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Efficient radical addition of tertiary amines to alkenes using photochemical electron transfer*

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Abstract: An efficient photoinduced radical addition of tertiary amine, mainly cyclic derivatives, to electron-deficient alkenes was developed. The reaction was applied to the asymmetric synthesis of the pyrrolizidine alkaloids laburnine and isoretronecanol. The method was then optimized for the addition of a larger variety of tertiary amines, in particular acyclic ones. Radical tandem addition cyclization reactions with unsaturated tertiary amines have also been investigated. A detailed mechanistic study using isotopic labeling enabled the optimization of a corresponding reaction with *N*,*N*-dialkylaniline derivatives. The origin of the high reaction stereoselectivity achieved with menthyloxyfuranone was elucidated. The radical addition of tertiary amines was also performed with heterogeneous photocatalysis using inorganic semiconductors as sensitizers.

Keywords: photochemistry; radical reactions; electron transfer; heterocycles; stereoselectivity.

INTRODUCTION

Radical reactions have become important tools in synthetic organic chemistry [1]. Currently, reactivity, selectivity, and, particularly, stereoselectivity are intensively studied in order to optimize these reactions for application [2]. In many cases, these reactions need toxic reagents such as tin derivatives [3], and efforts have been undertaken to make the processes more environmentally friendly. Photoinduced electron-transfer reactions open a quite efficient access to radical intermediates [4]. In cases where electron transfer at the ground state is not possible, electronic excitation of one of the reaction partners enables exothermic electron transfer between them. This relationship is described by the Rehm–Weller equation [5]. In this way, these processes considerably enrich the redox chemistry of organic compounds. After proton exchange, neutral radical intermediates are generated. The present article describes an efficient method for the addition of tertiary amines to electron-deficient alkenes. The interest for application to organic synthesis (a convenient approach to a variety of nitrogen-containing heterocycles), mechanistic, and stereochemical and catalytic aspects are important points discussed in this article.

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PHOTOINDUCED RADICAL ADDITION OF TERTIARY AMINES TO ALKENES

Radical addition of tertiary amines to alkenes has been known for many years [6]. Thus, in this simple way, a large variety of amines can be synthesized, many of which possess biological activity. For instance, cyclic amines such as *N*-methylpiperidine **1** can be added to alkenes and derivatives of piperidine alkaloids are obtained (Fig. 1) [7]. However, this reaction has rarely been applied to organic synthesis since yields and selectivities are generally low. Photochemical reaction conditions have also been applied. For instance, in a photosensitized reaction, *N*-methylpyrrolidine **2** was added to the furanone **3** [8]. In this case, benzophenone was used as sensitizer in high quantity. Such reactions are also unselective since large amounts of products resulting from decomposition of the sensitizer or its reaction with the substrates are obtained. The highest yields reach only 60 %. Corresponding intramolecular reactions are more efficient, as shown by the transformation of **4** [9].

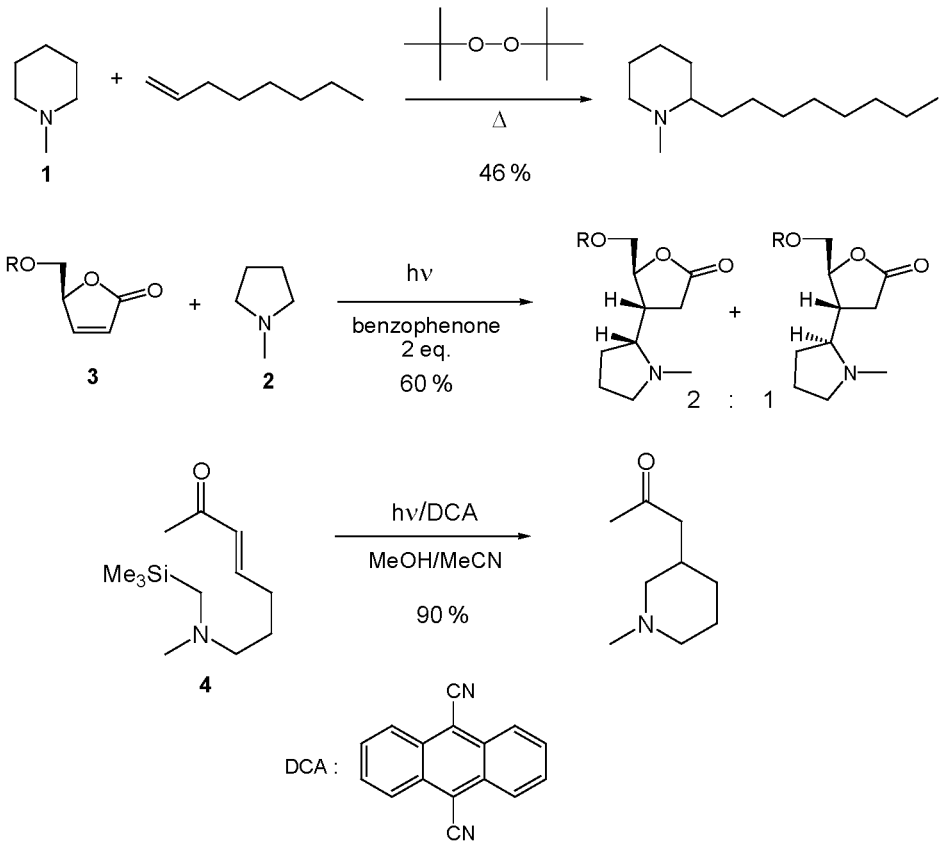


Fig. 1 Radical addition of tertiary amines to olefinic double bonds.

The intermolecular version of the reaction becomes efficient when electron-donor-substituted aromatic ketones such as **5**, **6**, or **7** are used as sensitizers (Fig. 2) [10]. In this way, *N*-methylpyrrolidine **2** was efficiently added to menthyloxyfuranone **8**. The radical addition occurred stereospecifically *anti* with respect to the menthyloxy substituent. The configuration of the chiral center in the α-position of the nitrogen atom in **9a,b** was not controlled. The products were formed with yields up to 94 % and a quantum yield of 4. When compared to more conventional sensitizers such as benzophenone or acetophenone, it can be concluded that in the case of the new sensitizers:

- Yields are particular high.
- The reactions are significantly faster, which facilitates large-scale transformations.
- The new sensitizers are used only in catalytic amounts and can be recovered up to 80 % after the reaction.

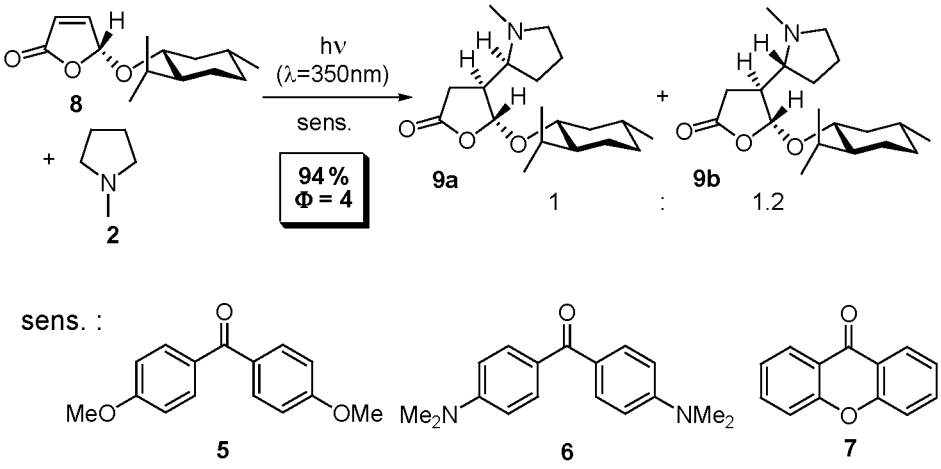


Fig. 2 Efficient photoinduced radical addition of *N*-methylpyrrolidine **2** to menthyloxyfuranone **8** using electron-donor-substituted aromatic ketones as sensitizer.

