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Heterocyclic Compounds in Enantioselective Photochemical Reactions

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1.1 Introduction

The present chapter deals with different key topics. Heterocyclic compounds play a central role in many domains of chemistry such as the search of new biologically active compounds in pharmaceutical and agricultural chemistry [1]. Also, many new materials such as semiconducting compounds contain heterocyclic moieties [2]. In these domains, a large structural diversity and molecular complexity is highly needed. Here, traditional methods of organic synthesis find their limits. Photochemical reactions extend such limits. As electronic excitation completely changes the chemical reactivity of compounds or whole family of compounds [3], products, which cannot be synthesized by more conventional methods become accessible and are of high interest for application in the field of bioactive compounds [4, 5]. Furthermore, the outcome of known reactions, especially catalytic reactions, can be improved when they are carried out under photochemical conditions. Based on the enormous quantity of recent and past results in the field of photochemical reactions, it makes sense to subdivide chemical reactions into two classes: reactions that occur in the electronic ground state and reactions in which electronic excitation is involved. From the economic and ecological point of view, photochemical reactions are particularly interesting, since many of them can be carried out without an additional chemical reagent. The photon is considered as a traceless reagent [6, 7]. For these reasons, these reactions are now highly appreciated in chemical and pharmaceutical industry [8–10].

Stereoselectivity also plays a central role in organic synthesis. Biological activity and material properties strongly depend on the stereochemistry of chemical compounds. Sooner or later, almost all synthesis methods will face this problem. In the past, photochemical reactions have been considered as being inherently stereo-unselective. It was thought that the high energy uptake by light absorption induces uncontrolled relaxation processes that lead to unselective reactions with large amounts of degradation either of the substrates or the photoproducts [11].

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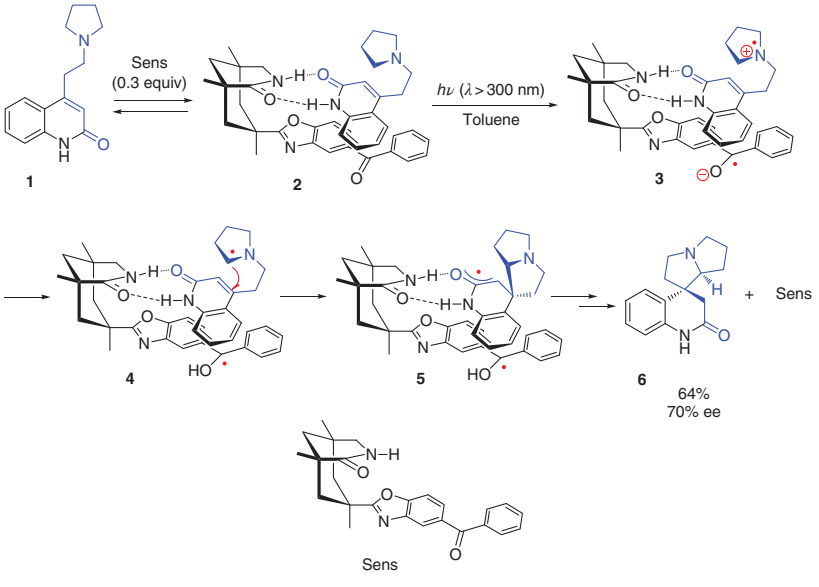
In this regard, it must however be pointed out that stereoselective and stereospecific photochemical reactions have been known from the very beginning of this research area [12, 13]. The controlled dissipation of the high electronic excitation energy in photochemical reactions is the reason for the high stereoselectivity in such reactions [11]. In particular, photochemical reactions can be conducted enantioselectively in chiral supramolecular structures [14, 15]. Enantiopure compounds are obtained in different ways: they can be prepared directly from other chiral precursors such as natural products ("chiral pool") or by optical resolution using different types of chromatography or crystallization techniques. Asymmetric syntheses using chiral auxiliaries, which are removed after the stereoselective reaction, also provide enantiopure compounds. Asymmetric catalysis and enzymatic catalysis directly yield enantioenriched compounds. A chiral enantiopure environment in a supramolecular structure or in a crystal may be the inductor of chirality in asymmetric reactions. In the present chapter, methods will be discussed leading directly to enantiopure heterocyclic compounds via photochemical reactions.

1.2 Asymmetric Catalysis with Chiral Templates

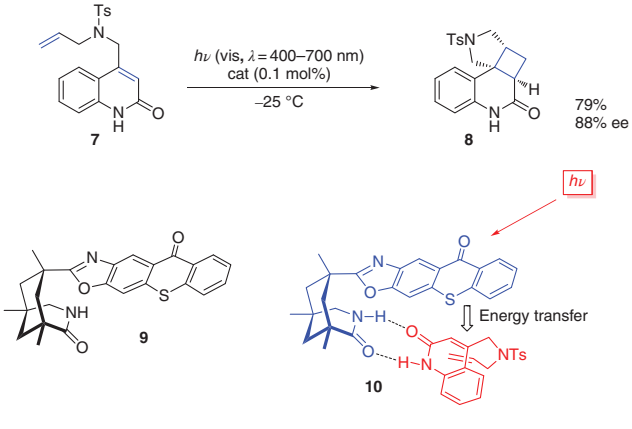
Photochemical substrates may be complexed with chiral structures that induce chirality [16]. A typical example is described in Scheme 1.1 [17]. The quinolone derivative **1** carrying a pyrrolidine moiety undergoes an intramolecular cyclization leading to the spirocyclic indolizidine compound **6**. The substrate is complexed with the enantiopure Kemp acid derivative (**2**) via hydrogen bonds between two lactam



Scheme 1.1 Enantioselective synthesis of a spirocyclic indolizidine compound induced by a photochemical electron transfer.

