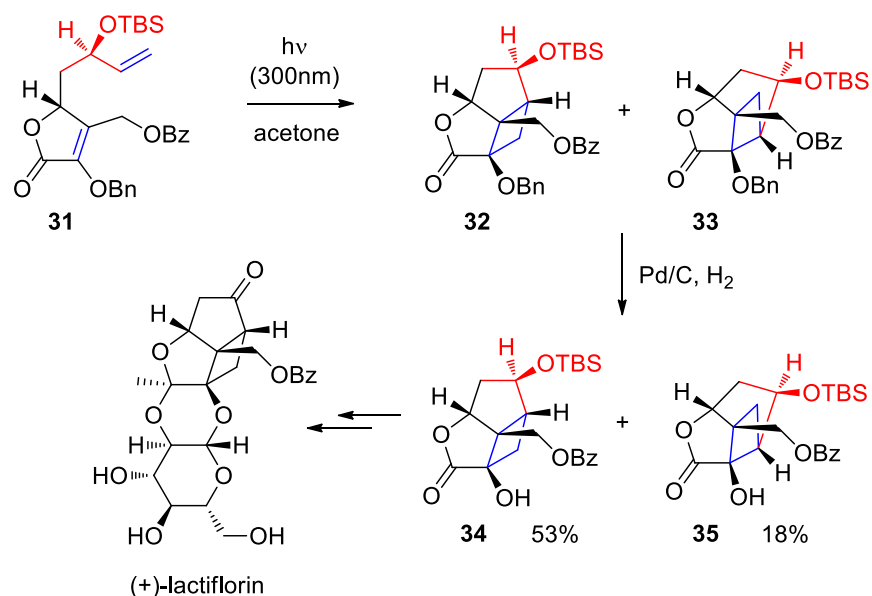


Scheme 6. Diastereoselective intramolecular [2+2] photocycloaddition using a lactate containing tether for chiral induction.



Scheme 7. Diastereoselective intramolecular [2+2] photocycloaddition using a L-(+)-valinol containing tether for chiral induction.

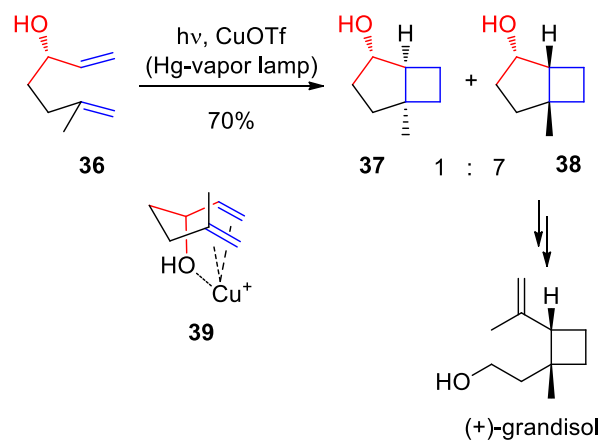
The diastereoselectivity of such reaction can be increased when the chiral information is localized on the olefinic reaction partner which is not electronically excited or when the reaction in an intramolecular way. In the case of **31** (Scheme 8) both criteria are fulfilled. When this compound was irradiated in the presence of acetone, triplet sensitization is induced and regioisomeric cyclobutanes **32** and **33** are formed.⁶⁰ The minor isomer results from a cross addition while the major isomer is formed from a straight addition. The benzyl protecting group was removed under hydrogenation conditions and the resulting tertiary alcohols **34** and **35** were characterized. The major regioisomer **34** was transformed into (+)-lactiflorin. It is the first synthesis of this compound. Two other structures of this natural product have been suggested in previous literature. The present synthesis finally confirms one of them.⁶¹



Scheme 8. Intramolecular photosensitized [2+2] cycloaddition and its application to the total synthesis of (+)-lactiflorin.

2.3 [2+2] Photocycloaddition with alkenes

Cu(I) catalyzed photocycloaddition between two alkenes function has frequently been applied to the synthesis of cyclobutane derivatives.^{42,43,62,63} When the diene compound **36** was irradiated in the presence of a Cu(I) salt, the cyclobutane diastereoisomers **37** and **38** have been isolated (Scheme 9).^{64,65} Although allowed by the Woodward-Hoffmann rules⁶⁶, [2+2] photocycloadditions between alkenes cannot always be efficiently applied to organic synthesis. To become efficient, the alkene functions need to be well oriented.⁶⁷ When conformational mobility inhibits such an orientation, complexation by Cu(I) ions may approach them (**39**). In such complexes, electronic excitation occurs by metal to alkene ligand charge transfer (MLCT).^{68,69,70} In the present case, further complexation with the hydroxyl function favors the formation of the diastereoisomer **38**. The reaction has been applied to the asymmetric synthesis of the pheromone component grandisol. A similar synthesis of this compound starts with chiral (*R*)-(+)-glyceraldehyde.⁷¹

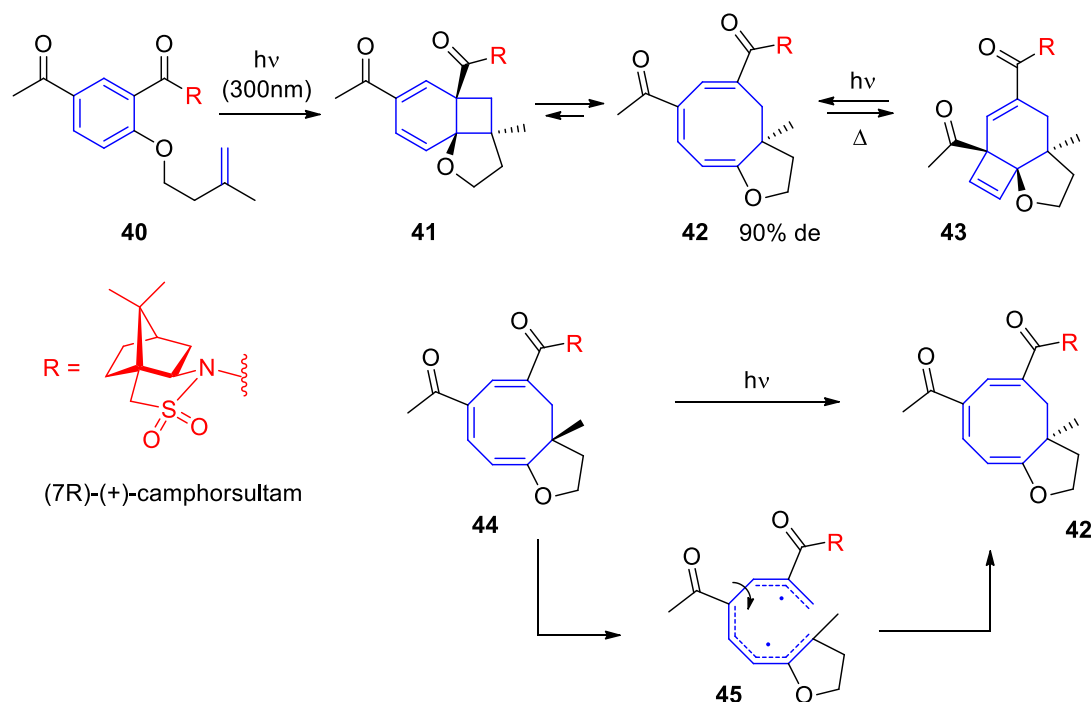


Scheme 9. Copper(I) catalyzed intramolecular [2+2] photocycloaddition with alkene moieties. Application to the asymmetric synthesis of grandisol.

2.4 Photocycloadditions with aromatic compounds

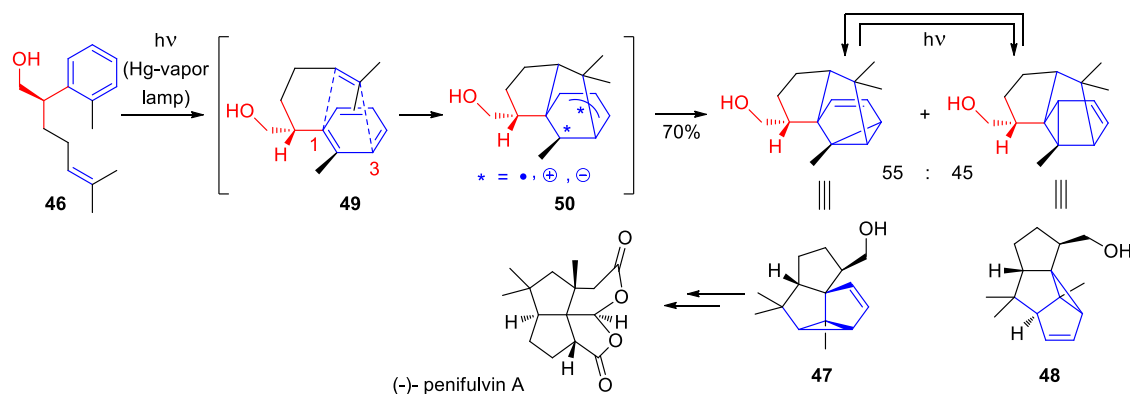
Photocycloadditions of aromatic compounds with alkenes are an important tool in organic synthesis.^{11,72,73,74,75,76} Starting from relatively simple compounds, in only one step a high degree of molecular complexity is generated. When electronically excited, benzene derived aromatic compounds undergo [2+2] (*ortho*), [2+3] (*meta*) or more rarely [2+4] cycloaddition with alkenes. Especially, [2+3] and [2+2] photocycloaddition are competing processes. Most frequently, the [2+3] photocycloaddition has been applied to organic synthesis.

In the case of the diastereoselective intramolecular Photocycloaddition of the aromatic ketone **40**, (+)-camphorsultam was used as chiral auxiliary (Scheme 10).⁷⁷ After excitation to the triplet state, [2+2]-photocycloaddition occurs leading to the tricyclic cyclobutane derivative **41**. As in many cases of such reactions, consecutive steps are observed. Thus the cyclooctatriene derivative **42** is formed in a thermal disrotatory ring opening. In a further photochemical disrotatory cyclization, the cyclobutene derivative **43** is formed. The formation of the latter compound is reversible so that **42** is accumulated. At the beginning of the transformation the diastereoselectivity is rather low (30% at 20% of conversion). As the reaction advances to full conversion of **40**, the diastereoselectivity increases up to 90%. This indicates that chiral induction in the [2+2] photocycloaddition step (formation of **41**) is rather weak. Since this step is irreversible, it has been suggested that an epimerization in **44** should take place which would be in competition with the cyclization to the corresponding tricyclic cyclobutene compound. The latter process is a singlet reaction. However, the ketone function attached to the cyclooctatriene moiety in **44** favors intersystem crossing to the triplet state. At this electronic state, C-C bond cleavage can take place leading to the diradical intermediate **45**. Conformational flexibility in this intermediate enables the formation of the major and thermodynamically more stable diastereoisomer **42** in the ring closure step. Thus the initially low diastereoselectivity is increased by this epimerization process during the advancing of the conversion.



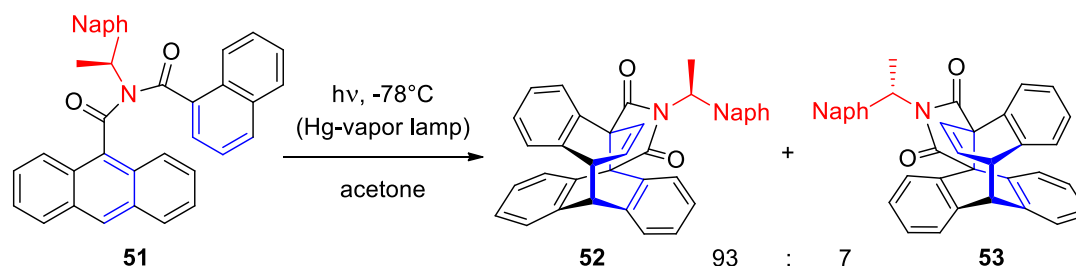
Scheme 10. Diastereoselective intramolecular [2+2] photocycloaddition followed by thermal and photochemical rearrangements.