The mechanism depicted in Fig. 3 explains these observations. After photochemical excitation of the sensitizer, a ketyl radical **I** and a nucleophilic α-aminoalkyl radical **II** are generated via hydrogen abstraction. **II** easily adds to the electron-deficient double bond of menthyloxyfuranone **8** leading to the oxoallyl radical **III**. After hydrogen abstraction, the final products **9a,b** are obtained and an α-aminoalkyl radical **II** are generated. Since quantum yield is only 4, the resulting radical chain process is not very efficient. Photoinduced radical reactions may have quantum yields of several thousand. For the present reaction, this means that the termination step should play an important role. Oxoallyl radicals **III** can react with ketyl radicals **I** in order to form additional **9a,b** and to regenerate the sensitizer (catalyst). The starting reaction and the termination step are linked together in a second efficient radical cycle [11]. Certainly, these processes are efficient because they occur in two steps. In the case of the starting reaction, first the electron transfer from the tertiary amine to the excited sensitizer takes place, leading to a radical ion pair (Fig. 4). After proton exchange, the neutral radicals **I** and **II** are generated. A similar mechanism can be discussed for the termination step when electron transfer occurs from the ketyl radical **I** to the electrophilic oxoallyl radical **III**. In this step, an enolate ion **IV** and a particularly stabilized carboxonium ion **V** are formed. The neutral products **5** and **9a,b** are obtained after proton exchange. Polar effects or even electron transfer in the radical addition and the hydrogen abstraction steps of the radical chain (cycle I, Fig. 3) also contribute to the efficiency of the overall reaction [12].

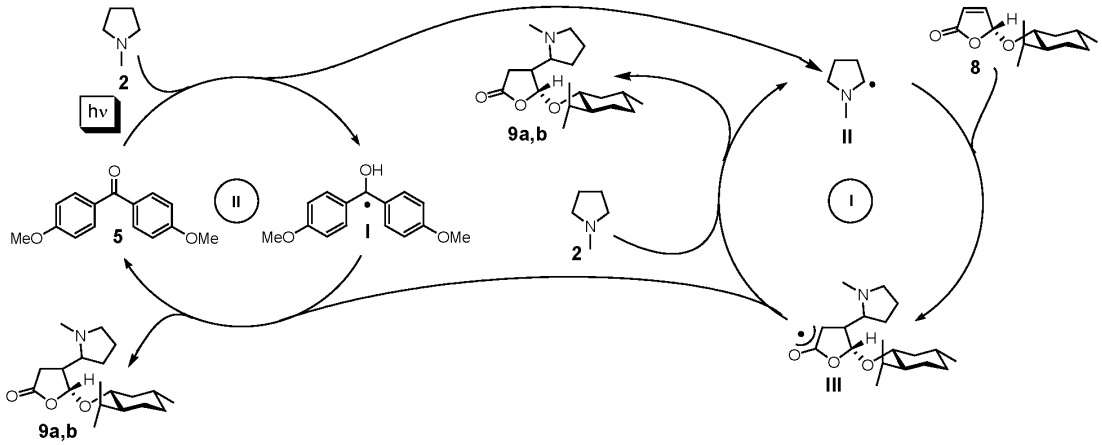


Fig. 3 Mechanism of the photoinduced radical addition of *N*-methylpyrrolidine **2** to menthyloxyfuranone **8**.

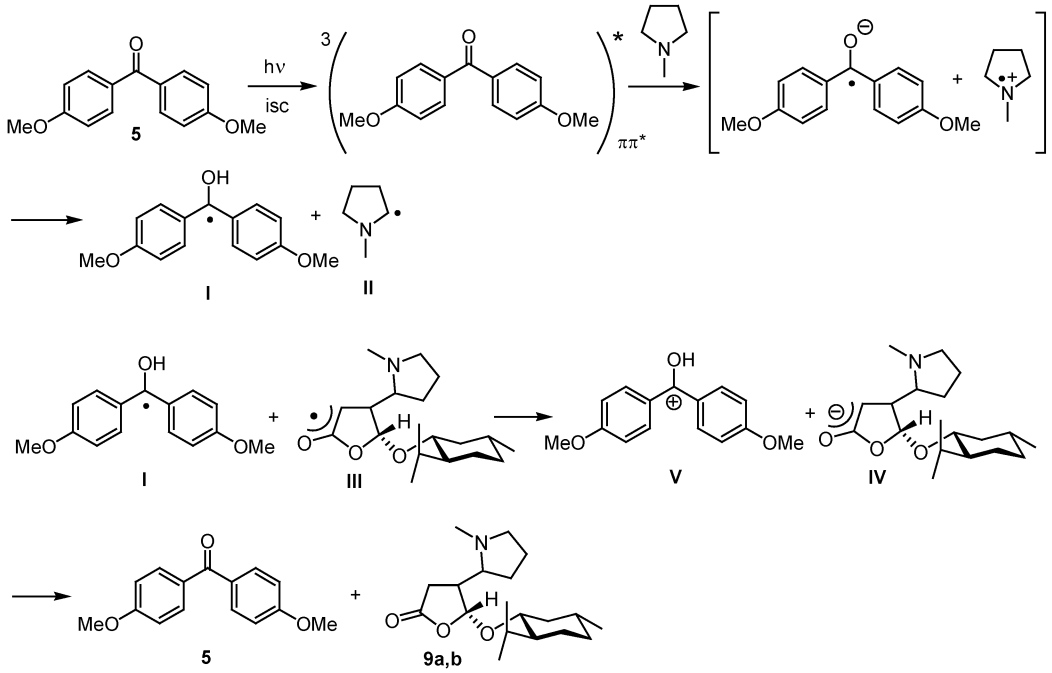
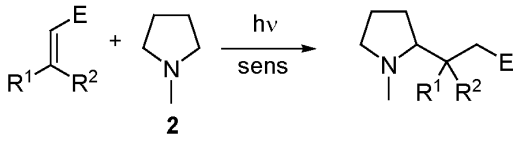


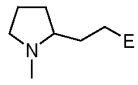
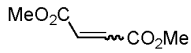
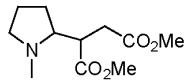
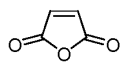
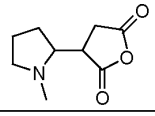
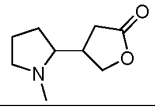
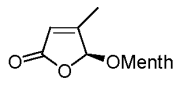
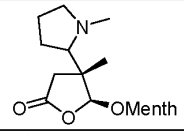
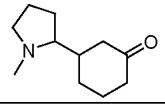
Fig. 4 Electron-transfer steps of the radical cycle II (Fig. 3).

The reaction was performed with a variety of electron-deficient alkenes (Table 1). In the case of β-unsubstituted acrylic derivatives, *N*-methylpyrrolidine **2** was used as solvent (entry 1). Using these conditions, photopolymerization was almost completely inhibited as side-reaction. In all other cases, acetonitrile was used as a polar solvent. Reactions of β-disubstituted Michael-acceptor compounds are generally slow. A similar observation was made with a corresponding furanone (entry 5). In this case, a prolonged irradiation of 2 h under otherwise identical reaction conditions was necessary to obtain a significant conversion. α,β-Unsaturated ketones such as cyclohexenone (entry 6) could also be successfully transformed. In this case, Michler's ketone [4,4'-(*N,N'*-dimethylamino)benzophenone] **6** was

used as sensitizer and the reaction was carried out with visible light in order to prevent photodimerization of the enone.

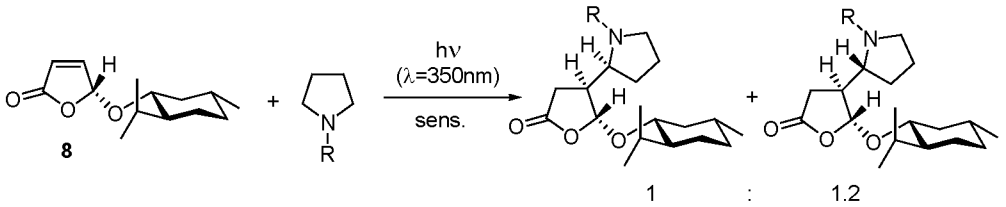
Table 1 Efficient photoinduced radical addition of *N*-methylpyrrolidine **2** to various electron-deficient alkenes.



Entry	Alkene	Product	Yield (%)
1[a]			
	E = CN		80
	E = CO_2Me		87
2			
	cis		69
	trans		73
3			76
4			86
5			71[b]
6			90

[a]**2** was used as solvent.
[b]Based on a conversion of 55 %.