moieties. In this arrangement, the pyrrolidine approaches the reaction center mainly by one diastereotopic half-space. In this complex, the shielding group acts also as an aromatic ketone sensitizer (sens). After photochemical excitation of the latter, electron transfer from the tertiary amine moiety to the ketone leads first to a radical ion pair **3** and after proton transfer to intermediate **4** [18]. The nucleophilic α-aminoalkyl radical attacks with 70% of stereoselectivity the electrophilic double bond of the quinolone moiety. Thus, an electrophilic oxoallyl radical is generated affording the diradical intermediate **5**. The final product **6** results from a hydrogen transfer from the ketyl radical to the oxoallyl radical. It must be pointed out that in the present case this step is favored because it is an intramolecular process. In these radical steps, polar effects play an important role [19–21]. In the corresponding intermolecular stereoselective reactions, these effects contribute essentially to the efficiency of these processes [18]. The intermolecular addition of tertiary amines to indolone derivatives with an exocyclic electron-deficient olefinic double bond has been carried out with similar Kemp acid derivatives [22]. In this case, however, ruthenium or iridium complexes have been used as external photoredox catalysts that were excited by visible light absorption.

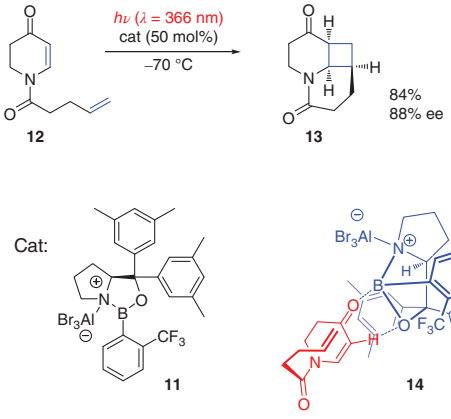
Using a similar chiral sensitizer, an intramolecular [2+2] photocycloaddition has been carried out with high enantioselectivity (Scheme 1.2) [23]. The quinolone derivative **7** is transformed, under visible light irradiation, into a complex polycyclic compound **8** containing a pyrrolidine moiety. It must be pointed out that the same [2+2] photocycloaddition is also induced by UV irradiation via direct light absorption but no chiral induction takes place. It is therefore necessary to choose a sensitizer that absorbs in the visible domain of the light spectrum to ensure enantioselectivity. The thioxanthone derivative **9** absorbs in the visible light region and transfer its triplet energy to the complexed substrate (**10**). Again, this complexation occurs via hydrogen bonds between the two lactams of the substrate and the Kemp acid moiety of the sensitizer. In this structure the olefinic double bond in the side chain approaches the reactive center of the quinolone almost only by one



Scheme 1.2 Construction of a pyrrolidine moiety using an enantioselective [2+2] photocycloaddition. Source: Alonso and Bach [23] / John Wiley & Sons.

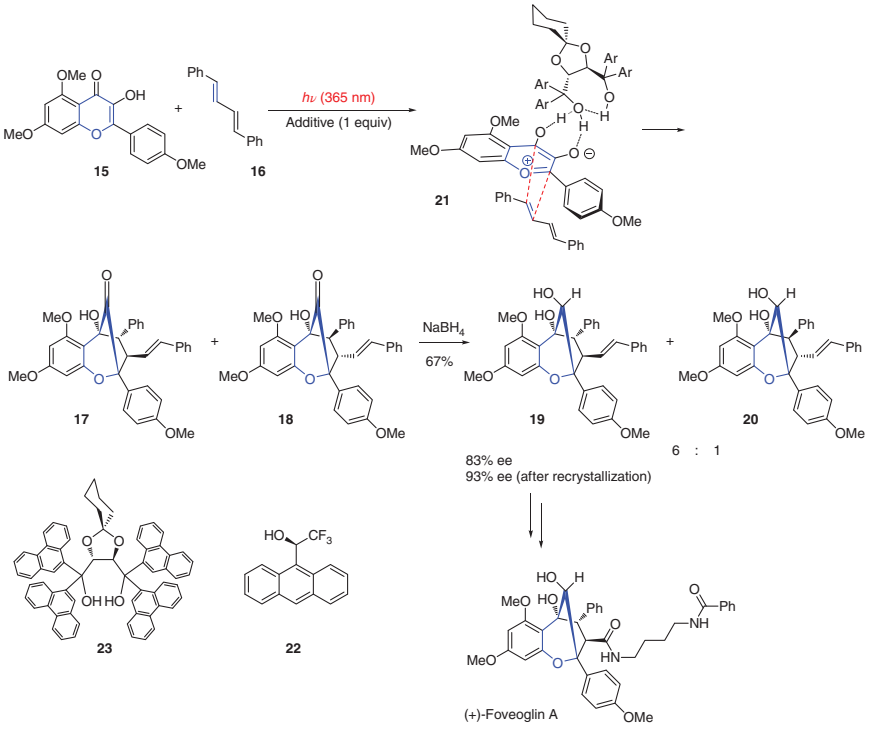
diastereotopic half-space. Similar asymmetric reactions have been performed with 3-alkylquinolones carrying a 4-*O* alkene side chain. In this case, tetrahydrofuran moieties are formed [24].

The substrate can also be complexed to a metal or a strong coordinating atom. In such a case, chirality is induced by a chiral ligand sphere [25]. In this context, chiral Lewis acid **11** was used to catalyze the asymmetric intramolecular [2+2] photocycloaddition of the dihydropyridinone derivative **12** (Scheme 1.3) [26]. In this reaction, a δ-valerolactam moiety (**13**) is formed. By complexation with a Lewis acid, the absorption maximum of compound **12** is shifted from 290 to 350 nm. Using fluorescent lamps with an emission λ_{max} = 366 nm, complex **14** was excited almost exclusively since the noncomplexed substrate **12** does not absorb light in this spectral range. Thus, the formation of racemic product as background reaction is suppressed. In the complex **14**, the approach of the olefin to the reaction center again occurs by one diastereotopic half-space.