The intramolecular [2+3] cycloaddition is the most frequently applied photocycloaddition between a benzene derived moiety and an alkene. While in many ground state reactions of benzene derivatives, the aromatic character is conserved in the products, in photocycloadditions of such compounds, the aromatic character is suppressed in the products. Generally such photoproducts possess a high degree of complexity. Thus the enantiopure compound **46** was transformed in only one photochemical reaction into the polycyclic compounds **47** and **48** (Scheme 11).⁷⁸ The approach of the alkene moiety to the electronically excited arene occurs regioselectively in the *ortho*-positions of the methyl group (**49**). The diastereoselectivity is completely controlled by the chiral center in the benzyl position which was explained by an allylic 1,3-strain effect.⁷⁹ Two σ -bonds are formed yielding intermediate **50**. As the reaction occurs at the singlet excited state, this intermediate possesses a certain zwitterionic character. The formation of a third σ -bond yields the final products **47** and **48**. The angular isomer **47** was transformed into then natural product (-)-penifulvin A. The photochemical products **47** and **48** are in photostationary equilibrium via a photochemical vinyl cyclopropane rearrangement. Consequently, the linear isomer **48** is transformed into **47** and can also be used the total synthesis of (-)-penifulvin A. The same strategy was applied to the asymmetric synthesis of two other members of this compound family.⁸⁰



Scheme 11. Intramolecular [2+3] photocycloaddition and its application to the asymmetric synthesis of (-)-penifulvin A.

[4+4]-Photocycloaddition between condensed aromatic compounds such as anthracene and naphthalene are easily performed. According to the Woodward-Hoffmann rules⁶⁶ for concerted reactions, such cycloaddition are forbidden at the ground state. Under photochemical conditions such transformations are readily feasible. They are applied to the synthesis of medium sized ring systems. Thus the imide **51** carrying an anthracenyl and a naphthyl moiety undergoes photocyclization yielding the adducts **52** and **53** in high diastereoselectivity. (Scheme 12).⁸¹

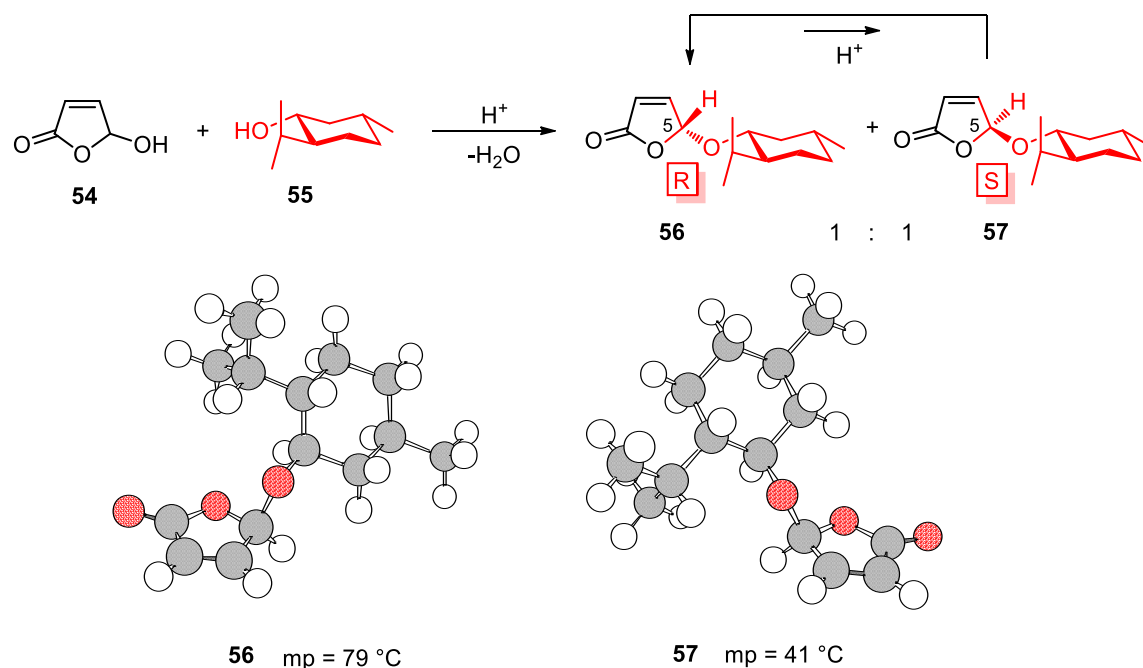


Scheme 12. Diastereoselective [4+4]-photocycloaddition between an anthracene and a naphthalene moiety.

3 Radical reactions

A photochemical addition cyclization reaction was used to quantify the diastereoselection of a photochemically induced radical addition. As already mentioned, the α,β -unsaturated lactones such as **56** are a valuable chiral synthon.⁴⁶ **56** is synthesized by condensation of 5-hydroxyfuranone **54** with enantiomerically pure (-)-menthol **55**. Two diastereoisomers **56** and **57** are obtained.⁴⁷ The diastereoisomer **56** possessing *R* configuration in the 5-position crystallizes preferentially (mp 79°C) while the diastereoisomer **57** with *S* configuration in position 5 (mp 41 °C) can be transformed into **56** (Scheme 13).⁸² Under particular crystallization conditions at low temperature the 5*S*-diastereoisomer **57** can also be obtained in pure form. A computational study based on NMR data shows that the degree of diastereodifferentiation for a reaction at the furanone C=C double bond is different. In the case of **56** the shielding of the diastereotopic half space of a *syn* reaction (*syn* with respect to the alkoxy substituent in

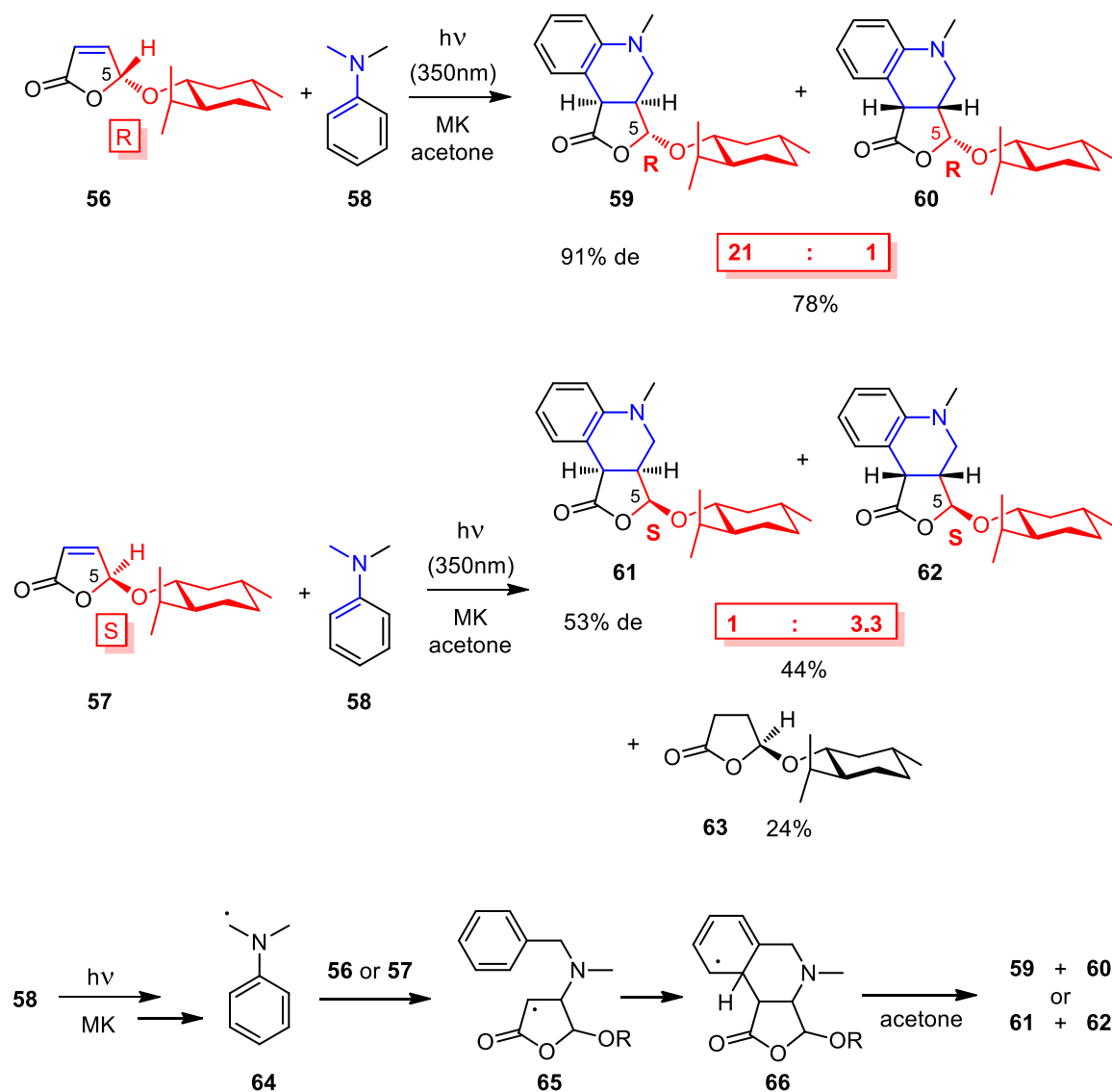
the 5-position) is higher than in the case of **57**. Therefore the diastereoselectivity of reactions with **56** should be higher than in the case of **57**.



Scheme 13. Synthesis of (5*R*)- and (5*S*)-5-*l*-Menthylxyfuran-2[5H]-one.

To get further insights into the diastereoselection process, the photochemically induced addition cyclization reaction with aromatic tertiary amines such as **58** was carried out (Scheme 14).⁸² In this reaction, α -aminoalkyl radicals **64** are generated via photochemical electron transfer or photoredox catalysis with Michler's ketone (Bis[4-(dimethylamino)phenyl]methanone, MK).⁸³ The addition of **64** to the furanone **56** or **57** leads to the oxoallyl radical intermediates **65**. After cyclization the resulting intermediates **66** are oxidized by a carbonyl compound such as acetone. Detailed mechanistic studies have been carried out on this reaction under homogeneous and heterogeneous conditions and their influence on the diastereoselectivity.^{84,85,86} When the reaction was carried with the diastereoisomer **56** in acetonitrile solution and in the presence of acetone, the dihydroquinoline compounds **59** and **60** were obtained with 91% of diastereoselectivity. The major diastereoisomer is formed by an attack of the α -aminoalkyl radical *anti* with respect to the menthyl substituent at the chiral center in 5-position. In contrast to the previously discussed [2+2] photocycloaddition (compare Scheme 4 and Figure 1), the chiral furanone reacts at its ground state. When the diastereoisomer **57** was transformed under the same reaction conditions, again diastereomeric tetrahydroquinolines (**61**, **62**) were obtained and again the major isomer resulted from a radical attack *anti* with respect to the menthyl substituent. However, the diastereoselectivity is significantly lower. Furthermore, the side product **63** is formed. In contrast, to reactions with **56**⁸³, the presence of acetone could not completely suppress the formation of this product. It should further be pointed out here that in the absence of Michler's ketone (MK) and in the presence of acetone, only slow and unselective transformation was observed. Thus sensitization by acetone under these conditions was not effective. Obviously, chirality is induced by two elements. The chiral acetal in 5-position and the menthyl substituent. In such cases, the phenomenon of double induction is observed.⁸⁷ The two elements act in the same direction (matched pair, the case of **56**) or in

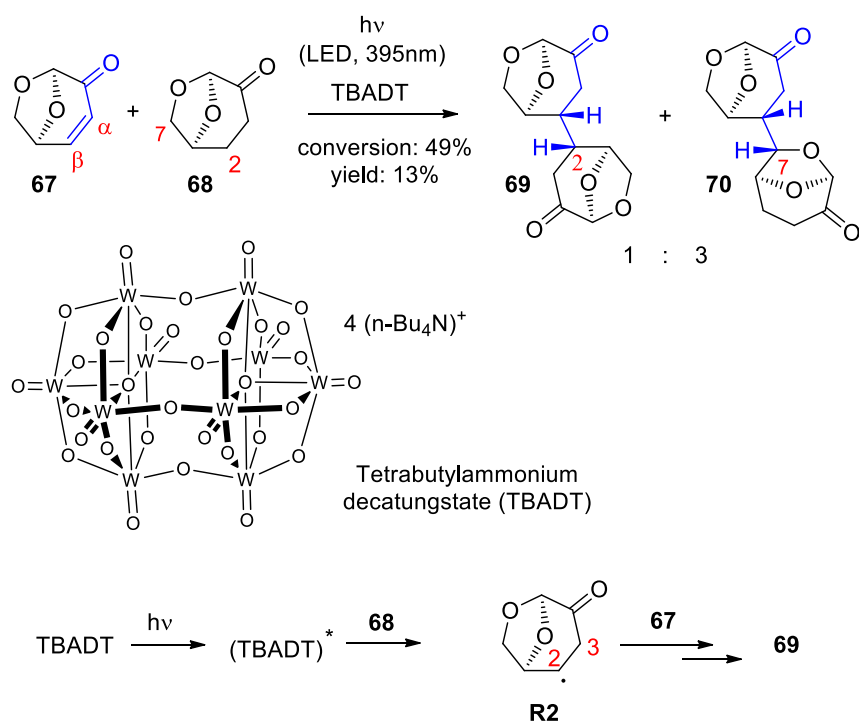
the opposite direction (mismatched pair the case of **57**). The dominant element is chiral center in 5-position which contributes with $\Delta\Delta G^\ddagger = 5.15 \text{ kJ mol}^{-1}$ to the chiral induction in the reaction depicted in Scheme 14. The menthyl substituent contributes with $\Delta\Delta G^\ddagger = 2.9 \text{ kJ mol}^{-1}$.