The reaction was mainly performed with cyclic tertiary amines (Fig. 5). In these cases, the addition only occurred on the ring and never on the side-chain, not even in the case of the *N*-isopropyl substituent (entry 3) where a thermodynamically more stable tertiary radical may be formed at the alkyl side-chain. Occasionally, acyclic tertiary amines such as diisopropylethylamine **10** were successfully transformed. The reaction occurred specifically at the ethyl substituent. The high regioselectivity at the amine can be explained by the fact that the deprotonation of the radical cation **VI** occurs under kinetic conditions (Fig. 6) [13]. This reaction step is particularly fast when the corresponding C–H bond is oriented parallel with respect to the radical cation carrying orbital of the nitrogen atom. Such an orientation is more easily established inside the ring (**VII**). In the case of **VIII**, such an orientation is only possible at the ethyl subsituent. The corresponding C–H bonds of the isopropyl substituents are orientated



Entry	R	Irradiation Time (min)	Isolated Yield(%)
1	Me	5	94
2	Et	5	81
3	i-Pr	5	82
4	t-Bu	5	81
5	t-BuMe$_2$Si	12	77

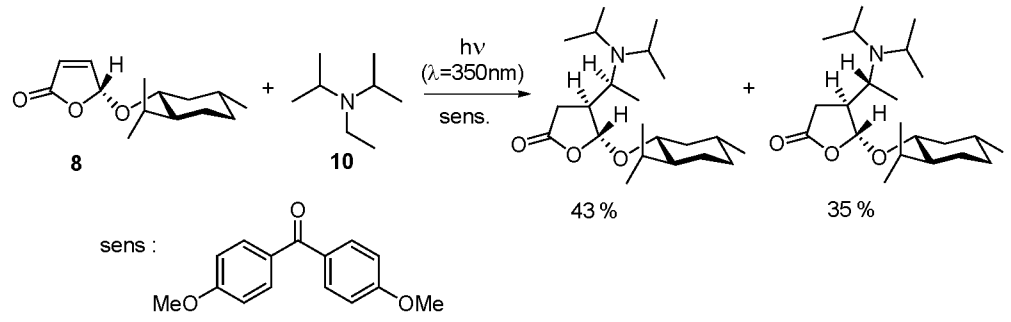


Fig. 5 Photoinduced radical addition of various tertiary amines to menthyloxyfuranone **8**.

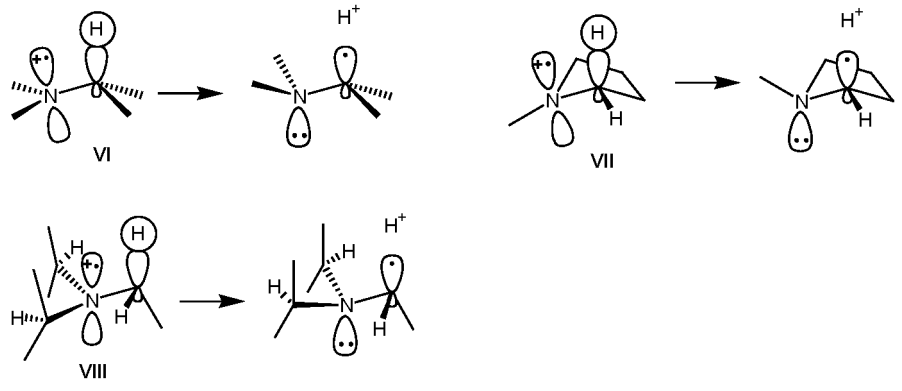


Fig. 6 Deprotonation of radical cations of tertiary amines.

orthogonal with respect to the radical cation carrying orbital at the nitrogen atom. For properties of α-aminoalkyl radicals, see ref. [14].

The reaction was successfully applied to the asymmetric synthesis of bicyclic alkaloids. The diastereomeric adducts **11a,b** could be easily separated by chromatography. In only a few steps, they were transformed into the pyrrolicidine alkaloids (–)-isoretronecanol and (+)-laburnine (Fig. 7). The same reaction sequence was used for the transformation of the *N*-methylpiperidine adduct **12** into the corre-

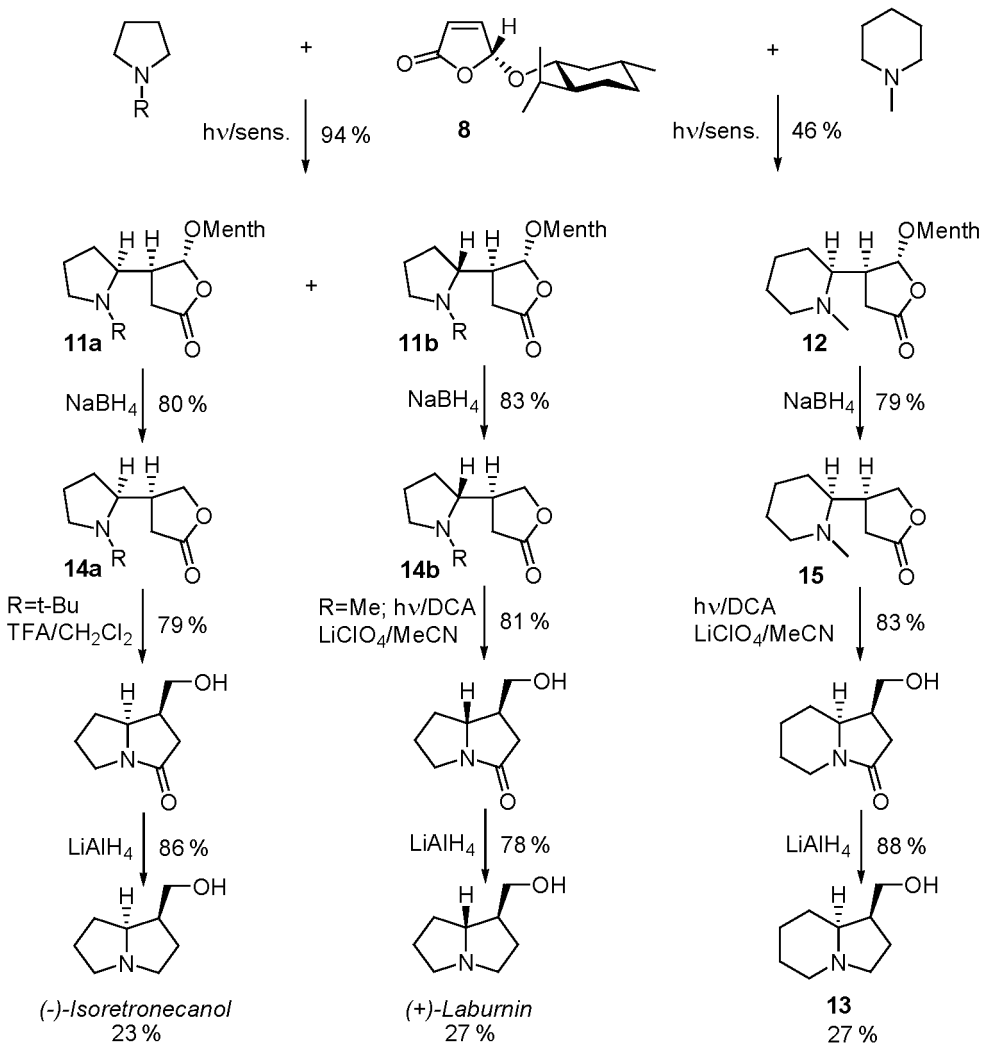


Fig. 7 Application of the photoinduced radical addition of tertiary amines to the asymmetric synthesis of bicyclic alkaloids.

sponding indolizidine alkaloid **13**. The selective dealkylation of **14a,b** or **15** represents a key step of the synthesis. Using photochemical electron-transfer conditions, compounds **14b** and **15** were selectively demethylated [15]. Under these reaction conditions, α-aminoalkyl radicals are oxidized. The resulting iminium intermediates react so that the bond of the less highly substituted alkyl group is cleaved.

Recently, an intramolecular version of the photoinduced radical addition of tertiary amines using enatioselective catalysis was published [16]. In this reaction, the sensitizer was attached to a chiral host structure, a derivative of Kemp's triacid. The aromatic ketone acted as a sensitizer and shielding group. The substrate was linked via hydrogen bonds.

PHOTOINDUCED RADICAL ADDITION OF TERTIARY AMINES IN THE PRESENCE OF THIOCARBONYL COMPOUNDS

As mentioned above, this method is particular efficient for the addition of cyclic tertiary amines while acyclic amines such as triethylamine could not be transformed. As already pointed out, the efficiency of the reaction is due to the sensitizer structure. Electron-donor-substituted aromatic ketones work well. A physicochemical study was performed in order to find out whether photophysical primary processes of the overall reaction may explain the favorable results. In this context, it should be mentioned that the conventional and weak sensitizers (benzophenone, acetophenone) possess T_1 states with $n\pi^*$ character, while the electron-donor-substituted ketones have T_1 states with $\pi\pi^*$ or charge transfer character. The latter compounds have significantly lower photoreduction quantum yields [17]. All possible reaction combinations with both efficient and inefficient sensitizers and amines were studied. No significant difference was detected [18]. Among other parameters, the triplet quenching rates were at the same order of magnitude.