Scheme 1.3 Enantioselective Lewis acid catalysis of an intramolecular [2+2] photocycloaddition reaction. Source: Brimioulle and Bach [26] / American Association for the Advancement of Science.

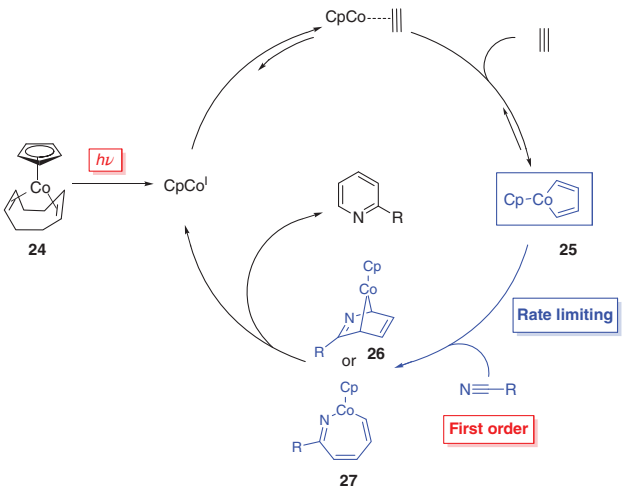
α,α,α′,α′-Tetraaryl-2,2-disubstituted 1,3-dioxolane-4,5-dimethanols (TADDOLs, e.g. **23**) are capable of complexing numerous substrates via hydrogen bonds [27]. When a photochemical substrate is complexed with such compounds, chirality can be induced. Under these conditions, when the flavone derivative **15** was irradiated with the diphenyl butadiene **16**, a [2+3] cycloaddition took place, leading to compounds **17** and **18** (Scheme 1.4) [28]. After reduction with $NaBH_4$, compounds **19** and **20** were isolated in good yields. Furthermore, the major diastereoisomer **19** was obtained in high enantioselectivity, and recrystallization led to almost enantiopure samples. The high enantioselectivity of the photochemical reaction was explained by the structure of complex **21**, which strongly favors the attack of the olefin by only one diastereotopic half-space. Interestingly, when the sterically much less encumbered chiral alcohol **22** was added instead of the TADDOL compound



Scheme 1.4 Asymmetric synthesis of (–)-foveoglin A using ESIPT-promoted [2+3] cycloaddition with a flavone derivative. Source: Wang et al. [28] / John Wiley & Sons.

23, an efficient chiral induction was still observed. The high enantioselectivity observed with hydrogen bond complexes can also be explained by the fact that excited state intramolecular proton transfer (ESIPT) plays a key role in the reaction mechanism [29]. In fact, it was shown that the cycloaddition occurred at the triplet state of **15** and that most probably single electron transfer is involved. Compound **19** was transformed into (+)-foveoglin A, which is the enantiomer of a natural product. This compound family plays an important role in medicinal chemistry as they possess anticancer and antiviral activities.

The cyclization reaction of two alkynes and one nitrile function is a convenient method for the preparation of pyridine compounds [30]. It can be carried out under particular mild conditions when simple and inexpensive cobalt catalysts such as **24** are used (Scheme 1.5) [31]. Under irradiation with visible light, the formation of the cobaltacyclopentadiene intermediate **25** is accelerated, and the addition of the nitrile leading to the intermediate **26** or **27** becomes the rate-determining step. The consumption of the nitrile substrate becomes the first-order reaction step. Under these particularly mild conditions, a variety of pyridine derivatives have been synthesized possessing fragile substituents (Figure 1.1) [32]. Asymmetric catalysis was also successfully performed. The cyclopentadienyl ligand in the



Scheme 1.5 Visible light-supported cobalt-catalyzed [2+2+2] cycloaddition applied to the synthesis of pyridines.

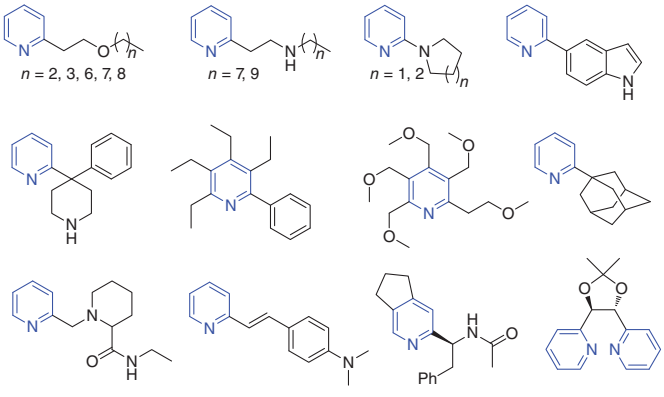
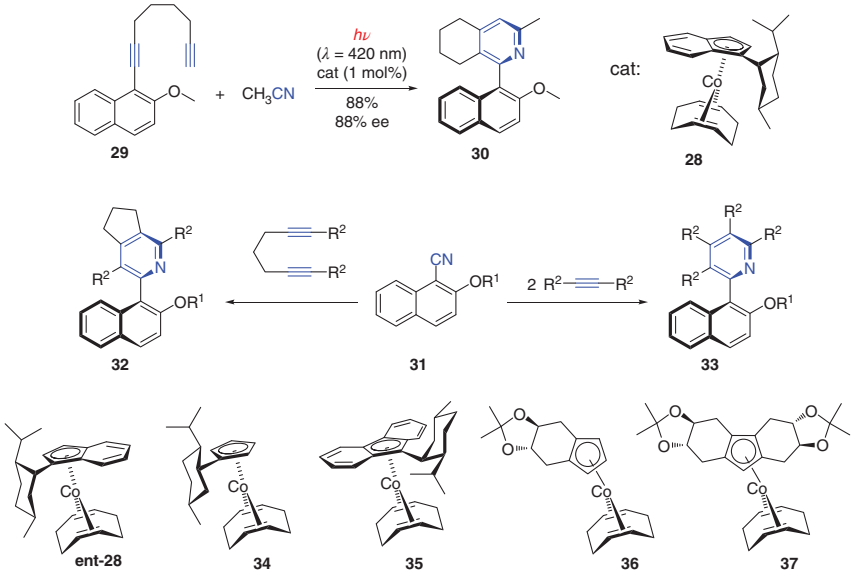