Scheme 14. Diastereoselective tandem addition cyclization reaction of an aniline derivative to 5-menthyloxyfuranone.

Radical intermediates are often generated by photochemically induced hydrogen abstraction or recently called hydrogen atom transfer (HAT). In the herein discussed reactions, this process can most frequently occur by two mechanisms: (1) The electron is transferred first and the proton follows (two-step process). (2) The electron and the proton are simultaneously transferred (one-step process).^{86,88} These two mechanisms are part of proton coupled electron transfer (PCET) processes.^{89,90} The mechanism of HAT affects also the regio and stereoselectivity of a reaction. Such regio and stereoselectivity effects can be discussed for the photocatalytic addition of cyrene to levoglucosenone. Levoglucosenone is a biobased renewable platform chemical obtained from cellulose by pyrolysis.⁹¹ It is an interesting synthon

for asymmetric organic synthesis.⁹² Currently, this compound also plays an important role as precursor of cyrene.⁹³ The latter is a new biobased solvent. Radical intermediates can be generated directly from alkane precursors using photocatalysis with tetrabutylammonium decatungstate (TBADT).⁹⁴ Under such conditions levoglucosenone **67** has been transformed with cyrene **68** (Scheme 15).⁹⁵ After photochemical excitation of TBADT, hydrogen abstraction at **68** occurs, for example in position 2. It is important to note that the reaction in this position is largely favored with respect to abstraction in position 3. This regioselectivity is general for such reaction with aliphatic ketones.⁹⁶ The resulting radical intermediate **R2** adds to **67** in the β -position which leads to compound **69**. This adduct possesses C_2 -symmetry. Only two products **69** and **70** from 32 possible regio and stereoisomers have been formed. The reaction takes place only in positions 2 and 7 of cyrene **68** and only one diastereoisomer of each regio isomer is formed. Consequently, the diastereodifferentiation is very high in both substrates **67** and **68**. The radical addition to levoglucosenone **67** occurs stereospecifically *anti* with respect to the (-CH₂-O)-bridge. In the formation of the symmetric adduct **69**, the same stereochemistry is induced in position 2 of the cyrene moiety.



Scheme 15. Regio and diastereoselective photocatalytic addition of cyrene **68** to levoglucosenone **67**.

In order to get a deeper insight in the origin of this regioselectivity of this reaction, computational studies have been carried out. Thus the C-H bond dissociation energies have been calculated (Figure 2a). The formation of radical **R1** should be favored. However, no reaction was observed in position 2 of cyrene **68**. This observation is in line with similar reactions of cyclic ketones that have previously been reported.⁹⁶ Only reactions have been observed in which **R2** and **R5** are involved. Partial charges have also been calculated (Figure 2b). The results of both studies well explain the experimental results. Calculations concerning the diastereoselectivity of the radical addition showed that the attack *anti* with respect to the (-CH₂-O)-bridge in **67** is favored by around 5 kcal/mol when compared to a corresponding *syn* attack.

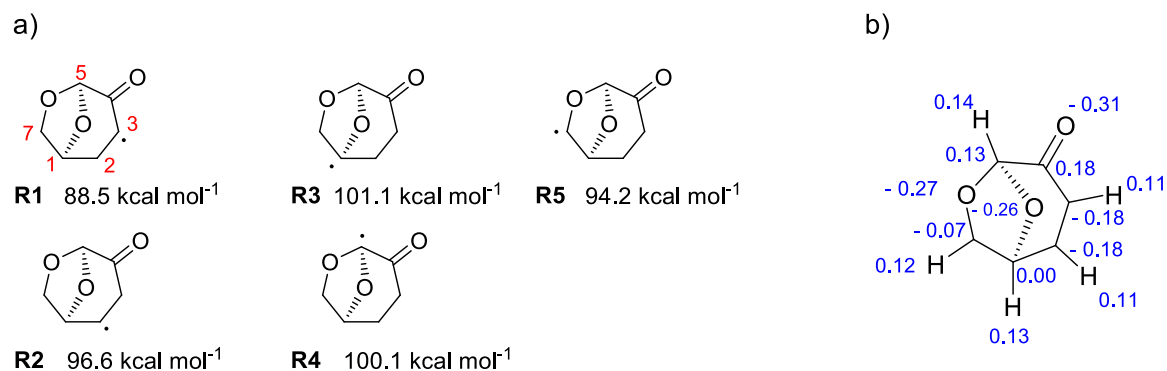
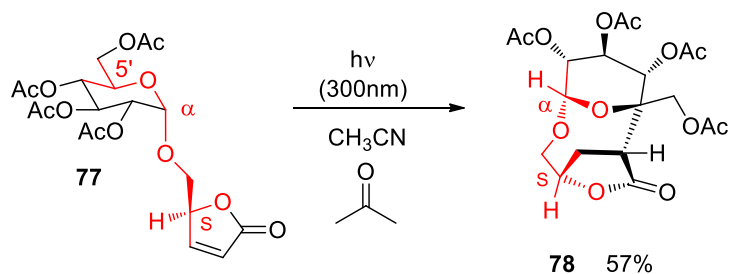
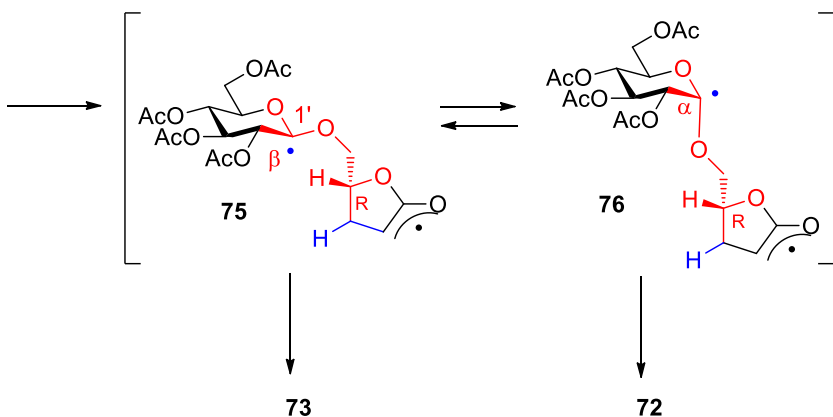
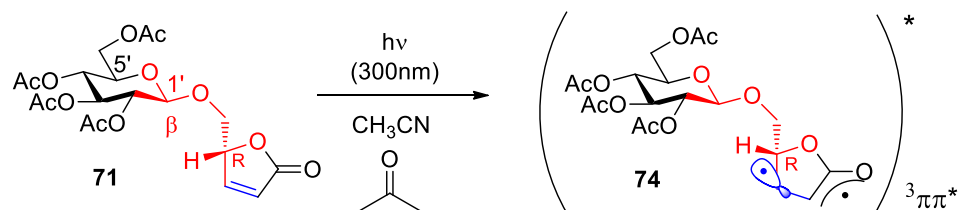
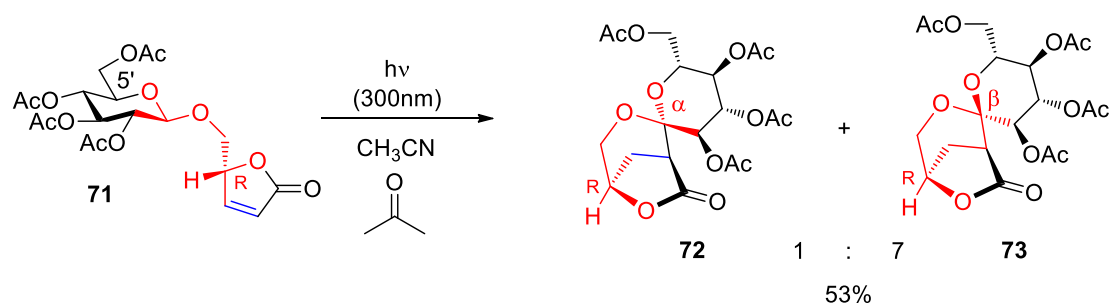


Figure 2. a) Calculation of C-H bond dissociation energies of cyrene **68**. b) Calculation of partial charges of **69**.

Photochemically excited α,β -unsaturated lactones such as **71** undergo intramolecular hydrogen abstraction (Scheme 16).⁹⁷ Complex spirocyclic compounds **72** and **73** are formed in a diastereoselective way. In the present case, electronic excitation was performed by sensitization involving triplet energy transfer from acetone to the furanone **71**. At the vibrationally relaxed state **74**, the C=C π -bond is cleaved and an increased spin density is localized in the β -position of the furanone moiety.⁴⁸ For this reason, hydrogen atom transfer takes place from the anomeric center of the sugar moiety into this position. Thus the diradical intermediates **75** and **76** are formed which are in conformational equilibrium. Radical combination yields the diastereoisomers **73** and **72** of the spiro cyclic products. Due the anomeric effect, conformer **75** should be more stable which could explain the favored formation of the β -anomeric product **73**. The configuration in the substrates also affect the regioselectivity of the hydrogen abstraction. When the (αS)-diastereoisomer **77** was irradiated under the same conditions, hydrogen atom transfer from the 5'-position of the sugar moiety led to the macrocyclic product **78**. Similar results have been observed when the reaction was carried out under direct light absorption of the furanone derivatives.⁹⁸ In this case the transformation was performed at low temperature. The triplet state is generated by intersystem crossing.

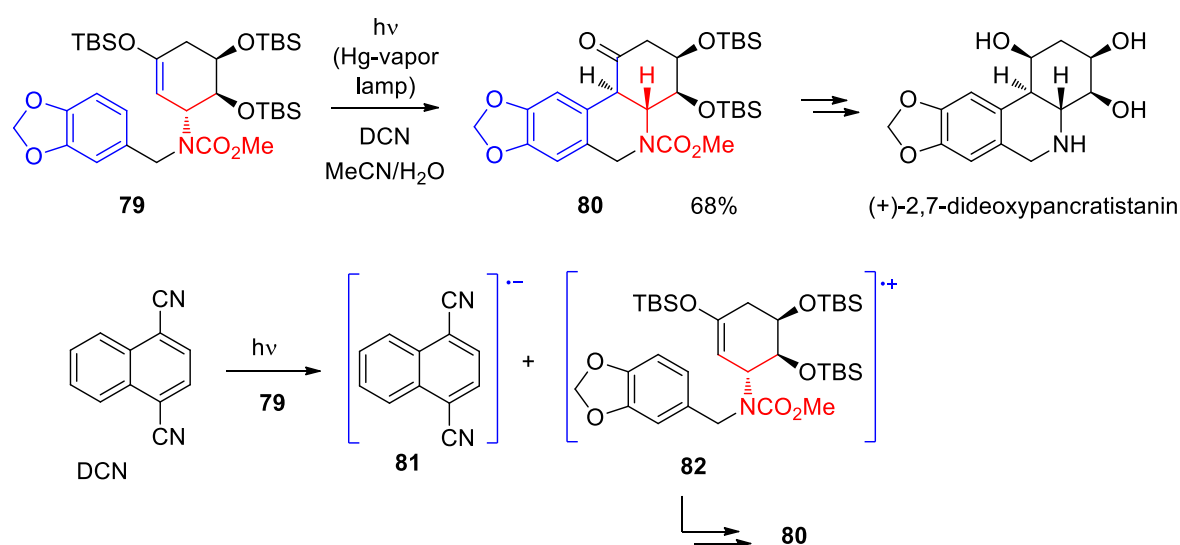


Scheme 16. Diastereo- and regioselective intramolecular hydrogen abstraction and radical cyclization of glucosyl substituted furanones.