At this stage, further optimization of the sensitizer would have little impact in improving the yields and extending the scope of the reaction. Affecting the complex interplay of various radical intermediates of the reaction should be more efficient. In the field of radical polymerization, it is well established that thiocarbonyl compounds which are added to the reaction mixture reversibly add to the radical chain end (radical addition fragmentation chain transfer, RAFT) [19]. Fragmentation of the initial function stops the polymerization and starts a new one. In this way, the polymer chain length can be controlled. Furthermore, this kind of mechanism is also discussed for the radical addition of xanthates to olefinic double bonds [20]. In the present case of the radical addition of tertiary amines to alkenes, no substrate carries a xanthate function. Therefore, thiocarbonyl compounds were added to the reaction mixture as regulators, and dithiocarbamate **16** was shown to be particular efficient (Fig. 8) [21]. In the presence of this compound, acyclic amines such as **19** and **20** or more complex amines such as **21** were successfully added to the furanone **17**. The addition of tertiary amines to less electron-deficient double bonds such as acrylamides (**22**) was also performed. In the case of more complex alkenes such as **8**, compound **16** was not efficient. During workup, the corresponding products partially decomposed. In this case, the xanthate **23** was more effective. In the case of the transformation of dimethylisoproypl amine **20**, the product resulting from the addition of the thermodynamically more stable teriary α-aminoalkyl radicals **IX** is favored. The resulting isomer **24** is the major reaction product. An interesting observation was made concerning the addition of *N*-methylpiperidine **1**. In the absence of **23**, only one isomer was obtained. In the presence of xanthate **23** however, two isomers **26a,b** were isolated in better yield. In the latter reaction, the configuration of the chiral center in the α-position of the nitrogen atom was not controlled. The presence of the thiocarbonyl compound can thus affect reactivity, regioselectivity, and stereoselectivity.

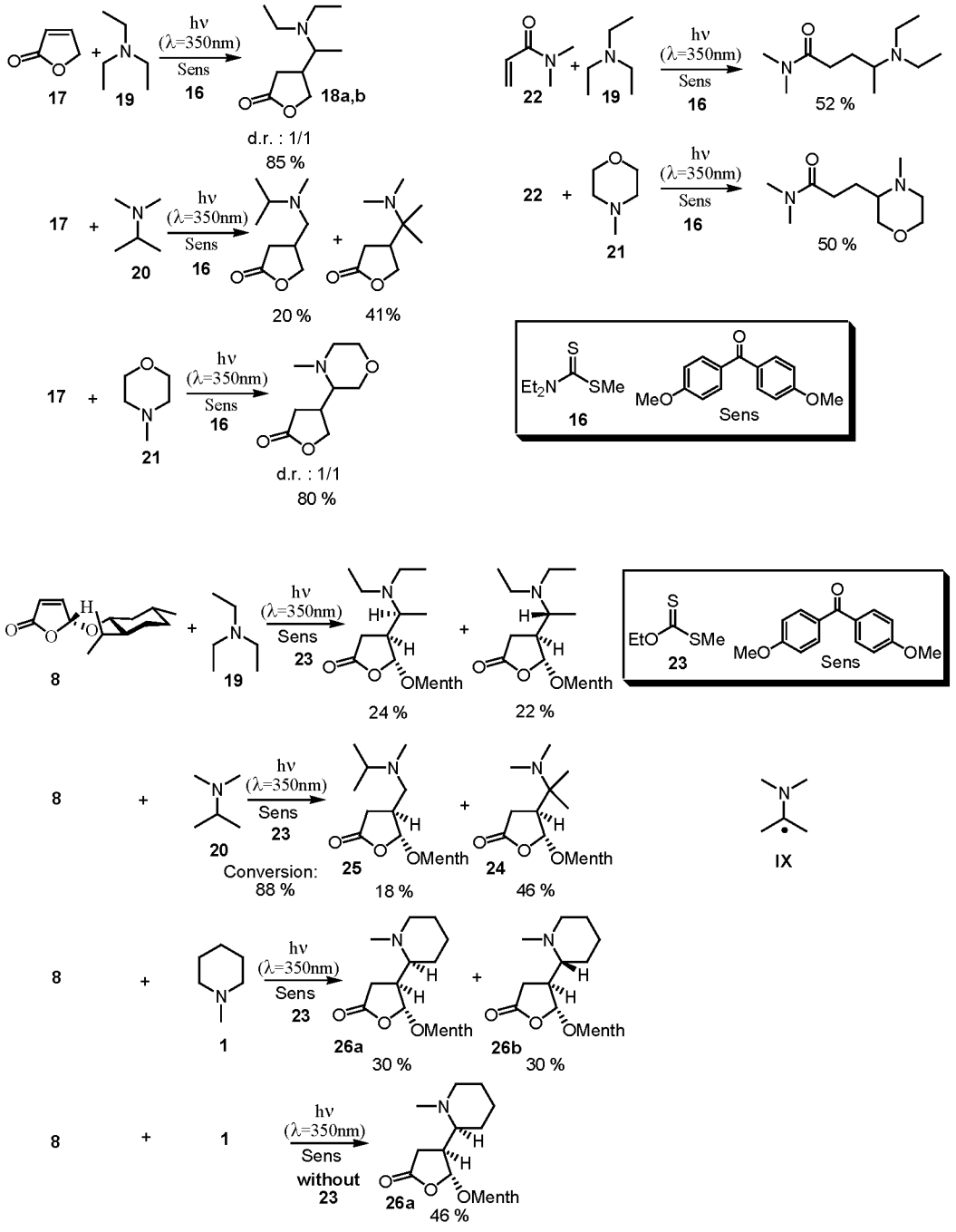


Fig. 8 Radical addition of tertiary amines in the presence of thiocarbonyl compounds.

Not all of these observations can be explained yet, but the more general mechanism depicted in Fig. 9 can be discussed. α-Aminoalkyl radicals **X** are generated via photochemical electron transfer. They add easily to the electron-deficient C=C double bond of the furanone **17** leading to oxallyl radicals **XI**. Due to its reversibility, this reaction step does not always positively contribute to the outcome of the overall reaction. The equilibria can be displaced by the reversible addition of thiocarbonyl com-

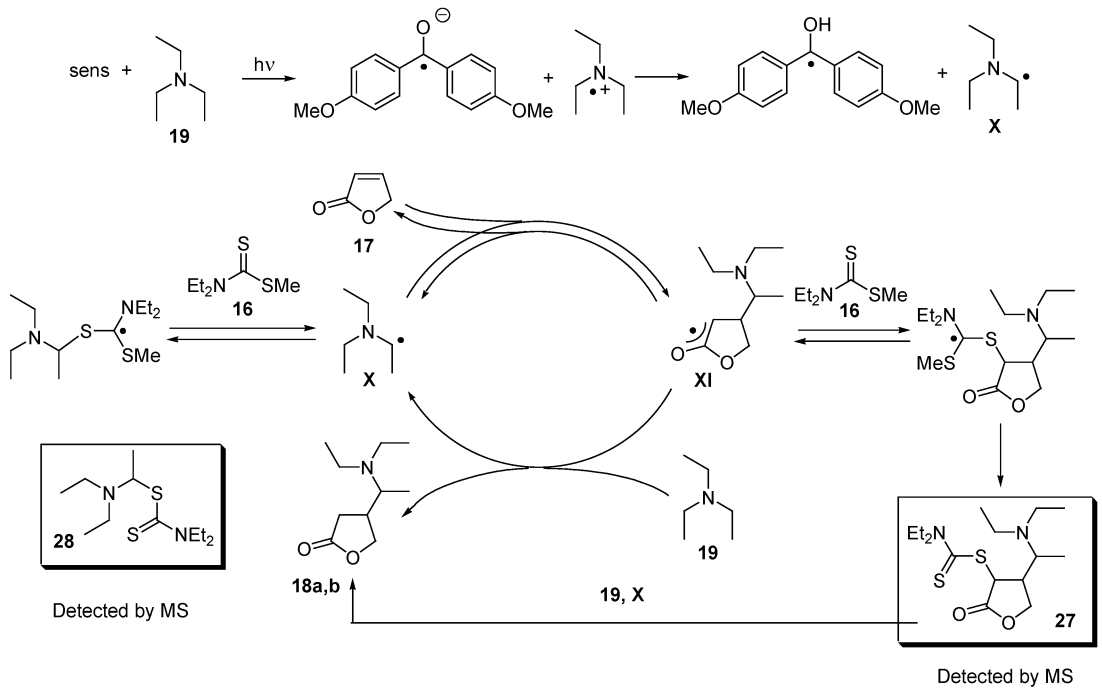


Fig. 9 Mechanism of the radical addition of tertiary amines in the presence of thiocarbonyl compounds.

pounds such as dithiocarbamide **16** to **XI**. This reaction step leads to the formation of the bisadduct **27**. Under the applied reaction conditions, this compound is unstable. Reaction with α-aminoalkyl radicals **X** and the tertiary amine **19** yields the desired final product **18a,b**. The bisadduct **27** was detected by electrospray mass spectroscopy. During this step as well as by trapping of **X**, the unstable thioaminal **28** was generated and was also detected by electrospray mass spectroscopy.