Figure 1.1 Pyridines that have been synthesized under mild conditions using photochemically promoted cobalt-catalyzed [2+2+2] cycloaddition.

cobalt catalyst was replaced by chiral analogs, best results being obtained with catalyst **28** (Scheme 1.6) [33]. With this reaction axial chirality can be efficiently induced as shown by the transformation of compound **29** into naphthyl pyridine **30**. Similar reactions have been carried out starting from 2-alkoxy-1-naphthonitriles **31** using different chiral cobalt complexes as catalysts. Either diines were used, leading to tetracyclic compounds **32**, or 2 equiv of a monoalkyne were employed, yielding the corresponding tricyclic products **33**. In this part of the study, the chiral catalysts **ent-28**, **34**, **35**, **36**, and **37** have also been tested. The study of this type of chirality, atropisomerism, has recently gained particular attention in photochemistry [34].

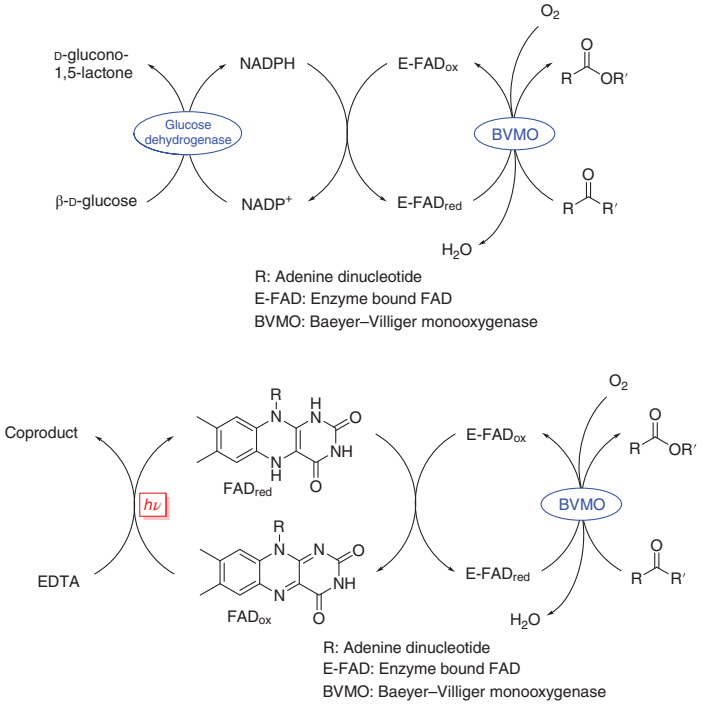


Scheme 1.6 Visible light-supported asymmetric [2+2+2] cycloaddition using chiral cobalt catalysts.

1.3 Asymmetric Photo-Enzyme Catalysis

Enzyme catalysis is a general method to produce enantiomerically enriched or pure compounds. Many such transformations need multi-enzyme systems that complicate the application to organic synthesis. In some cases, however, the replacement of one or more enzyme activities by a chemical transformation facilitates the transformations. As they tolerate a large variety of reaction conditions, photochemical reactions were efficiently applied in this context [35].

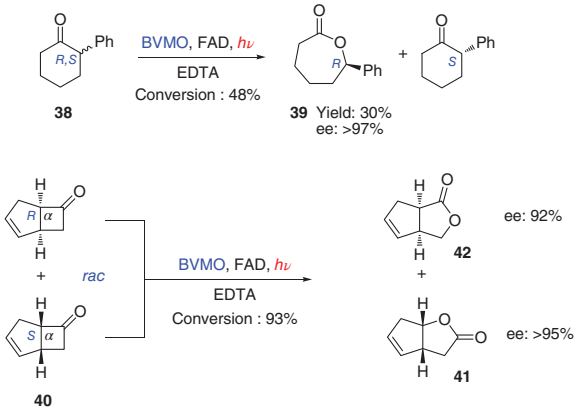
The Baeyer–Villiger monooxygenase (BVMO) asymmetrically catalyzes the transformation of ketones into esters or lactones in the case of cyclic ketones (Scheme 1.7) [36]. This enzyme contains a flavin adenine dinucleotide (E-FAD_{red}) unit, which reduces molecular oxygen into hydrogen peroxide capable of oxidizing the ketone substrate. The oxidized flavin species (E-FAD_{ox}) is reduced by nicotinamide adenine dinucleotide phosphate(H) (NADPH). The resulting nicotinamide adenine dinucleotide phosphate ($NADP^+$) is reduced via a glucose dehydrogenase-catalyzed reaction. This second enzyme activity can be replaced by adding flavin (FAD) to the reaction mixture. The reduced form of the nonbound FAD_{red} is capable of reducing the enzyme-bound E-FAD_{ox}. At the excited state, FAD_{ox} (generated by irradiation with visible light) is easily reduced via electron transfer from a sacrificial electron donor such as ethylenediaminetetraacetic acid (EDTA).