In the previously discussed examples of this section, the photochemical reactions are induced by sensitization or photo-catalysis. Different kinds or mechanisms of photocatalysis exist; they offer numerous perspectives for application of photochemical reactions to organic synthesis.⁹ A particularly

efficient method is photoredox catalysis. As it has already been pointed out, photochemical excitation significantly change properties and especially chemical reactivity of chemical compounds. Concerning redox reactions, most frequently electron transfer from or to an electronically excited compound is facilitated.^{99,100,101,102,103} It is therefore obvious, that under these conditions, numerous redox-catalytic reactions can be successfully carried out.

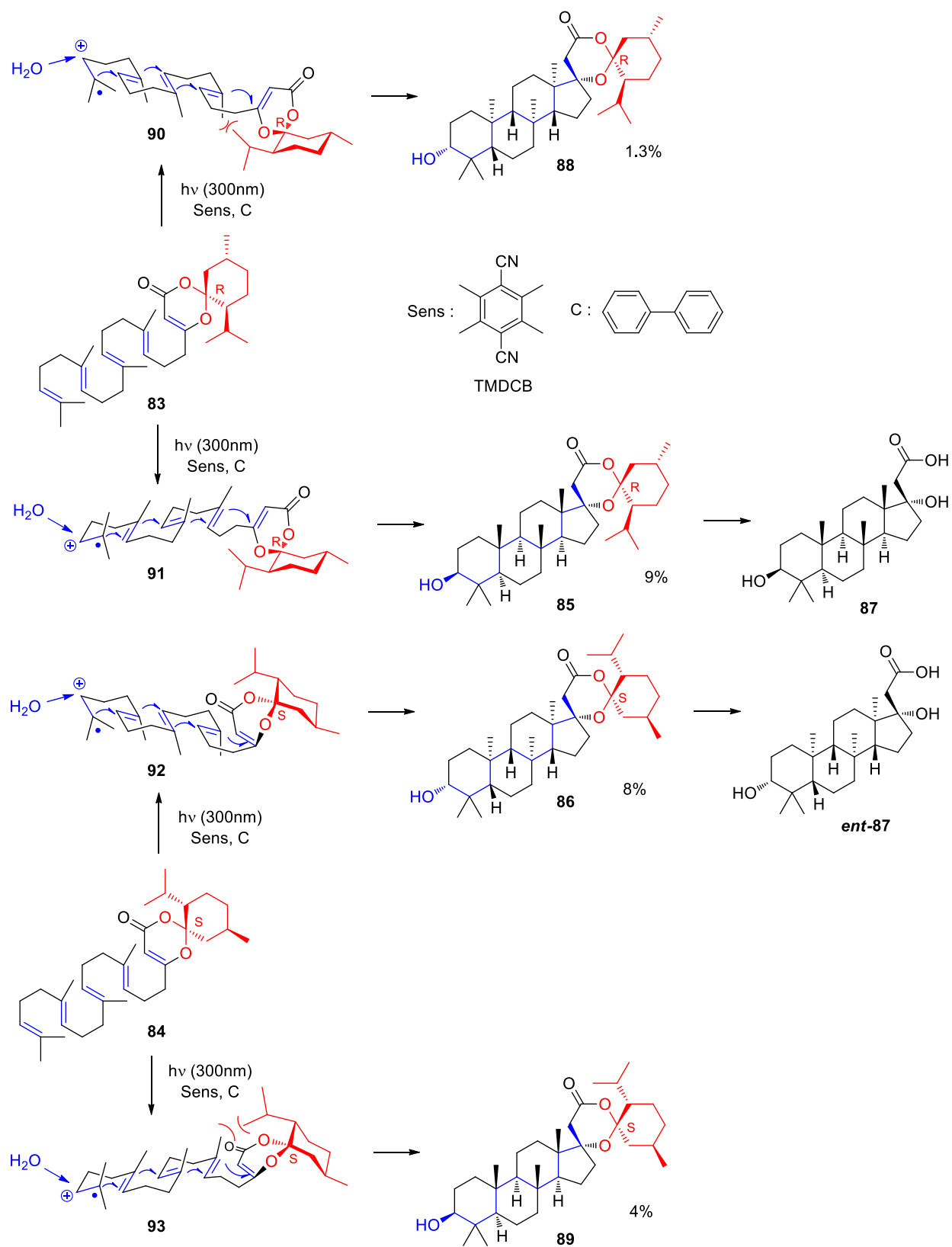
When compound **79** was irradiated in the presence of dicyanonaphthalene (DCN) cyclization occurred and the tetrahydroisoquinoline derivative **80** was isolated (Scheme 17).¹⁰⁴ Only, one epimer is formed in this reaction. Photochemical excitation of DCN induces electron transfer from **79** to DCN leading to the radical ion pair **81** and **82**. Cyclisation occurs in the radical cation **82**. Further synthesis steps leads to the target compound (+)-dideoxypancratistatin which is a phenanthridine derivative. It should be pointed out that the photoredox catalytic conditions enable an easy coupling of two electrophilic reaction partners. In this case, an enolether is coupled with an electron rich aromatic moiety.



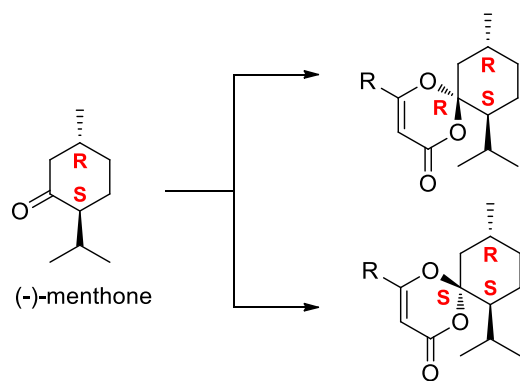
Scheme 17. Intramolecular Photoredox catalytic coupling of two nucleophilic reaction partners, an enolether and an electronically rich benzene derivative, and its application to organic synthesis.

Diastereoselective tandem or cascade reactions have been carried out under photochemical induced electron transfer conditions. Thus the (*E,E,E*)-geranylgeranylmethyl dioxinons **83** and **84** undergo four cascade cyclization to build-up the steroid skeleton (Scheme 18).¹⁰⁵ The reaction starts with electron transfer from the terminal olefinic double bond to the photoredox catalytic system. In this case, a co-sensitizing system of tetramethyldicyanobenzene (TMDCB) and diphenyl (C) has been employed. Using such a system enables a rapid intermolecular charge separation in cases when ionization of the substrate by the primary sensitizer is less efficient.¹⁰⁶ In this case, it is TMDCB. Such conditions also inhibit early back electron transfer in the reaction sequence. The cationic part is trapped by water while the radical cascade takes place. It must be pointed out that in this step the relative configuration of all chiral centers in the steroid part is completely controlled despite the fact that the reactions are carried out in solution. Only two diastereoisomers are formed with respect to the menthone moiety in the dioxinones. In the case of the transformation of compound **83**, the diastereoisomer ratio is 7:1 and **85** is the mayor product. In the case of the reaction of compound **84**, the ratio is 1:2 and **86** is the major isomer. In the

case of the minor isomers **88** and **89**, the formation of the corresponding conformers **90** and **93** are slightly inhibited by steric hindrance when compared to conformations **91** and **92** yielding the mayor isomers **85** and **83**. After removing of the menthone chiral auxiliary, **85** and **86** yield **87** and *ent*-**87** respectively. Concerning the application to the synthesis of enantiopure targets, the overall process is less efficient. The problem is related to the topology of chiral induction. In the present case, it results from the fact that menthone is an asymmetric chiral auxiliary. As a consequence two dioxinone diastereomers are formed from menthone (Scheme 19).^{107,108} Often, the diastereoselectivity of such synthesis is hardly controlled. The problem can be circumvented when C₂-symmetric chiral ketones are used instead of asymmetric ketones.^{109,110} This photochemically induced cascade reaction resembles the biosynthesis of lanosterol by similar cascade cyclizations in squalene. Lansterol is a synthesis intermediate of biochemical production of steroids.



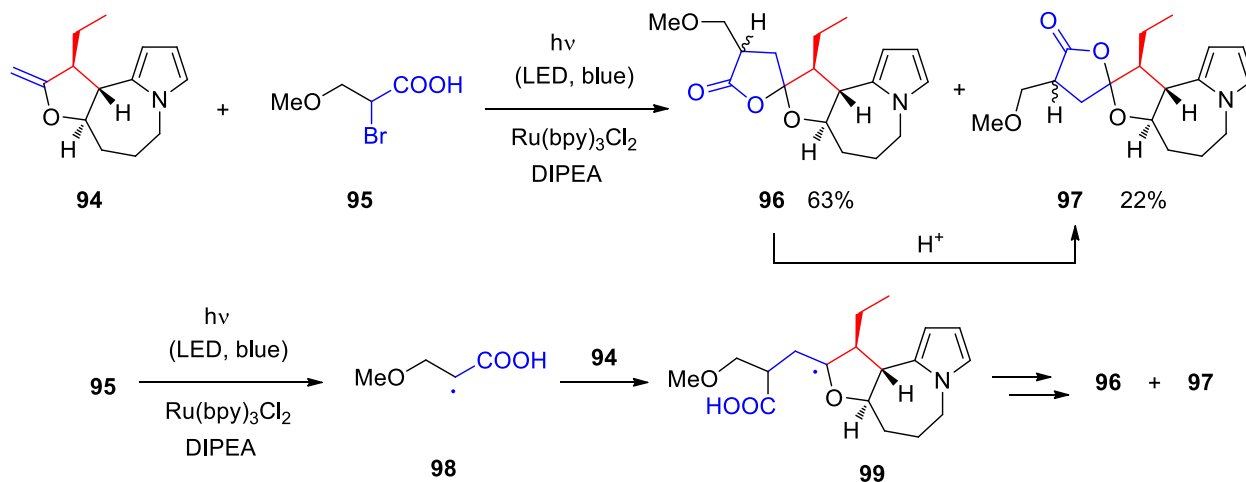
Scheme 18. Diastereoselective cascade reaction induced by photochemically induced electron transfer. Application to the synthesis of the steroid skeleton.



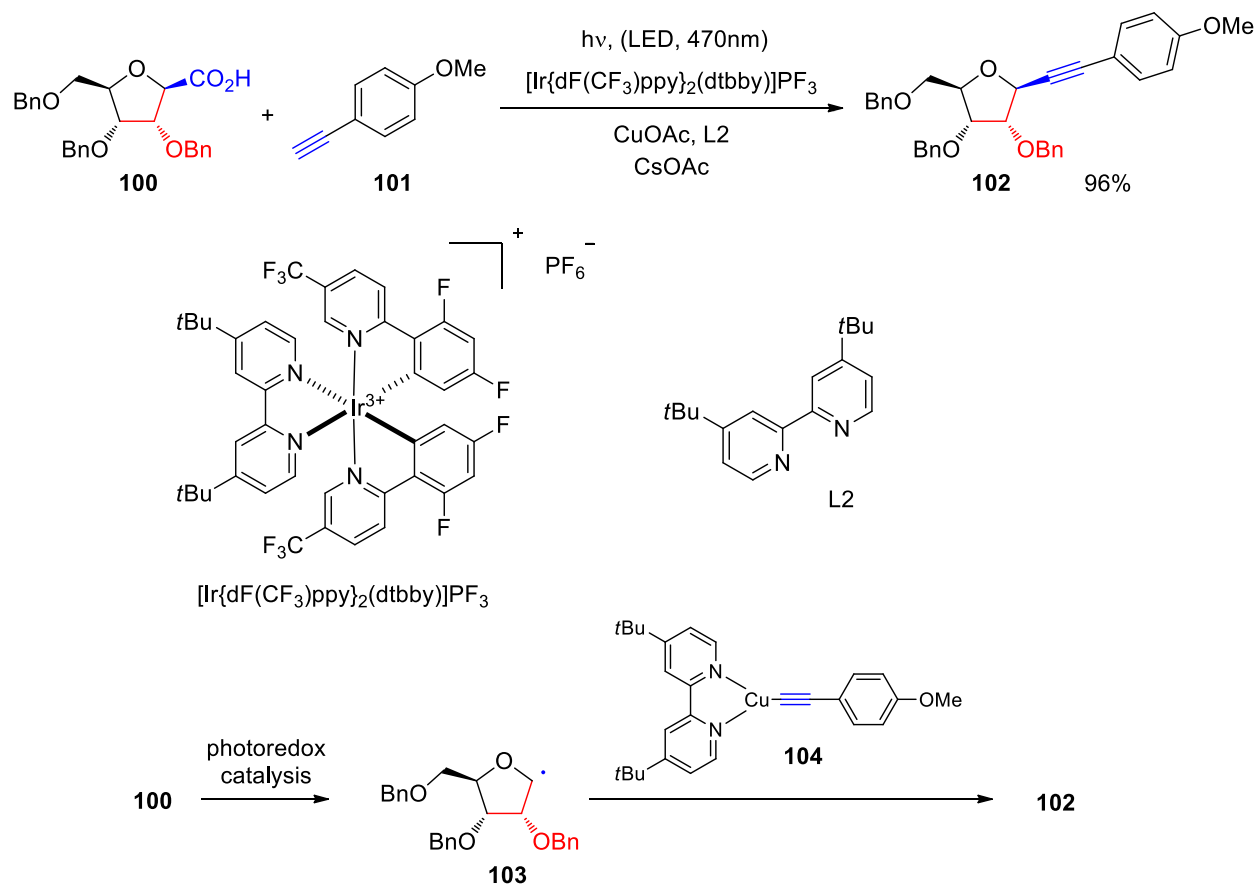
Scheme 19. Diastereoisomeric dioxinones.