PHOTOINDUCED RADICAL TANDEM ADDITION CYCLIZATON REACTIONS OF TERTIARY AMINES TO ALKENES

Electron-rich aromatic ketone sensitizers were also applied to more complex reactions such as radical tandem addition cyclization processes using unsaturated pyrrolidine derivatives (Fig. 10). The formation of the α-aminoalkyl radical should take place in the ring (**XII**). After addition to the alkene, cyclization should occur in either an *endo* or an *exo* way. This reaction was successfully performed with the *gem*-dimethyl-substituted pyrrolidine derivative **29** and menthyloxyfuranone **8** [22]. The reaction occurred stereospecifically *anti* with respect to the menthyloxy substituent. The configuration of the chiral center in the α-position of the nitrogen atom was not controlled (compounds **30**, **32** vs. **31**, **33**). *Exo*- and *endo*-cyclization (compounds **30**, **31** vs. **32**, **33**) were obtained. The *gem*-dimethyl substitution certainly favors the cyclization [23]. The reaction was more selective with the corresponding alkyne pyrrolidine derivative **34**. In this case, only *endo* cyclization products (**35** and **36**) were obtained. It should be noted that depending on the configuration of the chiral center in the α-position of the nitrogen atom, double-bond isomerization occurred. Under the reaction conditions, the intermediate **XIII** is transformed into **36**.

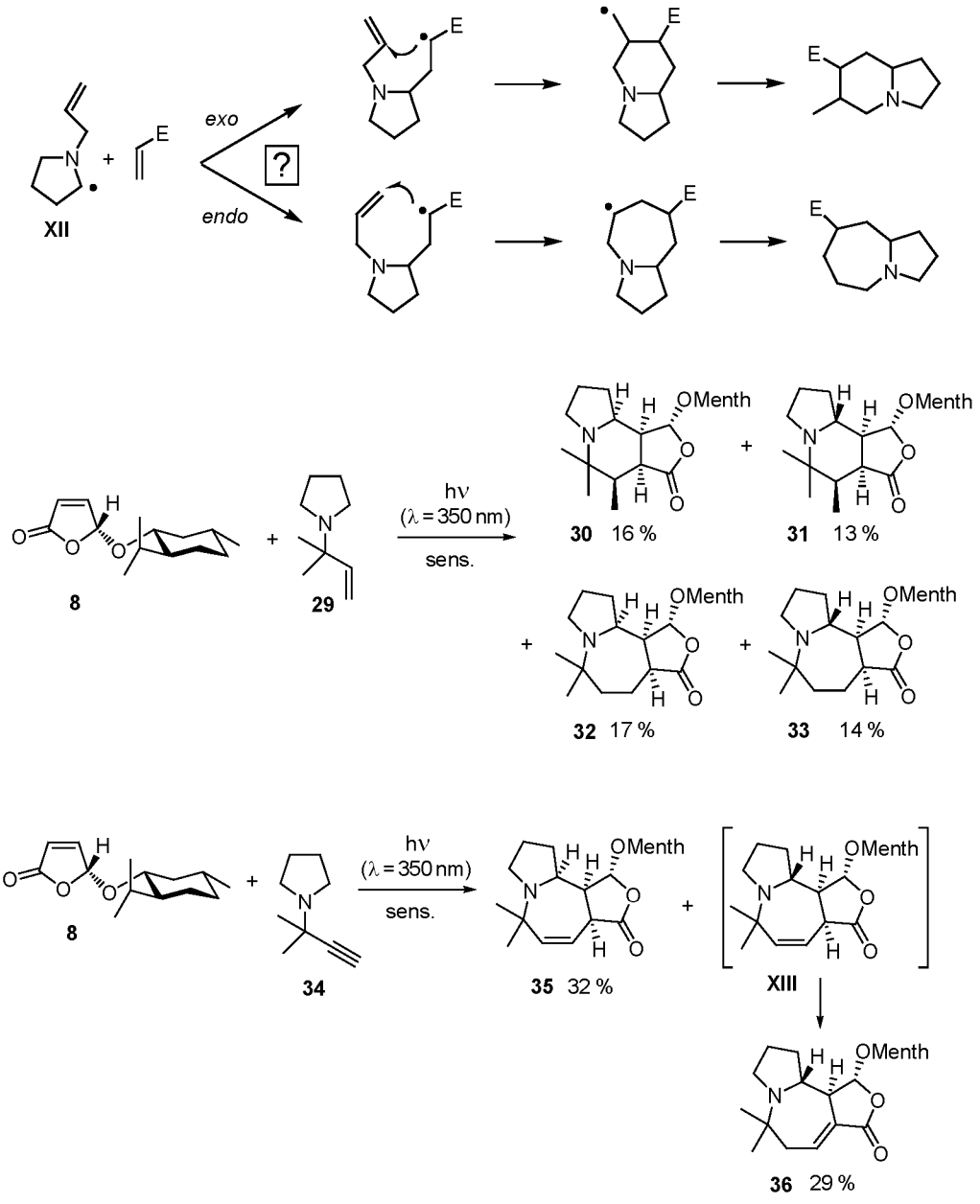


Fig. 10 Radical tandem addition cyclization reaction with unsaturated pyrrolidine derivatives.

An interesting reaction is observed with derivatives of aniline such as *N*,*N*-dimethylaniline **37** (Fig. 11) [22]. Michler's ketone **6** was used as sensitizer since this ketone could be more easily separated by chromatography. In the reaction with menthyloxyfuranone **8**, tetrahydroquinoline derivatives **38a,b** were formed with 90 % diastereoselectivity. The yield, however, was rather low, and the side-products **39** and **40** resulting from partial reduction of **8** were isolated in comparable amounts. It was estimated that both reactions could be coupled. In order to prove this hypothesis, isotopic labeling experiments were performed. In the reaction of the deuterated aniline derivative **37'**, deuterium transfer was observed from the *ortho*-position into the α-position of the lactone side-product **39'** and into one

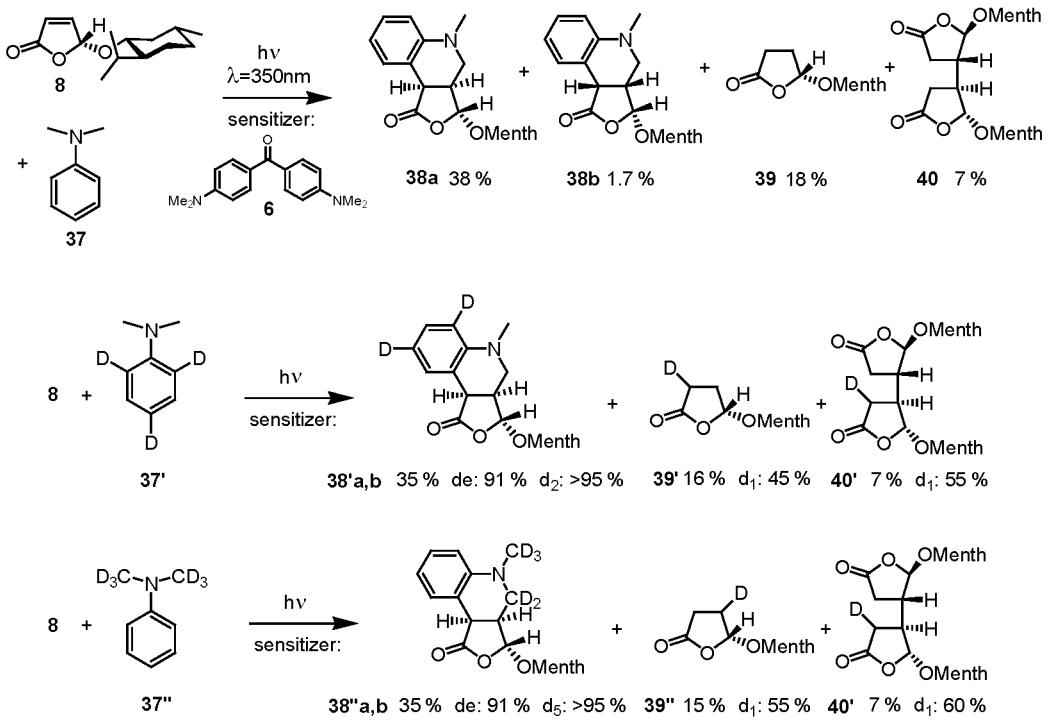


Fig. 11 Radical tandem addition cyclization reaction with unsaturated aniline derivatives and isotopic labeling experiments.