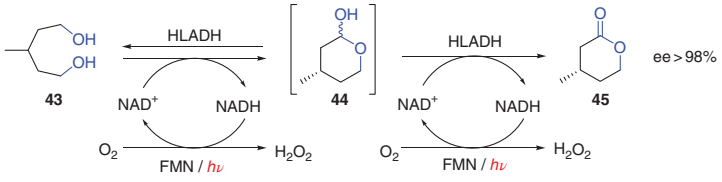
Scheme 1.7 Replacement of the glucose dehydrogenase by a simple photoredox catalytic system based on nonbound FAD.

Under these conditions the asymmetric Baeyer–Villiger reaction was carried out with the racemic 2-phenylcyclohexanone **38** (Scheme 1.8) [37]. Only the *R*-enantiomer was oxidized, and the phenylcaprolactone **39** was obtained in high enantioselectivity. The racemic cyclobutanone derivative **40** has been transformed under the same conditions. Interestingly both enantiomers were oxidized but different outcomes were observed. The α-*S*-enantiomer yields the bicyclic butyrolactone **41**, whereas the α-*R*-enantiomer is transformed into regioisomer **42**. Both compounds are formed in high enantioselectivity. Compound **41** is the expected regioisomer of a Baeyer–Villiger reaction. Depending on the stereochemistry of the starting ketone, the enzyme activity is therefore capable of directing the regioselectivity of the reaction [38]. It should be pointed out that under such reaction conditions, hydrogen peroxide is generated in low stationary concentration that reduces the enzyme degradation [39].

Combined photo- and enzyme catalysis was also carried out with alcohol dehydrogenases (ADH) [40]. These enzymes use NAD(P)H/NAD(P)$^+$ as cofactor [41]. In order to optimize the enzyme activity, this cofactor system must be regenerated [42]. One of the hydroxyl functionalities of the achiral diol **43** is dehydrogenated to an aldehyde by horse liver alcohol dehydrogenase (HLADH) with molecular oxygen (Scheme 1.9) [43]. Cyclization leads to the lactol **44**, a reversible step. In a second dehydrogenation also catalyzed by HLADH, the lactol is oxidized



Scheme 1.8 Enzyme-catalyzed enantioselective Baeyer–Villiger reaction applied to the synthesis of lactones. Source: Hollmann et al. [37] / John Wiley & Sons.



Scheme 1.9 Enantiospecific oxidation of the achiral diol **43** to 4-methyl-δ-valerolactone **45** using a photobiocatalytic process. Source: Rauch et al. [43] / Royal Society of Chemistry.

to the 4-methyl-δ-valerolactone **45**, obtained with complete enantioselectivity. In these steps, hydrogen is transferred to NAD^+ and NADH is formed. NAD^+ is regenerated by hydrogen transfer to oxygen leading to hydrogen peroxide. This step is photocatalyzed by flavin mononucleotide (FMN). The irradiation was carried out with blue LED ($\lambda_{max} = 465$ nm). Under similar reaction conditions and using a flavin-dependent "ene"-reductase, a variety of lactams have been obtained in high enantioselectivity [44].

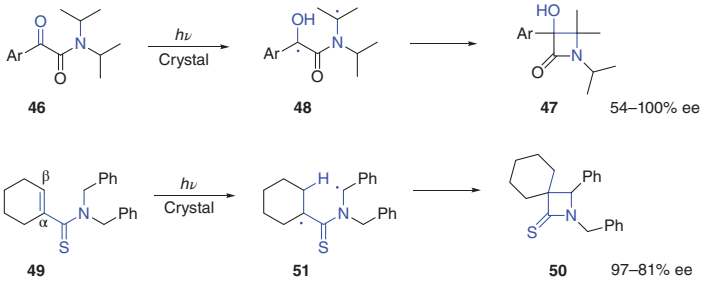
The combination of enzymatic reactions with photochemical, in particular photoredox processes, offers numerous perspectives for organic synthesis [45]. This combination is a particularly efficient approach in connection with sustainable or green chemistry. As these processes are the basis of photosynthesis in green plants, they have been suggested of potential relevance for a sustainable chemical industry by G. Ciamician more than 100 years ago [46]. It was the beginning of green chemistry [47] although it has been almost forgotten over the decades.

1.4 Asymmetric Photochemical Reactions in Crystals

Asymmetric synthesis is often based on selection of conformations. An efficient method to do this is to carry out reactions at the crystalline state. Molecular

symmetry and crystallography are strongly linked [48]. Particularly impressive photochemical reactions have been reported with achiral substrates that crystallize in Sohncke space groups [49, 50]. When achiral compounds crystallize in these space groups, most frequently, one enantiopure conformer is present in such homochiral crystals [51, 52].