Photoredox catalytic reactions with visible light have become a decisive part of organic synthesis methodology. Books^{7,8} and numerous special or thematic issues of chemical journals deal with this topic.^{111,112,113,114,115,116} Many of these reactions are investigated in the context of asymmetric catalysis. These reactions are now also applied to multistep syntheses, for example, of natural products.^{3,117,118,119}

Under photoredox catalytic conditions 2-bromo-3-methoxypropionic acid **95** reacts with the enolether function in compound **94** (Scheme 20).¹²⁰ In photoredox catalytic reaction with $\text{Ru}(\text{bpy})_3\text{Cl}_2$ as photocatalyst and diisopropylethyl amine (DIPEA) as sacrificial electron donor, electron deficient radicals **98** are generated from **95**. Such radical intermediates readily react with electron rich alkenes such as in the case of **94**. Similar reactions have also been carried out via direct excitation by irradiation with UV light¹²¹ or by copper catalysis.¹²² The resulting intermediates **99** undergo cyclization with the carboxyl function which leads to the final product diastereoisomers **96** and **97**. Under acidic conditions, epimerization was observed at the acetal function and the **96** can be transformed into the former minor isomer **97**. The diastereoselectivity of the photochemical step is kinetically controlled.

Scheme 20. Diastereoselective photoredox catalytic radical addition of electrophilic radicals to an enolether, application to the synthesis of skeleton of some *Stemona* alkaloids.

Photoredox catalysis is often coupled with other kinds of catalysis, for example organometal or organo catalysis.^{123,124,125,126,127,128,129,130} In the reaction of the 1- β -D-glucopyranose derivative **100** with *p*-methoxyphenylacetylene **101**, only one diastereoisomer of the C-glucoside **102** was formed (Scheme 21).¹³¹ In a photoredox catalytic step, **100** is decarboxylated and the intermediate **103** is formed. In the copper catalysis cycle, the complex **104** is formed which reacts with the radical species **103** leading to the final product. In this case organic photocatalysts were less efficient. In this way, 28 C-glucosides have been synthesized with yields up to 96%. Heteroaromatic and alkyl acetylene derivatives have also been added to furanosyl radicals.

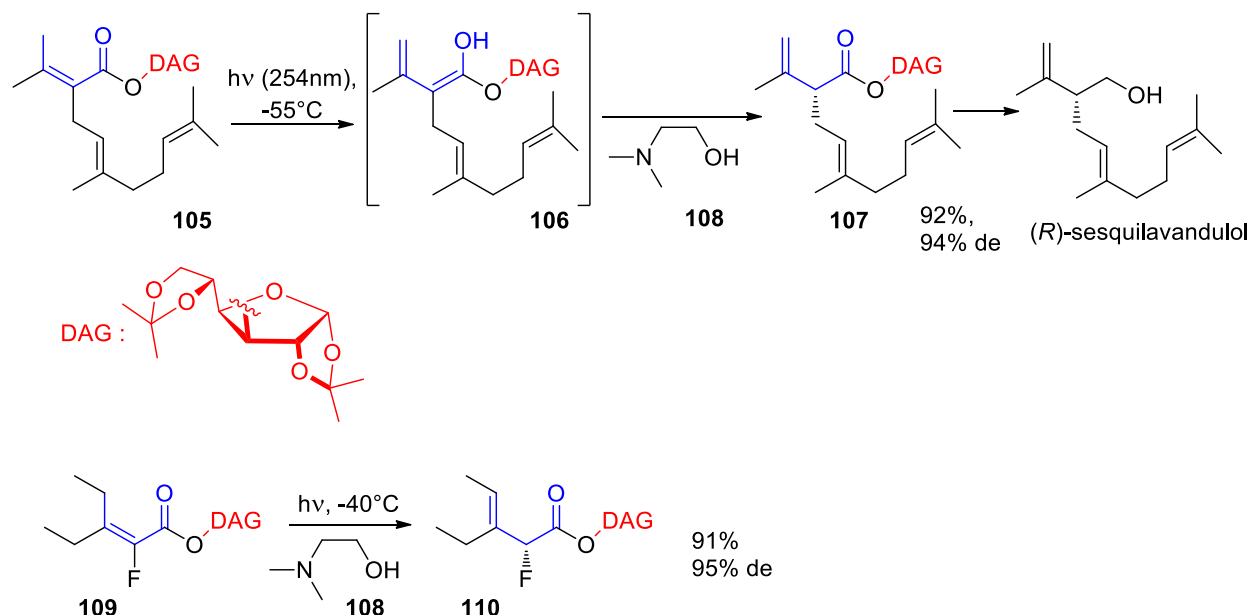


Scheme 21. Diastereoselective synthesis of alkynyl C-glucosides using dual copper and photocatalysis.

4 Photo-tautomerization

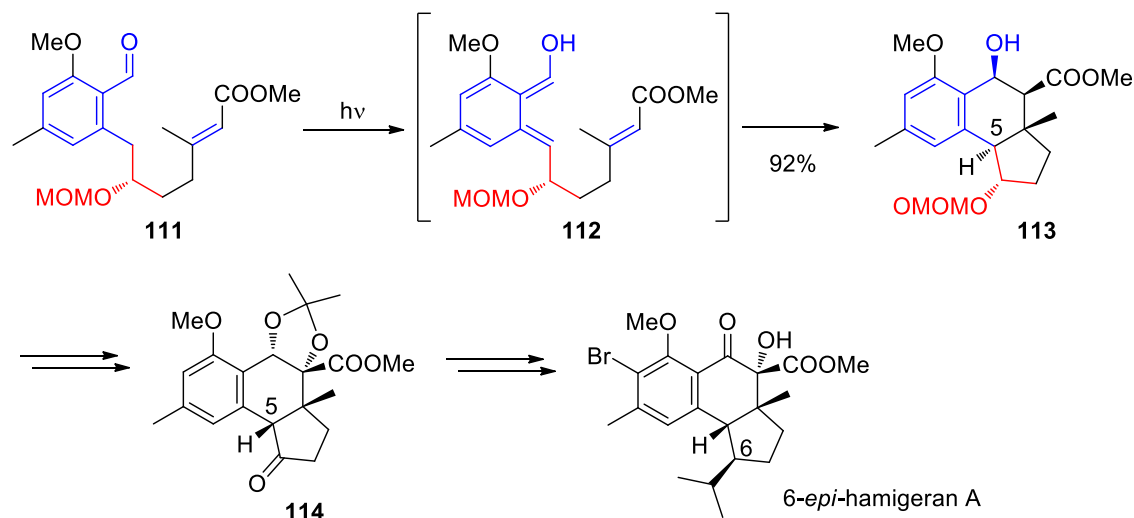
Keto-enol tautomeric equilibria are well known in organic ground-state reactions. They are controlled by the thermodynamical stability of the compounds involved in these equilibria. Under photochemical conditions, especially enol species are available which cannot or difficultly be generated at the ground-state.^{132,133,134,135,136} When α,β -unsaturated esters are irradiated, the $\text{C}=\text{C}$ double bond can be displaced into the β,γ -position.¹³⁷ This is observed when the α,β -unsaturated esters **105** is irradiated. Regioselective γ -hydrogen abstraction occurs at the methyl group and the dienole intermediate **106** is generated (Scheme 22).¹³⁸ Protonation in the α -position yields the final product **107**. This process is catalyzed by the aminoalcohol **108** and it is accompanied by a deprotonation of the enol moiety. Chirality was also induced, when chiral aminoalcohols were used instead of a chiral auxiliary.^{139,140} When

diacetone-D-glucose (DAG) is used as alcohol part and chiral auxiliary, **107** is isolated in high diastereomeric excess. The reaction was used as key step in the synthesis of (*R*)-sesquilandulol. The synthesis strategy was used to confirm the structure assignment of anhydrobisfarnesol by synthesis, a natural compound isolated from the latex of *E. lateriflora*. The same reaction can be applied to the asymmetric synthesis of fluoroorganic compounds. Thus, **109** was transformed into **110** in high yield and high diastereoselectivity.¹⁴¹



Scheme 22. Diastereoselective photodeconjugation applied to the asymmetric synthesis of natural products and fluoroorganic compounds.

When carrying alkyl substituents in *ortho* position, aromatic carbonyl compounds also undergo photo-tautomerization leading to quinodimethane intermediates.¹⁴² Various ground state reactions are then observed and a high degree of molecular diversity and complexity can be generated. In the case of compound **111**, the quinodimethane **112** is formed (Scheme 23).¹⁴³ In a stereospecific intramolecular Diels-Alder reaction, this intermediate is trapped and the tricyclic compound **113** is obtained in high yield. As far as the carbon skeleton is concerned, this synthesis intermediate contains already almost all elements of the target. An important stereochemical modification is the epimerization in position 5 of compound **114**. This was accomplished via a keto-enol tautomerization in **113** under basic conditions. This is a thermal reaction. Further steps led to 6-*epi*-hamigeran A. A large variety of analogs and stereoisomers of this tricyclic compound have been prepared with the same synthesis strategy.¹⁴⁴

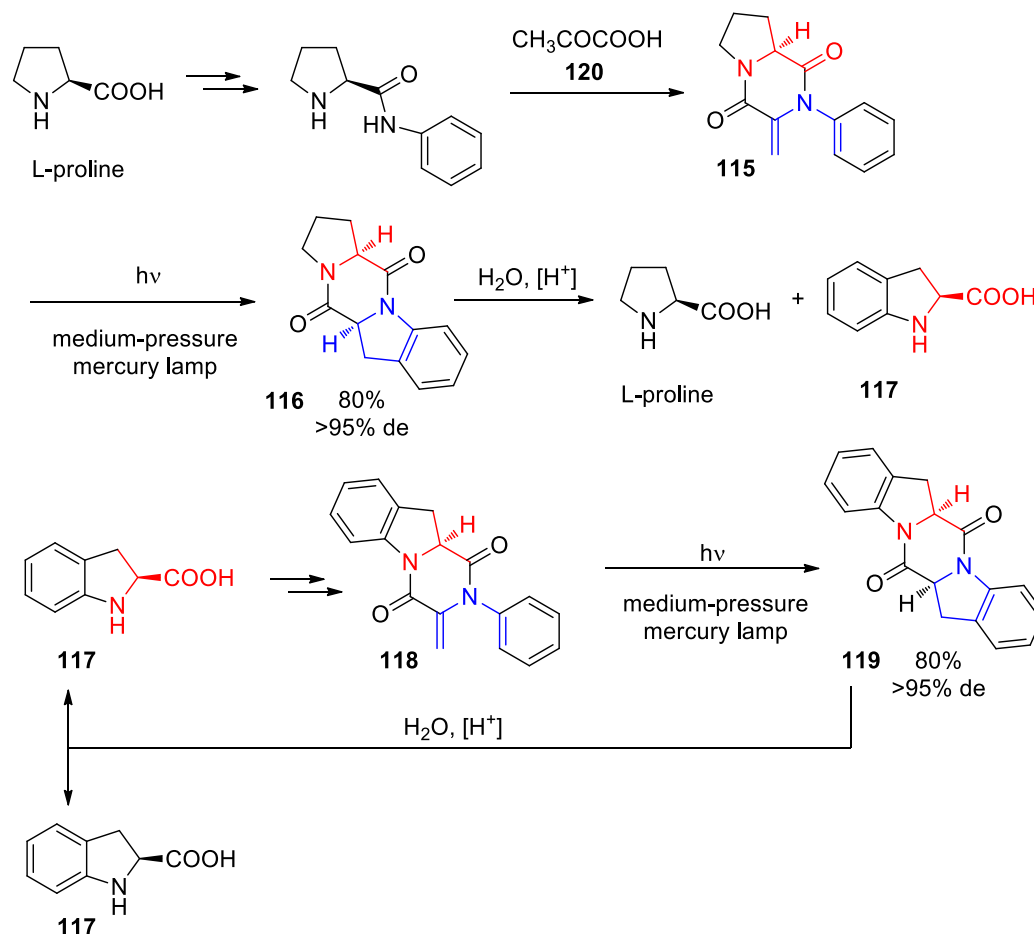


Scheme 23. Diastereoselective photochemical generation of a quinodimethane intermediate and its application to the synthesis of tricyclic compounds.