of the α-positions of the second side-product **40'**. Furthermore, deuterium transfer was observed from a methyl group of the deuterated derivative **37''** into the β-position of the lactone **39''** and once again into one of the α-positions of the second side-product **40'**. In order to explain these results, the mechanism with deuterium transfer from the *ortho*-position of **37'** depicted in Fig. 12 was proposed. As previously explained, α-aminoalkyl radicals **XIV** are generated via photochemical electron transfer. After addition to menthyloxyfuranone **8**, the oxoallyl radical **XV** is generated. In an intramolecular step, this electrophilic radical adds easily to the electron-rich aromatic ring leading to the tricylic radical intermediate **XVI**. In order to obtain the final product **38'a,b** in a rearomatization step, deuterium must be transferred. It can be transferred to **8** leading to the deuterooxyallyl radical **XVII**. After tautomerization and hydrogen abstraction at the methyl group from *N*,*N*-dimethylaniline **37'**, the lactone **39'** is isolated with one deuterium atom in the α-position. The deuterooxyallyl radical **XVII** is nucleophilic, and facile addition to **8** is therefore possible. Hydrogen abstraction of the resulting oxoallyl radical **XVIII** leads to the second side-product **40'**. When the deuterated aniline derivative **37''** is used, deuterium transfer occurs one step later in the mechanism. In this case, the hydroxyallyl radical **XVII** abstracts deuterium from **37''** at the β-position.

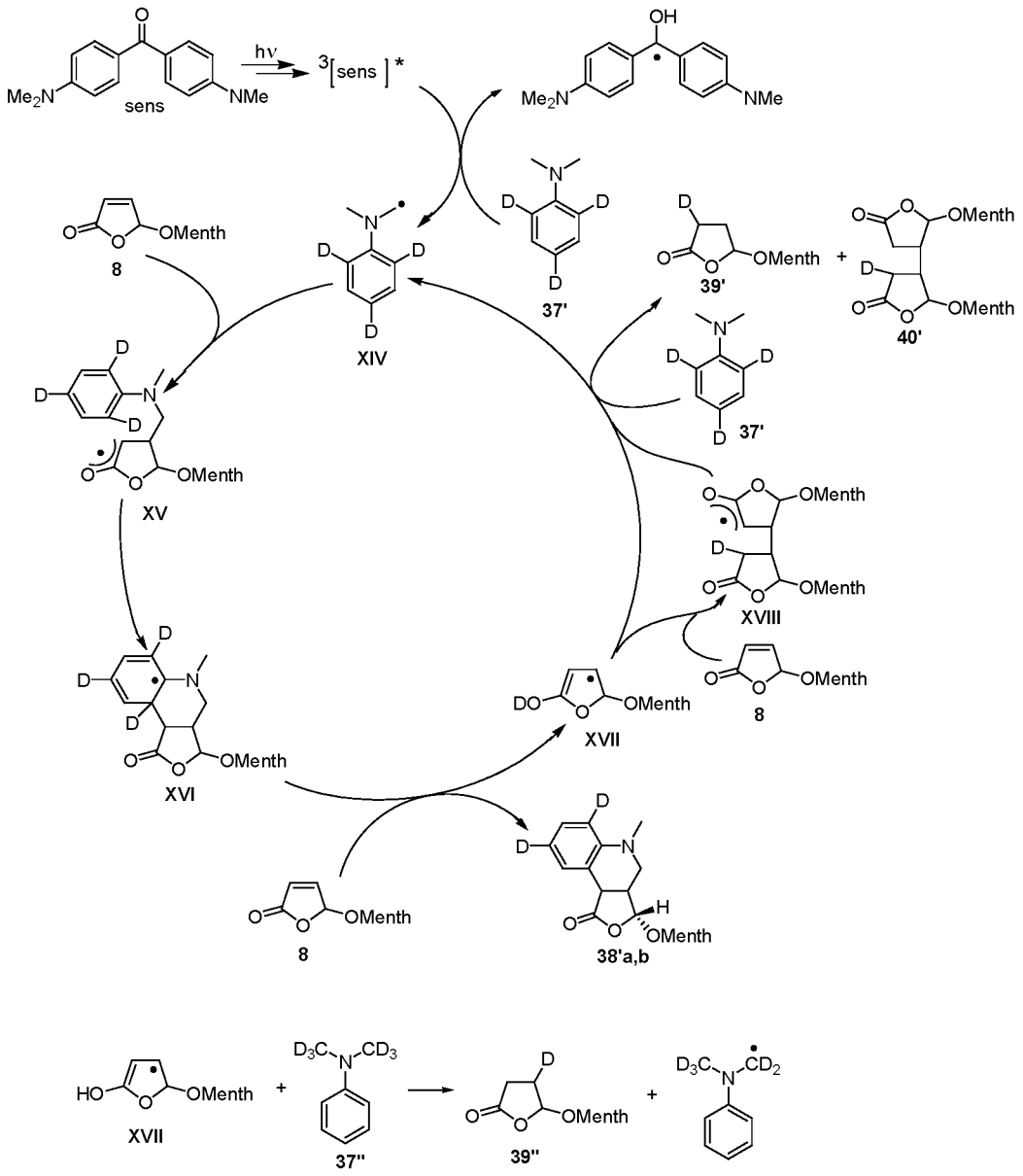


Fig. 12 Mechanism and deuterium transfer of the radical tandem addition cyclization reaction with unsaturated aniline derivatives.

The conclusion that has to be drawn from this mechanistic study in order to optimize the reaction and to make it applicable to organic synthesis is that menthyloxyfuranone **8** has to be replaced in its function as mild oxidant in the rearomatization step. This has been done by adding simple ketones such as acetone to the reaction mixture (Fig. 13) [22]. Under these conditions, the yield of tetrahydroquinoline derivatives **38a,b** was doubled, and the formation of reduction side-products was completely suppressed. It should be mentioned that acetone is also capable of sensitizing the reaction. However, only traces of an adduct resulting from the addition of hydroxyisopropyl radical were detected [24]. In order to check this reactivity, the transformation was performed in the absence of a sensitizer but in the pres-

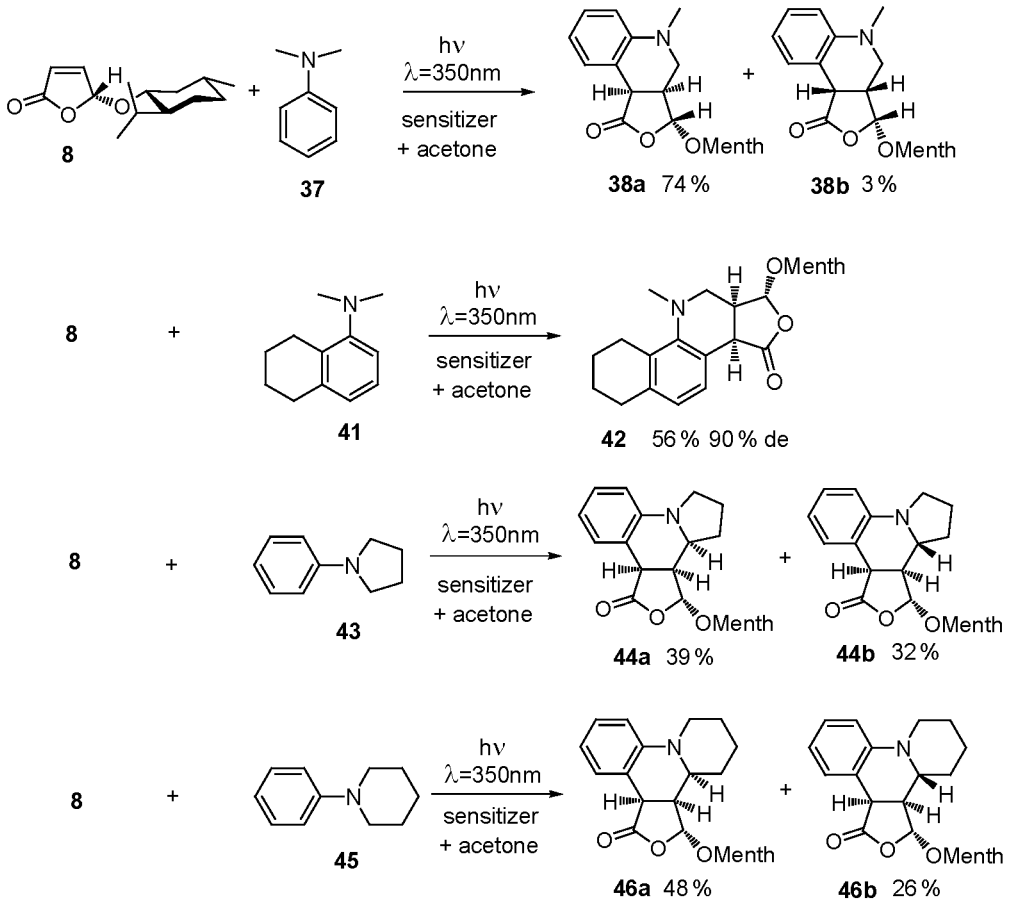


Fig. 13 Radical tandem addition cyclization reaction of various *N*,*N*-dialkylated aniline derivatives under optimized reaction conditions.