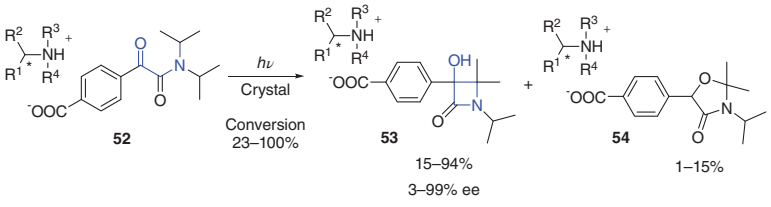
When α-ketoamides **46** are irradicated at the solid state, the hydroxy-β-lactams **47** are obtained in high enantioselectivity (Scheme 1.10) [53]. After light absorption, a hydrogen atom is transferred from an isopropyl group to the α-keto function leading to the diradical **48**. Radical cyclization yields the final product **47**. All these reaction steps occur under conformational control exerted by the crystal environment. In most cases, enantiomeric excesses (ee) were higher than 90%. In the case of Ar = Ph, the substrate crystallized in the chiral space group $P2_12_12_1$ [54]. Irradiation of the homochiral crystals yields product **47** (Ar = Ph) in 93% ee, which crystallized in the same space group $P2_12_12_1$. Both enantiomers have been selectively prepared choosing the corresponding homochiral crystals of the substrate. Under similar conditions the achiral α,β-unsaturated thioamide **49** was transformed into the thio-β-lactam **50** [55]. After photochemical excitation, a hydrogen was transferred from one of the benzyl positions into the β-position of the cyclohexene moiety (**51**). Radical combination yields the final product **50**. The starting product crystallized in the $P2_1$ space group, and when homochiral crystals were irradiated, one enantiomer of **50** was obtained in high enantiomeric excess. It is noteworthy that, when compound **49** was irradiated in solution, the same product **50** was isolated but as a racemic mixture along with side products [56]. Various other examples of this approach to chiral compounds have been reported [57].



Scheme 1.10 Synthesis of β-lactams using absolute asymmetric synthesis with homochiral crystals of the achiral substrates. Each enantiomer has been selectively produced from the corresponding homochiral crystal of the substrate.

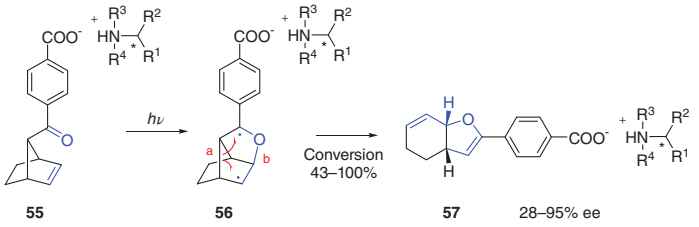
This method for the production of only one enantiomer without external chiral induction is part of absolute asymmetric synthesis. Using particular crystallization methods, e.g. seeding crystallization with the desired homochiral crystal, the achiral starting compound can be selectively transformed into only one of the homochiral crystals [58]. It should further be pointed out that such solid-state photochemical reactions can also be carried out on larger scale when suspensions are irradiated [59].

A certain control of the crystal symmetry can be obtained by attaching a homochiral element to the substrate. In this case, the number of possible space groups is reduced to 65 (Sohncke groups). A defined chiral environment is thus created around the photochemical substrate [48–51]. In order to obtain enantiomerically pure or enriched photochemical products, the chiral element should not be covalently bonded to the photochemical substrate [60]. In this context, ammonium salts of chiral amines and α-ketoamide **52** carrying a carboxylate function have been prepared, and the crystalline phase was irradiated (Scheme 1.11) [61]. In most cases, the resulting hydroxyl β-lactams **53** have been obtained in high yield and enantioselectivity. The oxooxazolidine derivatives **54** were formed in minor amounts. Both enantiomers of carboxylates **53** or **54** have been obtained as major stereoisomers depending on the configuration of the chiral ammonium cation. The absolute configuration of the carboxylates has not been determined in this study.



Scheme 1.11 Synthesis of β-lactams by irradiation of crystalline chiral ammonium salts. Source: Natarajan et al. [61] / American Chemical Society.

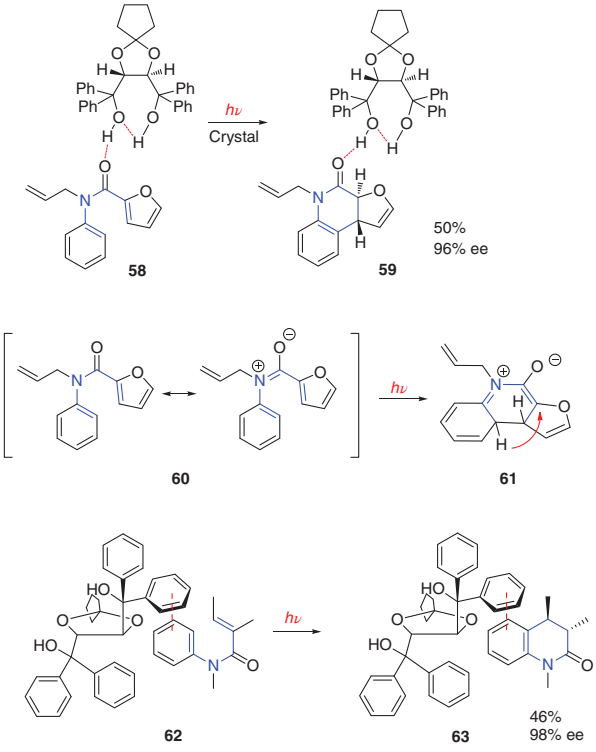
A similar norbornene **55** derivative has been transformed under the same conditions (Scheme 1.12) [62]. Upon irradiation, the carbonyl is added to the alkene function leading to the triplet 1,4-diradical intermediate **56**, which is a typical intermediate of the Paternò–Büchi reaction [63]. Such intermediates may undergo C—C bond formation leading to oxetanes. Bond cleavage of the newly formed C—O bond (b) can also take place regenerating the starting compound. This reaction step plays a key role in the stereoselective Paternò–Büchi reaction in solution [11, 64]. However, in the present case, a C—C bond (a) of the norbornene moiety is cleaved, yielding the final product **57**, a bicyclic dihydrofuran derivative. In most cases, high stereoselectivity was observed. The reaction is a photo-Claisen rearrangement [65] with intersystem crossing taking place.