5 Electrocyclization

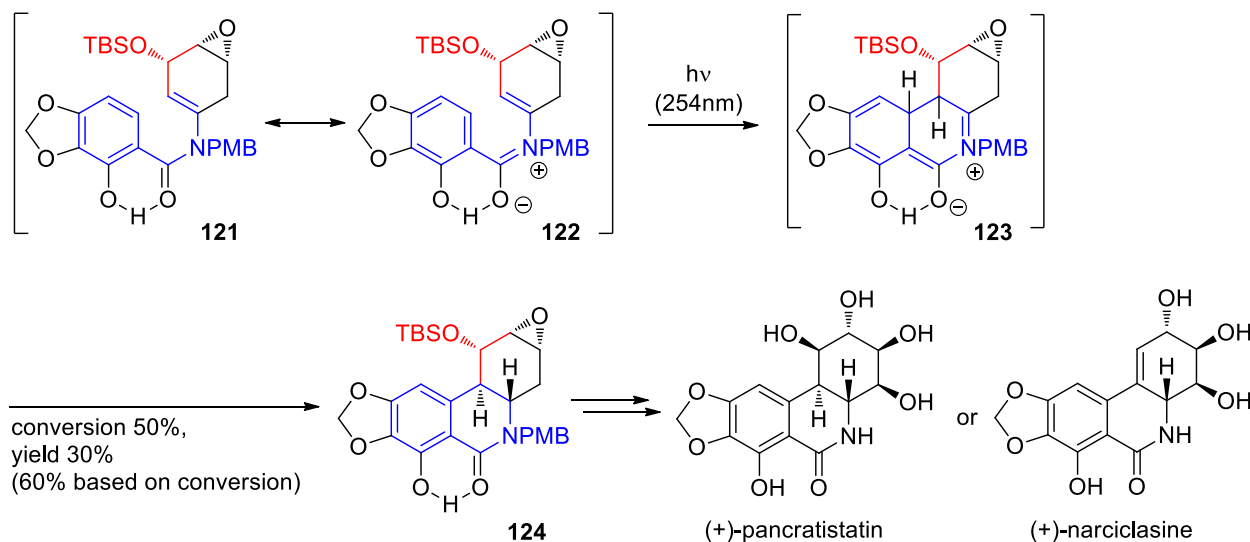
Photochemically induced electrocyclizations have frequently been applied to the synthesis of heterocyclic compounds.^{145,146,147,148} According to the Woodward-Hoffmann rules on orbital symmetry conservation in concerted reactions, symmetry-forbidden reactions at the ground state are allowed at the excited state.⁶⁶ Thus, photochemical conditions provide a significant extension of the application of electrocyclizations to organic synthesis. Furthermore, both ground state and excited state electrocyclizations are generally stereoselective.

A very elegant asymmetric synthesis has been developed for (*S*)-2-indoline carboxylic acid **117** at the industrial scale. Compound **115** which is easily prepared from L-proline, undergoes photochemical electrocyclization leading to the indoline derivative **116** in high yield and almost complete diastereoselectivity (Scheme 24).^{149,150} After hydrolysis (*S*)-indoline-2-carboxylic acid **117** is obtained as target. This compound is an important synthesis intermediate in medicinal chemistry. In this step L-proline is used as chiral auxiliary. In the further process, (*S*)-indoline-2-carboxylic acid **117** is used in this function. In the same way **117** is condensed with aniline and pyruvic acid **120** yielding the substrate **118** for the photochemical reaction. The transformation of **118** efficiently yields the tetracyclic product **119** in almost complete diastereoselectivity. Hydrolysis of the photoproduct yields two equivalents of (*S*)-indoline-2-carboxylic acid **117**. Repeating the process yields four equivalents of the initial compound. The process is repeated until the desired industrial scale is attained. In the further production, one half of the isolated **117** is reused as chiral auxiliary and the other half is removed from the production process. In the overall process, the amount of chirality is exponentially increased. Chiral amplification is observed in many processes.^{151,152,153,154,155,156} It is a useful tool in asymmetric synthesis.



Scheme 24. Diastereoselective synthesis of (*S*)-indoline-2-carboxylic acid using stepwise amplification of chirality.

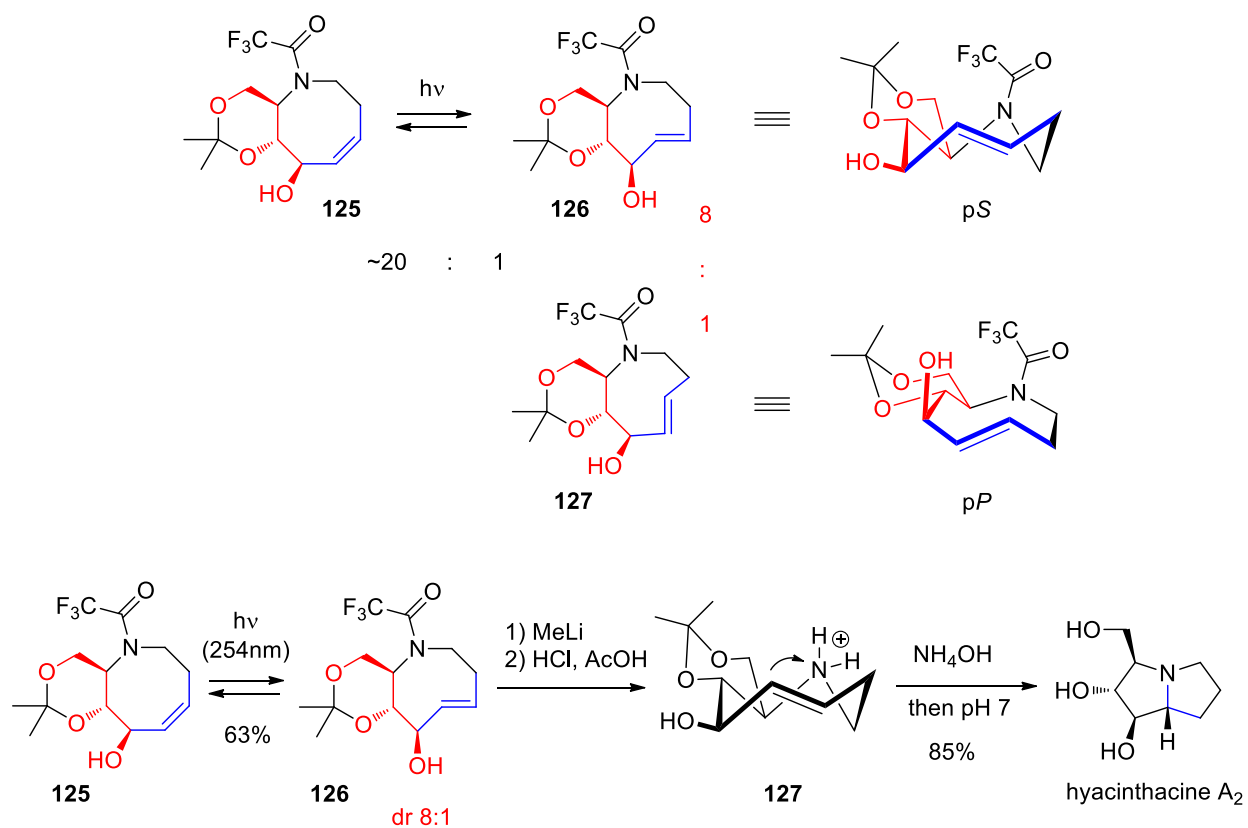
Generally, under photochemical conditions, the reactivity of chemical compounds is increased. Under these conditions electrocyclization can easily be carried out. Drastic reaction conditions are needed when such transformations are thermally performed. The aromatic compound **121** possesses an enamide function (Scheme 25).¹⁵⁷ With the mesomeric form **122** and with the participation of the phenyl ring, a 6π -system is formed. In such systems thermal disrotatory or photochemical conrotatory electrocyclizations are possible. However, in the case of compound **121/122** and only under photochemical conditions an electrocyclization could be performed yielding the intermediate **123**. This reaction step is favored by a hydrogen bond which stabilizes the negative charge on the carbonyl function. Tautomerization regenerating the aromatic character of the benzene group yields the final product **124**. It must further be pointed out that the reaction was smoothly carried out with highly functionalized substrate, for example, with a fragile epoxy function. This photochemical electrocyclic reaction was applied as key step to the total synthesis of (+)-narciclasine and (+)-pancratistatin. These compounds are interesting due to their anti-cancer activities, for example against murine P-5076 ovarian sarcoma and P-388 lymphocytic leukemia.



Scheme 25. Diastereoselective electrocyclic reaction involving an amide function and its application to the total synthesis of narciclasine alkaloids.

6 Photochemical rearrangements and isomerizations

cis/trans-Isomerization of alkenes is a typical photochemical reaction. As both compounds absorb light the isomers are in photochemical equilibrium.^{158,159} Cyclic alkenes may also undergo *cis* to *trans* isomerization. In the case of larger rings such as cyclooctene, a certain stability of the *trans* isomer is observed.^{160,161} While *cis* cycloalkenes are inherently achiral, the corresponding *trans* isomers are chiral and possess C_2 -symmetry.¹⁶² Compound **125** possesses a (*Z*)-1,2,3,4,7,8-hexahydroazocine core structure, nitrogen analog of cyclooctene. Upon irradiation, a *cis/trans* isomerization takes place and the diastereoisomers **126** and **127** are formed (Scheme 26).¹⁶³ A new stereogenic element is created by this isomerization. Under the reported reaction conditions, the photostationary equilibrium is very unfavorable with regard to the production of the *trans* isomer. During the irradiation the reaction solution was continuously pumped through a column which was packed with silver nitrate impregnated silica and recycled to the photochemical reaction vessel (Figure 3).¹⁶⁴ The *trans* isomers **126** and **127** were retained on the column by complexation with $AgNO_3$. After the reaction, the products were decomplexed with an ammonia solution and isolated in a ratio of 8:1. The major isomer **126** was transformed into the corresponding ammonium compound **127** which underwent a transannular cyclization to hyacinthacine A_2 . Such compounds have glucosidase inhibition and anti-viral properties. The herein described flow process is a particular case. Continuous flow processes have become an important tool in organic photochemistry.^{165,166,167,168,169,170} Most frequently and in combination with micro reactor technology, it is used to optimize light penetration of the reaction mixture in order to circumvent problems in connection with the Lambert-Beer law which often requires low concentrations. In other cases, when the product itself is photo-reactive, the reaction mixture must rapidly leave the irradiation field after partial or complete conversion. In the present case, the flow technology is used to shift a photo-stationary equilibrium towards the product side.



Scheme 26. Diastereoselective *trans* isomerization of a 1,2,3,4,7,8-hexahydroazocine core structure.