ence of acetone. In this case, the reaction was significantly slower and highly unselective. (As in previous cases, the irradiation was performed at λ = 350 nm.) This result resembles transformations performed with conventional sensitizers such as acetophenone or benzophenone. Under the optimized reaction conditions, a variety of aniline derivatives were transformed. *N*,*N*-Dimethylaniline derivatives such as **41** were transformed with a diastereoselectivity of about 90 %. The product **42** resembles azasteroids. In the cases of higher N-substituted aniline derivatives such as *N*-phenylpyrrolidine **43** or *N*-phenylpiperidine **45**, the radical attack occurred stereospecifically *anti* with respect to the menthyloxy subsituent. The configuration of the chiral center in the α-position of the nitrogen atom was not controlled. The latter transformations lead to benzoindolicidine **44a,b** and benzoqinolicidine derivatives **46a,b**.

SYNTHESIS OF (5*R*)- AND (5*S*)-5-MENTHYLOXYFURAN-2[5*H*]-ONE AND ORIGIN OF STEREOSELECTIVITY IN THEIR GROUND-STATE TRANSFORMATIONS

(5*R*)-5-Menthyloxyfuran-2[5*H*]-one **8** is a very flexible synthon in organic chemistry [25]. A maximum of organic functional groups are localized on only four carbon atoms, enabling a large variety of transformations (Fig. 14). This compound has been frequently applied to the asymmetric synthesis of numerous natural products, products possessing interesting biological activities, chiral ligands, etc. [26,27]. The reason for that is because almost all ground-state reactions with this synthon are highly diastereoselective or diastereospecific. Furthermore, the configuration of the chiral center induced in the β-position can be predicted.

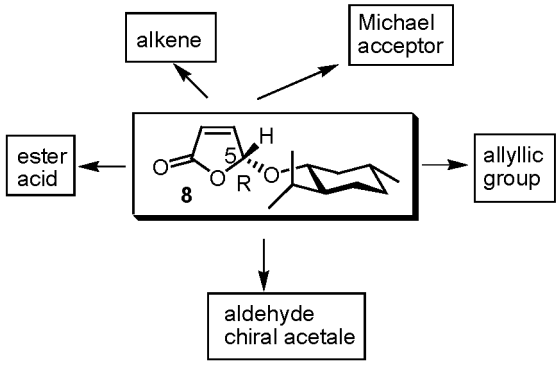


Fig. 14 (5*R*)-5-*l*-Menthyloxyfuran-2[5*H*]-one, a flexible synthon for organic synthesis.

During the synthesis of this synthon, an interesting observation was made enabling a more detailed investigation of the origin of this high diastereoselectivity. Menthyloxyfuranone **8** was obtained in two steps (Fig. 15) [25,27,28]. Efficient photooxygenation of furfural **47** yielded 5-hydroxyfuran-2[5*H*]-one **48** [29]. Acetalization with *l*-menthol led to a 1/1 mixture of (5*R*) **8** and (5*S*)-5-*l*-menthyloxyfuran-2[5*H*]-one **49**. The (5*R*)-diastereoisomer **8** crystallized preferentially in fine needles. The (5*S*)-isomer **49** could be transformed into the (5*R*)-isomer **8** in acid-catalyzed equilibrium reaction [30]. Particular crystallization conditions were applied, and the (5*S*)-isomer **49** could also be isolated in pure form [27]. When the crystallization is performed at low temperature (–28 °C) in strict absence of acid, massive crystals of the (5*S*)-isomer **49** were also formed. They possessed a size of 2 mm to 2.5 cm and were easily separated.

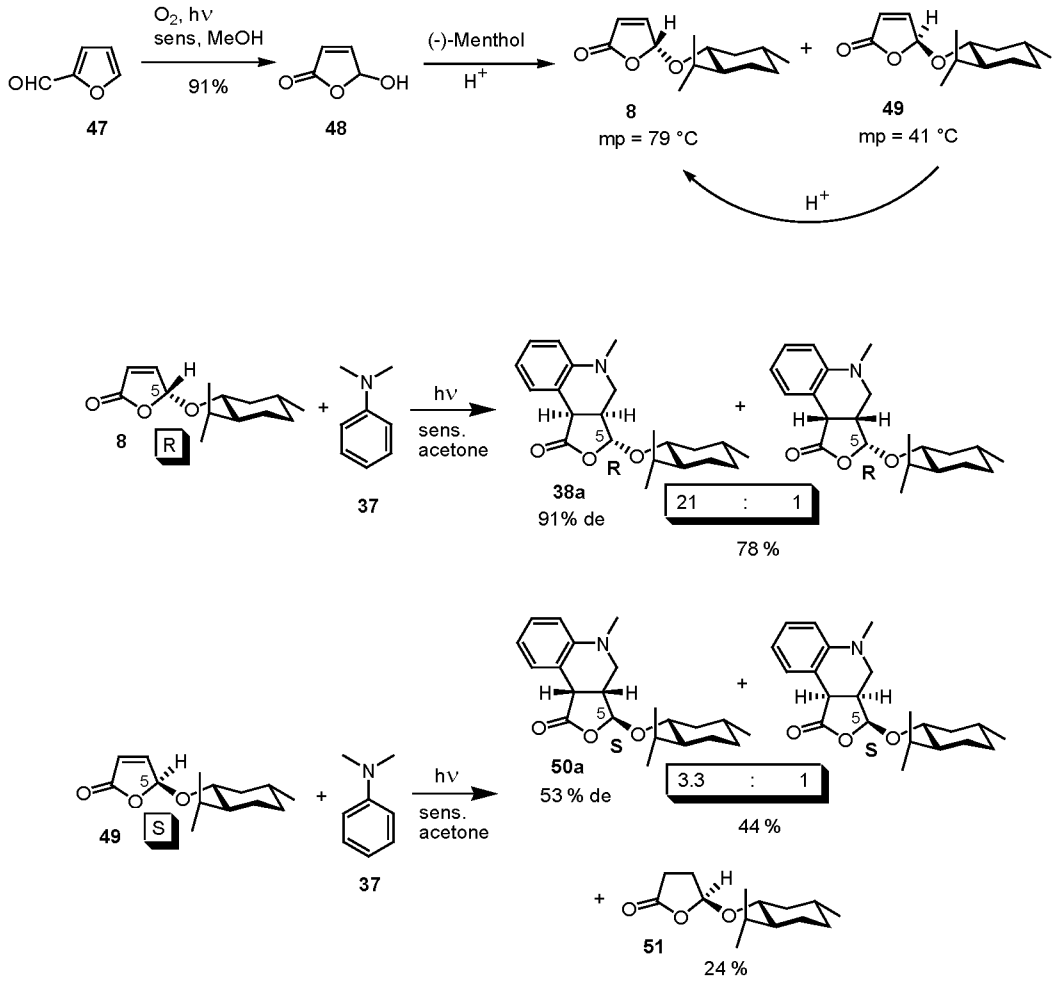


Fig. 15 Diastereoselective radical tandem addition cyclization reaction with (5*R*)- **8** and (5*S*)-5-*l*-menthyloxyfuran-2[5*H*]-one **49**, a flexible synthon for organic synthesis.