Scheme 1.12 Asymmetric photo-Claisen rearrangement by irradiation of crystalline chiral ammonium salts. Source: Xia et al. [62] / American Chemical Society.

1.5 Crystalline Inclusion Complexes

As pointed out earlier, TADDOLs are auxiliaries that efficiently induce chirality without being covalently bonded to the reacting molecule [27]. Using co-crystallization of these compounds with substrates of photochemical reactions is an interesting strategy for asymmetric synthesis [66, 67]. Crystals of TADDOLs are host structures with cavities that can be filled by guest molecules. When co-crystallized with a TADDOL derivative in a 1 : 1 ratio, the furoic acid amide **58** undergoes enantioselectively photocycloaddition yielding the quinolinone compound **59** (Scheme 1.13) [68]. Due to its polar mesomeric structure **60**, the amide constitutes a 6π system with benzene and furan moieties. Therefore, it undergoes conrotatory photocyclization leading to **61**. The final product **59** is formed via a tautomerization step. The same reaction was carried out with the acrylanilide derivative **62** (Scheme 1.13). Co-crystals of a 1 : 1 ratio with the same TADDOL have been irradiated. Again, the quinolinone compound (**63**) was obtained in high enantiomeric excess. Guest molecules can interact principally in two different ways with the TADDOL host matrix. They can approach the host molecules with their polar face, which may lead to the formation of hydrogen bonds. This was observed for the furoic acid amide **58** (Figure 1.2a). Guest molecules may also interact with the aryl substituents of the TADDOLs. In such cases, van der Waals, π–π-stacking, or



Scheme 1.13 Photocyclization in TADDOL co-crystals yielding quinolones in high enantioselectivity. Source: Toda et al. [68] / American Chemical Society.

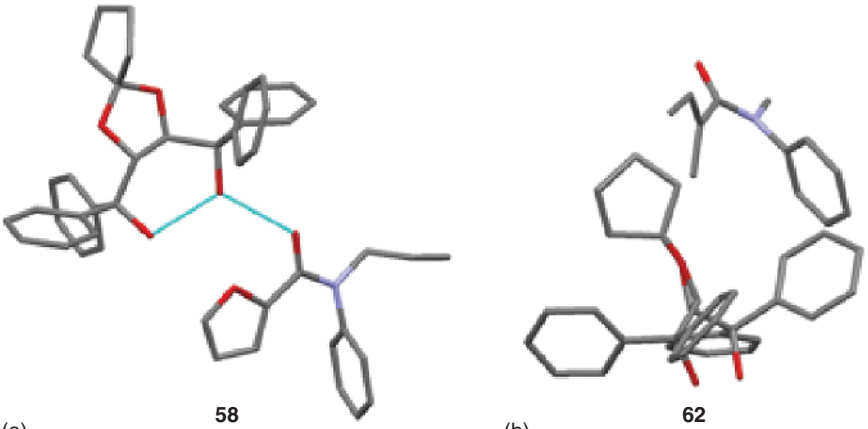
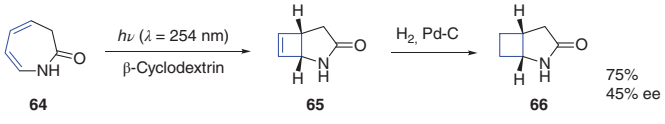


Figure 1.2 X-ray structures of compound **58** (a) and **62** (b) in 1 : 1 co-crystals with a TADDOL (compare Scheme 1.13).

edge-to-face interactions [69] can be observed. This may be the case in the reaction of compound **62** (Figure 1.2b).

Numerous photochemical reactions have been performed using cyclodextrins inclusion complexes [15, 70]. In water solution, cyclodextrins form such complexes with a variety of organic molecules. However, in many cases when β-cyclodextrin is used, the inclusion complexes are less soluble, and the corresponding suspensions, powders, or films are irradiated. In this context, a suspension of the 1 : 1 complex of β-cyclodextrin and the azepinone **64** has been irradiated with UV light (Scheme 1.14) [71]. The photochemical product **65** was hydrogenated, and the corresponding bicyclic γ-butyrolactam **66** was isolated in good yields and moderate enantioselectivity. Similar results have been obtained when films of the inclusion complex were irradiated. When the photochemical reaction of **64** in the presence of β-cyclodextrin was carried out in solution, followed by hydrogenation, **66** was isolated as a racemic mixture. Obviously, under these conditions, no inclusion of **66** takes place.

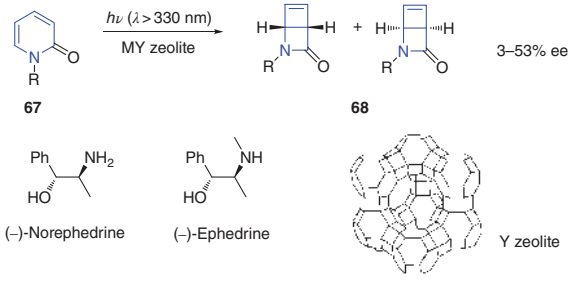


Scheme 1.14 Photocyclization of the dihydroazepinone **64** as part of an inclusion complex with β-cyclodextrin. Source: Mansour et al. [71] / American Chemical Society.