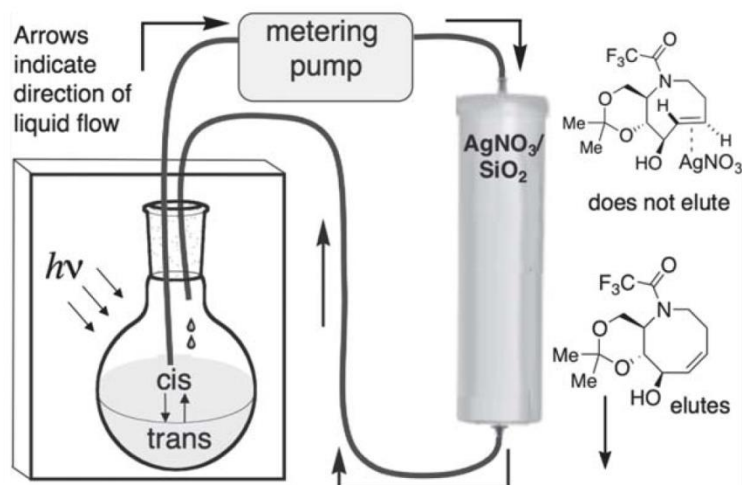
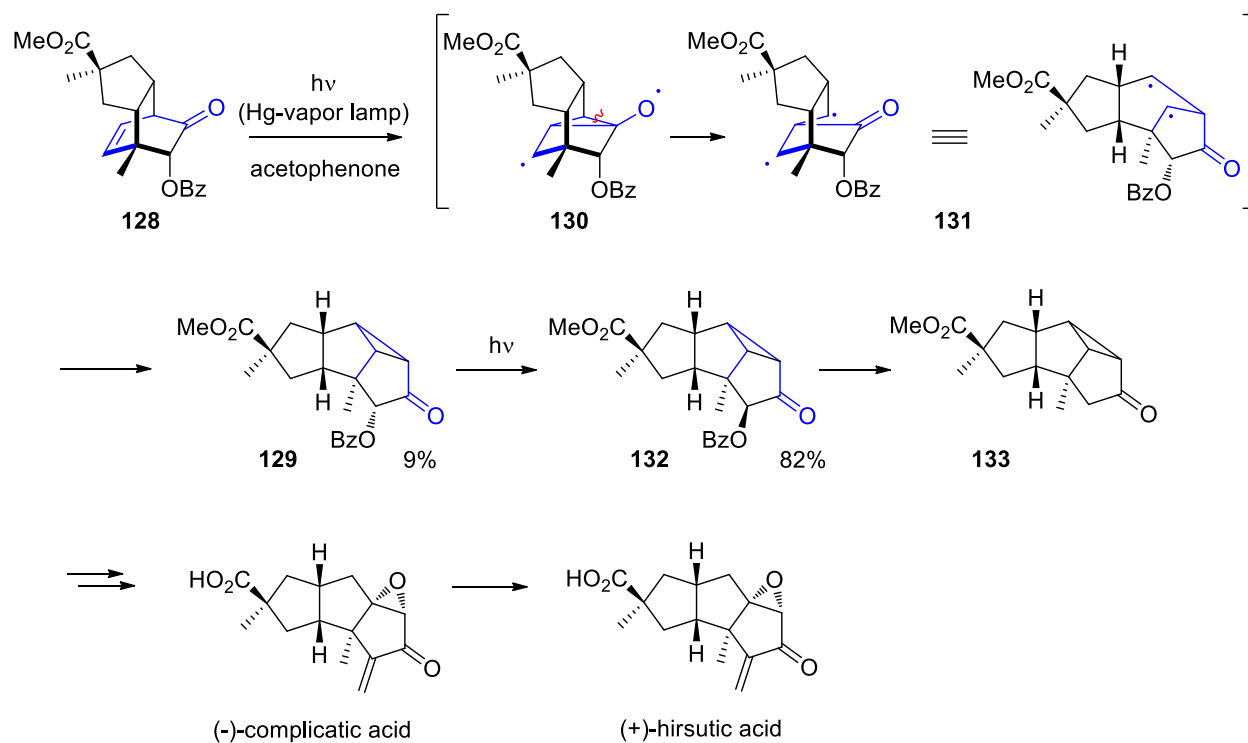


Figure 3. Flow system for the photochemical cis/trans isomerization (Scheme 26).¹⁶⁴

Photochemical rearrangements often occur under complete stereocontrol. Typical examples are found for di- π -methane rearrangements. The oxa-analog version (oxa-di- π -methane) of this reaction has been

frequently applied to organic synthesis.¹⁷¹ Thus the enantiomerically pure compound **128** was transformed into compound **129** (Scheme 27).¹⁷² The reaction is sensitized by acetophenone. After excitation, a 1,4-diradical intermediate **130** is formed which contains a cyclopropane unit. The latter opens in the way that the carbonyl function is regenerated and a 1,3-radical intermediate is formed (**131**). Radical combination yields compound **129**. This mechanism corresponds to that one of the di- π -methane rearrangement.¹⁷³ In several reports on mechanistic investigations, the direct (concerted) formation of **129** after excitation to the triplet state is suggested.^{174,175} In the present case, the oxa-di- π -methane rearrangement is followed by an epimerization (**132**). Most probably, a reversible Norrish Type I cleavage is involved in this step. In the context of the total synthesis, this epimerization doesn't matter. In next synthesis step the corresponding chiral center disappears as the BzO group is removed (**133**).



Scheme 27. Stereoselective oxa-di- π -methane rearrangement and its application to the asymmetric synthesis of (-)-complicatic and (+)-hirsutic acid.

7 Chiral induction in a constrained environment

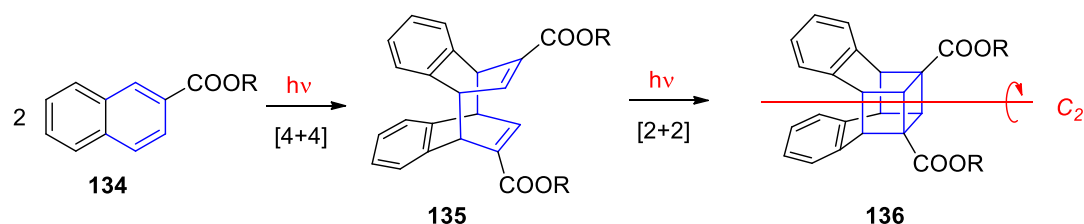
There were some debate on whether chirality is a binary or continuous property of an object, in particular a molecule.¹⁷⁶ Binary means: A molecule is chiral or not. A continuous property means that a molecule may be more chiral than another one. Formally, one of these descriptions exclude the other. Based on the definition of chirality, for example for geometrical objects, one would prefer the binary description. However, chirality of a molecular structure must be detected, for example by the physicochemical methods which provide continuous values. In this context, one would prefer the continuous property description.¹⁷⁷ These considerations are also relevant when chiral induction in the context of asymmetric synthesis is discussed. Although the molecules are described as chiral or achiral according to the definition of chirality and in the context of chirality a binary property, the transfer of the

chiral information during the corresponding chemical reaction is more or less efficient or the reaction is more or less stereoselective. Several models have been developed to parametrize or quantify the efficiency of chirality transfer. A typical example is the Ugi-Ruch model.¹⁷⁸ The application of this model to the diastereoselective reactions or properties of chiral compounds has been shown.^{179,180}

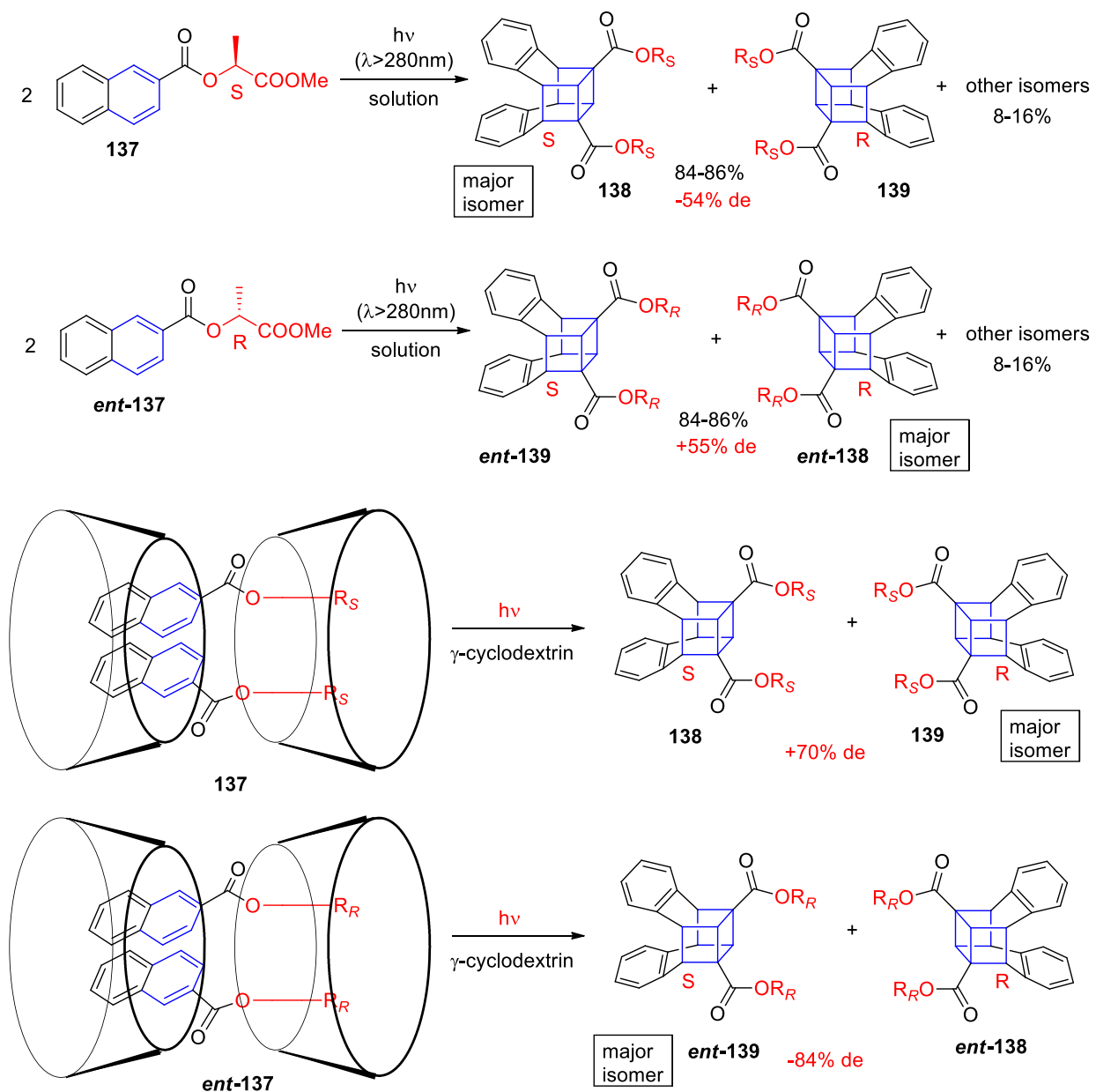
In the following, reactions will be discussed in which the chiral induction is significantly influenced by a constrained environment. 2-Naphthalenecarboxylic esters **134** undergo photodimerization, first via intermolecular [4+4] cycloaddition (**135**) then by intramolecular [2+2] photocycloaddition (**136**) (Scheme 28).¹⁸¹ The resulting major products possess a C_2 -symmetry. The reaction was carried out with chiral naphthoates (**137**, *ent*-**137**) carrying either *R* or *S*-lactate as chiral auxiliary (Scheme 29).¹⁸² In the of cyclohexane solutions **138**, **139**, *ent*-**138** and *ent*-**139** possessing C_2 -symmetry were the major regioisomers. As expected, the same diastereomeric excess was observed in both cases. The values have different signs in order to indicate the direction of the chiral induction. The reaction has then be performed with inclusion complexes with γ -cyclodextrins as host structure. Under these conditions, the diastereoselectivity is significantly increased. Obviously, the confinement improves the diastereoselectivity. However, the direction of induction is reversed. The minor isomer in solution is now the major one and vice versa. When the *R*-lactic ester *ent*-**137** was used in the inclusion complexes, the diastereoselectivity was higher than in the case of the *S*-enantiomers **137**. In the first case, *ent*-**139** is the major stereoisomer while in the second case **139** is the major isomer. This difference is explained by the fact that γ -cyclodextrin is chiral and also affect the diastereoselectivity. In this system of double induction⁸⁷, the major contribution of chiral induction results from the chiral auxiliary. The chiral induction by the host structure is rather weak. From these de-values the following absolute $\Delta\Delta G^\ddagger$ values are calculated for different contributions to chiral induction:

| | |
|--|--------------------------|
| $\Delta\Delta G^\ddagger$ (chiral auxiliary, in solution): | 3.0 kJ mol ⁻¹ |
| $\Delta\Delta G^\ddagger$ (chiral auxiliary, confinement): | 5.1 kJ mol ⁻¹ |
| $\Delta\Delta G^\ddagger$ (γ -cyclodextrin): | 0.9 kJ mol ⁻¹ |

It should be pointed out that the contribution of the two γ -cyclodextrins is weak. Cyclodextrins are very important bricks in supramolecular chemistry. Even in connection to chiral induction, they are often represented as a conical frusta or a truncated cone with an infinite number of mirror plains although the original cyclodextrins are chiral and have C_n -symmetry.^{183,184} This is not chosen arbitrarily. Chiral induction carried out only with not further functionalized cyclodextrins is often weak.