The radical tandem addition cyclization reaction with *N*,*N*-dimethylaniline **37** (also compare Fig. 11) was also performed with **49** [27]. Once again, the radical attack occurred preferentially *anti* with respect to the menthyloxy substituent, but the diastereoselectivity was significantly lower than in the case of **8**. Furthermore, the formation of the lactone by-product **51** could not be completely suppressed. In order to explain the different stereoselectivity of both reactions, a conformational analysis was carried out using NMR nuclear Overhauser enhancement spectroscopy (NOESY) measurements followed by MM3 calculations (Fig. 16). In the preferential conformation of the (5*R*)-isomer **8**, the diastereodifferentiation is more efficient because the isopropyl group of the menthyloxysubstituent reaches into one diastereotopic half-space. In the case of the isomer **49**, the orientation of this group is opposite, and the diastereodifferentiation is less expressed. The same orientation of the menthyloxy substituent was found in the major products **38a** and **50a** in solution and in the solid state [27,31]. It was concluded that the orientation of this substituent should control the diastereoselectivity of the reaction when the α-aminoalkyl radical attacks the furanone (compare Fig. 12). Chirality is induced by two elements, the chiral acetal center and the menthyl group. In the context of double induction, a matched, (5*R*)-isomer, and a mismatched, (5*S*)-isomer, pair can be distinguished. Applying the Eyring equation,

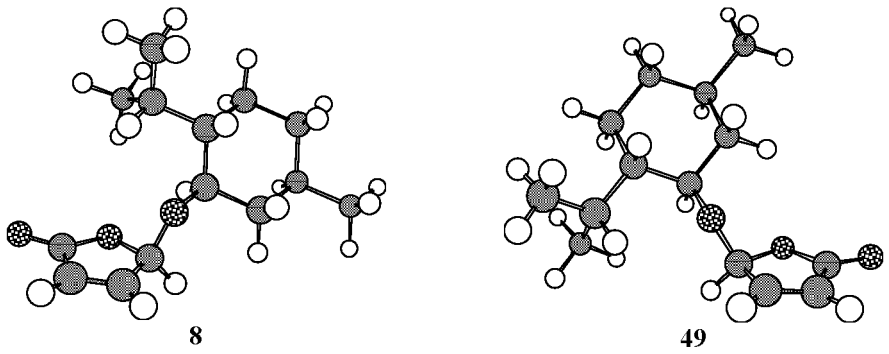


Fig. 16 Preferential conformations of (5*R*)- **8** and (5*S*)-5-*l*-menthyloxyfuran-2[5*H*]-one **49**.

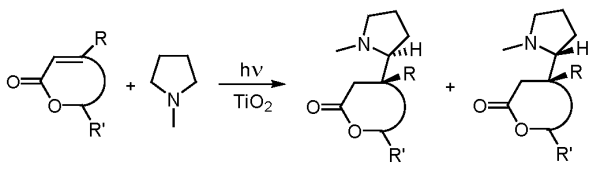
the contribution of the acetal function was estimated to be 70 % and that of the menthyl group to be 30 %.

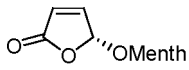
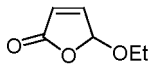
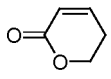
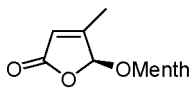
INORGANIC SEMICONDUCTORS AS HETEROGENEOUS PHOTOCATALYSTS

All previously discussed reactions use homogeneous photocatalysis with aromatic ketones as sensitizers. In order to perform the same reactions with heterogeneous photocatalysis, inorganic semiconductors such as TiO_2 or ZnS were chosen as sensitizers. After careful optimization, the addition of *N*-methylpyrrolidine **2** to menthyloxyfuranone **8** was performed with a yield of 90 % (entry 1, Table 2) [32]. The diastereoselectivity was the same as under homogeneous reaction conditions (compare Fig. 2). A variety of α,β-unsaturated lactones have been transformed in the same way, and yields up to 98 % (entry 3) were observed. As already mentioned above, the conversion of β-disubstituted unsaturated lactones is particular low (compare Table 1). Using heterogeneous photocatalysis, only a weak conversion of a corresponding derivative was observed (entry 5, Table 2). The mechanism is depicted in Fig. 17. After light absorption, an electron is transferred from the valence band to the conduction band. The semiconductor particle can now oxidize the tertiary amine. After deprotonation, α-aminoalkyl radicals **II** are generated. These radicals add to the furanone **8**, leading to oxoallyl radicals **III**. The high efficiency of reaction raises the question as to what happens with the electron in the conduction band. This electron can reduce the electrophilic radical **III**. After proton transfer from the surface of the semiconductor particle, the final product **9a,b** is obtained. It should be noted that the amine could be used as solvent. No additional polar solvent was necessary to stabilize intermediately generated radical ion pairs toward back electron transfer. Only in particular cases of homogeneous photocatalysis with aromatic ketones, the transformation could be performed with the amine as substrate and solvent.

The radical tandem addition cyclization reaction of menthyloxyfuranone **8** and *N*,*N*-dimethylaniline **37** (compare Fig. 11) was also studied using heterogeneous photocatalysis with inorganic semiconductors [33].

Table 2 Photoinduced radical addition of *N*-methylpyrrolidine **2** to various electron-deficient α,β-unsaturated lactones using TiO_2 as sensitizer.



Entry	α,β-Unsaturated lactone	Time of irradiation [h][a]	Conversion (%)	Yield[b] (%)
1		2.5	73	90
2		2	90	64
3		2	100	98
4	 [c]	3.5	100	90
5		13	20	76

[a]c(lactone): 5.10^{-1} mol L^{-1}, amine as solvent.
[b]Based on conversion of the α,β-unsaturated lactone.
[c]The starting concentration was 10^{-2} mol/L.

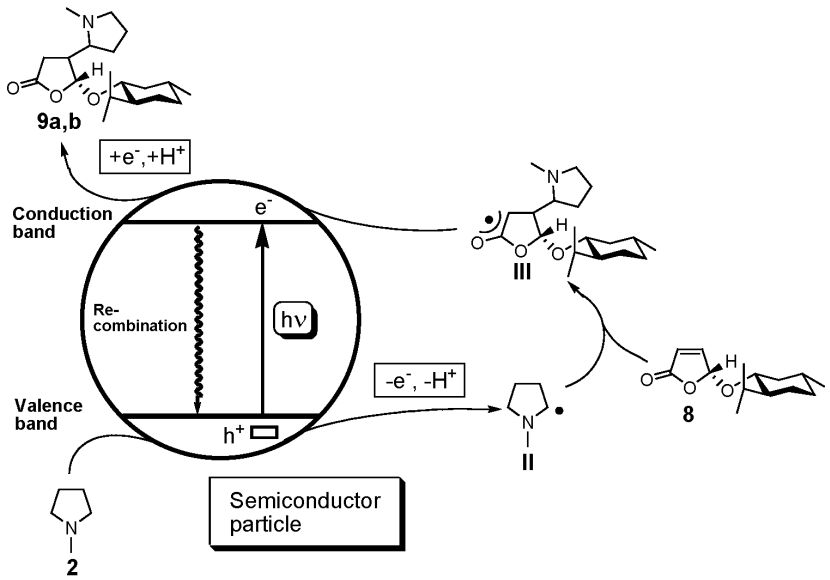


Fig. 17 Mechanism of the radical addition of tertiary amines to olefins using heterogeneous photocatalysts such as inorganic semiconductors.

CONCLUSIONS

Using photochemical electron transfer, numerous cyclic tertiary amines have been successfully added to electron-deficient C=C double bonds. The reaction was considerably improved when electron-donor-substituted aromatic ketones were used as sensitizer. The reaction was performed on large scale (15 g) and was applied to the asymmetric synthesis of alkaloids. In the presence of thiocarbonyl compounds such as dithiocarbamides, a larger variety of amines, in particular acyclic ones, have also been successfully added to alkenes. An influence on the regio- and stereoselectivity was detected. Using the new sensitizers, photoinduced radical tandem addition cyclization reactions with pyrrolidine derivatives possessing an unsaturated side-chain are possible. The reaction with *N*,*N*-dialkylated aniline derivatives posses a rearomatization step which led to considerable amounts of by-products. In the presence of ketones as mild oxidants, however, this side-reaction was completely suppressed and the reaction was applied to the asymmetric synthesis of a variety of nitrogen-containing heterocycles. Menthyloxyfuranone was frequently used in the reactions presented in this article, but this compound is an interesting synthon for asymmetric synthesis in general since almost all ground-state reactions are highly stereoselective. The origin of this selectivity can be attributed to preferential conformations of the menthyloxy substituent. Most of the reactions were performed with homogeneous photocatalysts. However, the photoinduced radical addition of tertiary amines to alkenes can also be carried out using heterogeneous photocatalysis with inorganic semiconductors as sensitizer.

ACKNOWLEDGMENTS

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