1.6 Inclusion in Zeolites

Zeolites are inorganic crystalline porous materials that absorb small- or medium-sized molecules depending on the cavity size [72]. They are frequently used as catalysts. Concerning photochemical reactions, they have been used as a

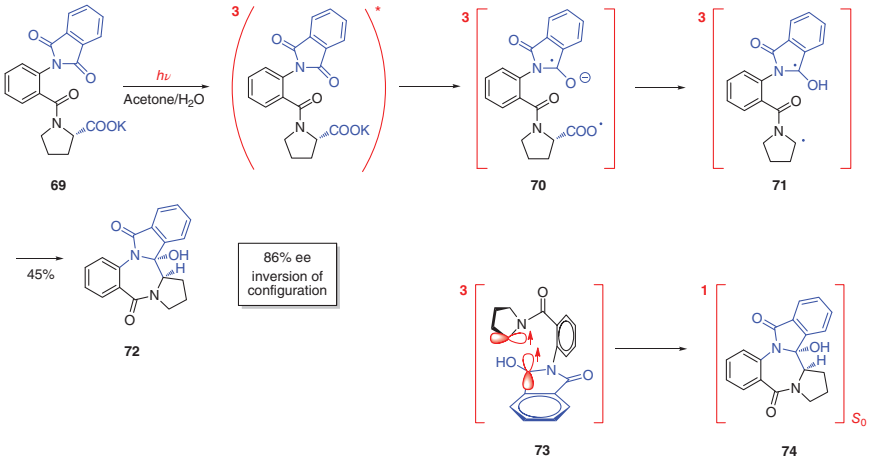
host structure for organic molecules [73, 74]. The photocyclization of pyridones **67** to the bicyclic β-lactams **68** has been performed in super cages of MY zeolites, where M are different alkali metal ions (Scheme 1.15) [75]. In order to create a chiral environment, inclusion into the super cages of MY zeolite of (−)-norephedrine or (−)-ephedrine together with the substrate **67** was carried out. In order to assure maximum interaction with the chiral inductor, the aminoalcohols were used in a 10-fold excess. In cases of larger substituents R, the bicyclic β-lactams **68** have been obtained with enantiomeric excesses up to 53%. The confinement of the non-covalently bonded chiral inductor with the pyridone substrates reduces the number of conformers. The proximity of the chiral inductor directs this selection in an enantioselective way. It must be pointed out that when the same reactions were carried out in solution, almost no chiral induction was observed. The reaction was also performed with pyridone substrates in which chiral amine derivatives were covalently bonded. In such cases, significant diastereoselectivity was observed when compounds were absorbed by Y zeolites.



Scheme 1.15 Photochemical transformation of pyridones **67** to bicyclic β-lactams **68** co-absorbed with chiral aminoalcohols in Y zeolites. Source: Sivasubramanian et al. [75] / Royal Society of Chemistry.

1.7 Memory of Chirality

In many stereoselective reactions, the chiral information is transferred from a chiral center, for example, a chiral carbon atom, to the reaction center [76]. The resulting products are formed with diastereoselectivity. In some cases, however, such a chiral center is destroyed, and the chiral information is conserved (memory of chirality) in more or less stable conformers or other non-covalent interactions. In this way, such reactions become stereo- or enantioselective. Such phenomena are part of chiral memory effects [77, 78]. In this context, the proline derivative **69** has been irradiated in an acetone/water mixture (Scheme 1.16) [79]. Under these conditions, sensitization occurs via triplet energy transfer from photochemical excited acetone to **69**. Intramolecular electron transfer occurs from the carboxylate functionality to the phthalimide moiety (**70**). Immediate decarboxylation takes place and an α-aminoalkyl radical (**71**) is generated. In this reaction step, the chiral information at the former proline moiety is lost. Radical cyclization leads to the final product



Scheme 1.16 Observation of a memory of chirality effect in a decarboxylative photocyclization. Source: Griesbeck et al. [79] / John Wiley & Sons.

72 with high enantioselectivity. It must be pointed out that the chiral information was conserved in relatively rigid conformations and transferred with inversion of configuration. This effect is explained by the fact that the spin multiplicity changes in this step. The triplet diradical **73** is transformed into the final product in its singlet state **74**. Radical combination and intersystem crossing concomitantly occur when the radical carrying p orbitals in the diradical are orthogonally oriented as depicted in structure **73** [80]. Such an arrangement increases spin–orbit coupling. As shown for the present and other examples, such an interaction has a significant impact on the stereoselectivity of these reactions [81]. In a similar electrochemical reaction, which takes place at the singlet ground state, almost the same enantioselectivity was observed but with retention of configuration at the pyrrolidine moiety [78, 82]. Memory of chirality effects have been observed in a variety of photochemical reactions involving radical intermediates [83].

1.8 Conclusion and Perspectives

Enantioselective synthesis of heterocyclic compounds plays an important role in many domains such as the search of new biologically active compounds for use in medicine or agriculture or for the preparation of new materials. Photochemical reactions significantly contribute to this research field. Currently, template-supported or organometallic catalysis is intensively investigated with considerable impact in photoredox catalysis and photosensitization [84, 85]. Enzyme catalysis represent an efficient method for the preparation of enantiopure compounds, among them many heterocyclic compounds. Photochemical reactions can simplify the catalytic systems. In many cases, the use of coenzymes has been replaced by simple photochemical processes. Solid-state photochemistry is an efficient method to control the equilibrium of conformers in an enantioselective way. Consequently, many of such

reactions are carried out with high or complete enantioselectivity. This research domain provides interesting perspectives for material science. Photochemistry of heterocyclic compounds also contributes to basic understanding of chemical reactivity. Memory of chirality is observed in some of these reactions. For example, the influence of spin–orbit coupling, the conformational rigidity on enantioselectivity, has been discussed in this context. It should also be pointed out that supramolecular structures [14] or supramolecular catalysis [86] play a key role in most of these reactions. Among the reaction discussed in this chapter, asymmetric photoredox catalytic reactions and photochemically modified enzymatic reactions are certainly the most attractive methods for application in organic synthesis. In the context of sustainable chemistry, photochemical reaction with crystalline substrate is particularly interesting since no solvent is needed [66, 87].

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