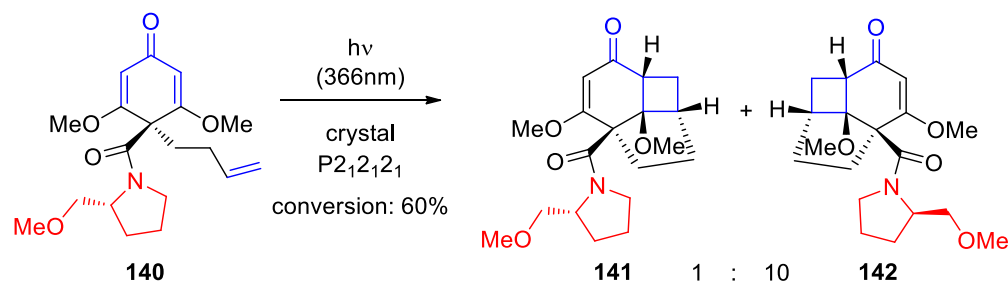
Scheme 28. Photodimerization of 2-Naphthoates via [4+4] and [2+2] cycloadditions.



Scheme 29. Diastereoselective photochemical dimerization of chiral naphthoates in cyclohexane solution and with corresponding inclusion complexes. The reactions depicted here were carried out at 20°C.

Many photochemical reactions have been carried out in the crystalline phase, especially in connection with asymmetric synthesis.^{185,186,187,188,189,190} In the solid state, conformations are frozen and highly stereoselective reactions are possible when the reaction centers are adequately oriented. Especially in the case of a crystal chiral environment, asymmetric synthesis is possible. Basic principles of crystallography permits the generation of such an environment.¹⁹¹ It is of particular interest, that enantiopure compounds can only crystallize in particular space groups (Sohncke groups) where the environment or confinement is chiral.^{192,193} In the case of compound **140**, the presence of the (*R*)-prolinol group as chiral auxiliary requires that it crystallizes in a Sohncke group. In the present case, two crystal modifications are observed, both having the space group $P2_12_12_1$. When crystals of the

α -modification of this compound are irradiated, the formation of the diastereomeric cyclobutane **142** via [2+2] photocycloaddition is favored (Scheme 30).¹⁹⁴ At higher conversions, the diastereoselectivity decreased. When the reaction was carried out in solution compounds **141** and **142** were obtained in a 1:1.5 ratio. In the case of the β -modification, the formation diastereoisomer **141** was favored. The same strategy for efficient chiral induction was also applied with with photochemical decarbonylation reaction.¹⁹⁵ Similar effects of increase of chiral induction by confinement is observed with zeolites as host structure. Zeolites are inorganic materials with large cavities.^{196,197} In most cases they are achiral. The chiral induction of auxiliaries is often significantly increased when the reactions occur in such cavities.¹⁹⁸

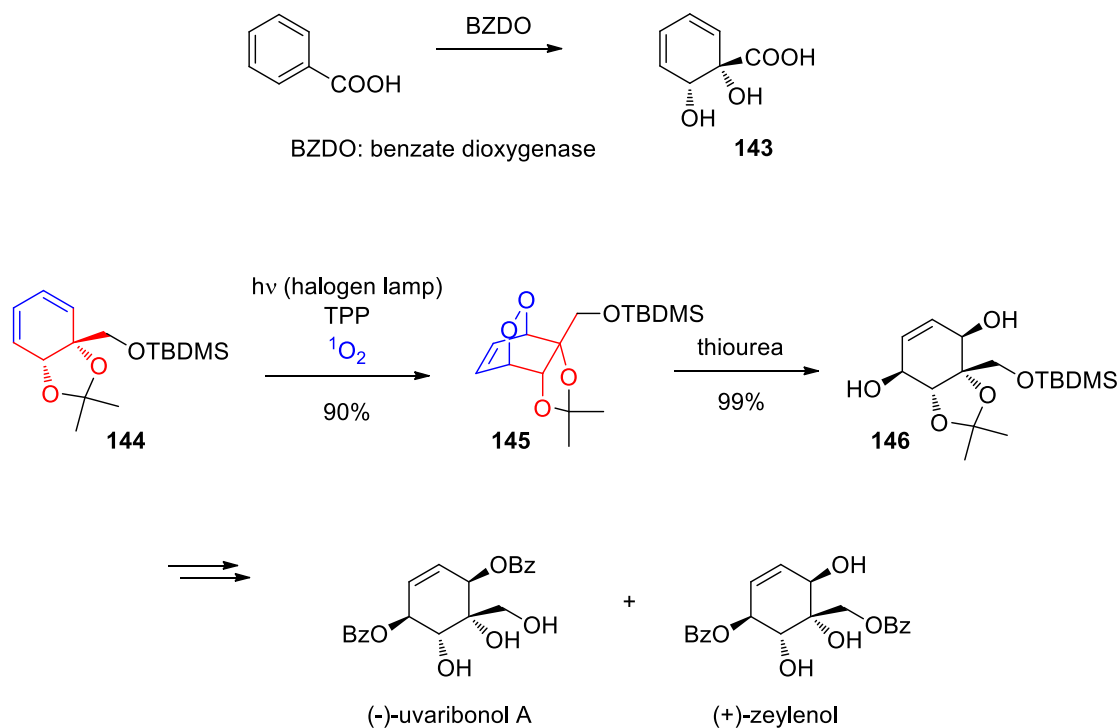


Scheme 30. Diastereoselective [2+2] photocycloaddition carried out in crystals.

8 Photooxygenation

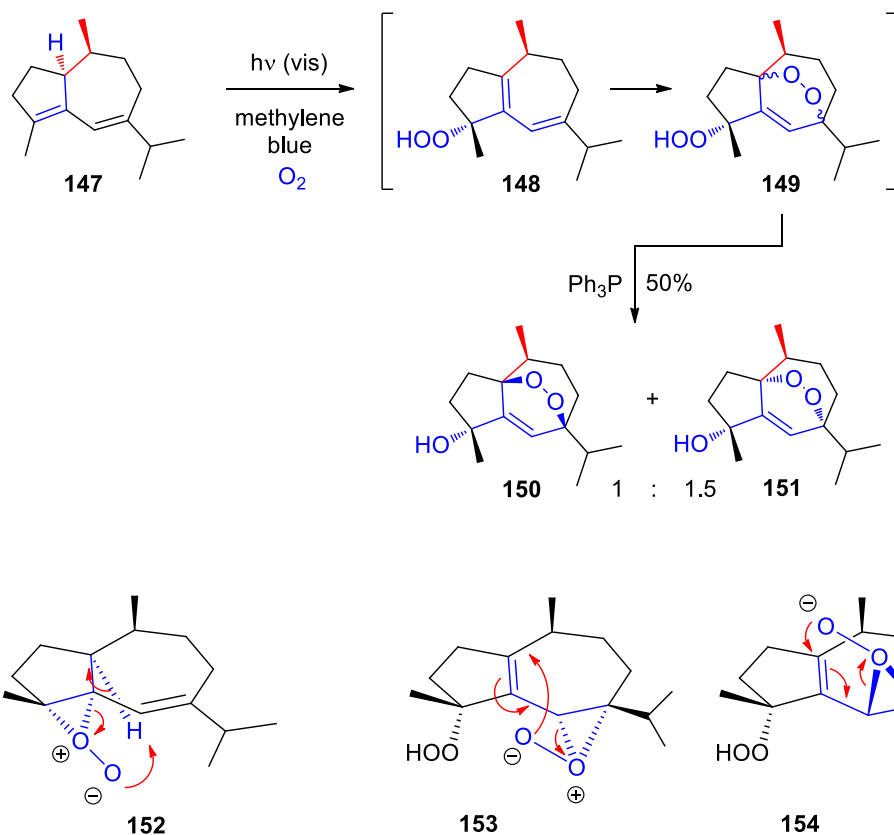
In contrast to ground state triplet oxygen, the reactivity of the singlet excited species undergoes preferentially polar reactions aside electron transfer.¹⁹⁹ Photosensitization is certainly the most convenient production process of singlet oxygen. The photooxygenation with singlet oxygen thus has become a very attractive oxidation method for organic synthesis.^{200,201} It is also interesting in the context of sustainable chemistry.¹⁰ Reactions of singlet oxygen with alkenes, especially ene reactions^{202,203} and the formation of endo peroxides^{204,205}, are most frequently applied to organic synthesis. The reactions are often highly regio and stereoselective. Also detailed mechanistic investigations of the stereoselectivity of such reactions have been reported.^{16,206}

Aromatic compounds are easily oxidized to dihydroxycyclohexadienes²⁰⁷ which react with singlet oxygen in a formal [4+2] cycloaddition. Using the enzyme benzoate dioxygenase (BZDO), the product **143** is obtained in high enantiopurity (Scheme 31). When a corresponding derivative (**144**) was transformed with photochemically generated singlet oxygen, only one stereoisomer of the endoperoxid **145** was obtained.²⁰⁸ Tetraphenylporphyrin (TPP) was used as sensitizer. The treatment with thiourea under particular mild conditions yields almost quantitatively the diol **146**. Further transformations lead to (-)-uvaribonol and (+)-zeylenol. The combination of photooxygenation with the consecutive reduction of the endoperoxides thiourea is an efficient method to prepare polyhydroxycyclohexenes. These compounds belong to a family of natural products. Such derivatives possess a variety of interesting biological activities such as selective cytotoxicity or antifeedant activity.



Scheme 31. Diastereoselective formation of endoperoxids via photooxygenation.

An ene reaction is observed with the guajadiene derivative **147** leading to the intermediate **148** (Scheme 32).²⁰⁹ Only one diastereoisomer is formed. In compound **148**, the diene moiety is *syn* oriented so that a second photooxygenation takes place yielding the endoperoxides **149**. The reaction mixture was treated under reductive conditions with Ph_3P yielding the final products **150** and **151**. The high diastereoselectivity in the ene photooxygenation is explained by the intermediate **152**. An allylic hydrogen atom at chiral center is then transferred leading to **148**. In the formation of the endoperoxides **149**, the diastereo differentiation for the formation of a corresponding intermediates **153** and **154** is less efficient.



Scheme 32. Photooxygenation of a guajadiene derivative, consecutive formation of a hydroperoxide and an endoperoxide.

9 Conclusion

Photochemical reactions play an important role in organic synthesis. The electronic excitation of a chemical compound modifies its chemical properties. Therefore, such transformations makes compounds or compound families available which cannot or difficultly be synthesized by conventional methods. Starting from simple substrates, in only one step a high degree of molecular complexity and diversity is generated. Photochemical excitation also have in impact on the stereoselectivity of organic reactions. The profound investigation of diastereoselectivity of such reactions is crucial for application of such reactions to asymmetric synthesis. Such studies also provide insight in fundamental aspects of chemical reactivity in general. Based on such knowledge, strategies can be developed in order to optimize reactions with regard to their stereoselectivity. For example, the stereoselectivity of chemical reactions can be increased when they are carried out in a confined environment, such as inclusion complexes or crystals. In order to induce diastereoselectivity, chiral auxiliaries are used which are most frequently linked by a covalent bond to the reacting moiety. Chiral induction also occurs from chiral elements already present in the substrate which are incorporated in the product of the photochemical reaction or in the target of a multi sept synthesis. Such transformations play an important role in connection with asymmetric synthesis. Most frequently, stereoselective photochemical cycloadditions from carbonyl compounds or aromatic compounds and electrocyclic are applied to organic synthesis especially for heterocyclic compounds. In this way complex, unusual compounds are obtained. Recently,

electron and hydrogen atom transfer reactions receive tremendous attention for application to organic synthesis. In this context, also the diastereoselectivity is systematically investigated. Photochemical reaction conditions are successfully used for oxidation. The most prominent example in this domain is the photooxygenation with singlet oxygen.

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