Diastereoselective Radical Tandem Addition-Cyclization Reactions of Aromatic Tertiary Amines by Semiconductor-Sensitized Photochemical Electron Transfer

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The diastereoselective radical tandem addition-cyclization reaction of *N*,*N*-dimethylaniline (**2**) with menthyloxyfuranone **1** was initiated by photochemically induced electron transfer using inorganic semiconductors (TiO_2, ZnS, SiC and SnO_2) as sensitizers. The rearomatization step, which also causes the partial reduction of **1**, was studied by isotopic labeling experiments using deuterated derivatives of **2**. The influence of the semiconductor surface on these processes has been characterized and compared with the results obtained under homogeneous conditions.

Introduction

Radical reactions have become an important tool in organic chemistry.[1,2] However, considerable effort is still needed to improve the selectivity of these reactions.[2,3] In this context, the radical addition of simple tertiary amines to alkenes represents an interesting example. Despite the great variety of products possessing biological activity, for instance in the field of pharmacology, this reaction has rarely been applied to organic synthesis since the products are isolated in low or moderate yields.[4] Recently, we reported an efficient photochemical method for the stereoselective radical addition of tertiary amines to electron-deficient double bonds.[5] The radical chain reaction was initiated by a single-electron transfer followed by a proton transfer from the tertiary amine to the electronically excited sensitizer.[6] Nucleophilic α-aminoalkyl radicals and stable ketyl radicals were formed as intermediates.[7−9] The best results were obtained when aromatic ketones possessing electron-donating substituents were used as the sensitizer. These sensitizers were used in catalytic amounts (5−10 mol%) of which up to 80% could be recovered after the reaction. More ambitious reactions like radical tandem addition-cyclization reactions have been successfully carried out under the same conditions.[10] For a recent review on these reactions see ref.[11]

We looked for a way to perform these reactions by heterogeneous catalysis since these methods often simplify the procedure as the separation of the catalyst is particularly easy. We wondered whether photochemically excited inorganic semiconductors such as TiO_2 could initiate the radical addition of tertiary amines to alkenes. The photochemical reactions of TiO_2 have been frequently studied: for detoxification of waste water,[12] oxidation and reduction reactions,[13,14] solar energy harvesting[15] or in the context of organic synthesis.[14,16] Metal sulfides like ZnS and CdS have been used for the formation of dehydrodimers of olefins or enol/allyl ethers and for the addition of allyl radicals to imines or diazo compounds.[17] Recently, we have shown that the radical addition of simple tertiary amines to electron-deficient alkenes can be successfully carried out with inorganic semiconductors like TiO_2 or ZnS.[18,19] The products were isolated with yields of up to 98% and a facial diastereoselectivity of > 95%. In this paper we report our first results of the tandem addition-cyclization reaction of aromatic tertiary amines with electron-deficient alkenes using semiconductors as the sensitizers.

Results and Discussion

The irradiation at 350 nm of a suspension of a semiconductor like TiO_2 (0.1 mol-equiv. with respect to **1**) in a solution of (5*R*)-menthyloxyfuran-2(5*H*)-one (**1**) and *N*,*N*-dimethylaniline (**2**) in acetonitrile yielded two stereoisomeric tetrahydroquinoline derivatives **3a** and **3b** and the lactone **4** (Scheme 1, Table 1). The major isomer of the tetrahydroquinolines, **3a**, results from radical attack *anti* to the menthyloxy substituent.[20] The side product **4** was formed in about the same yield as **3a**,**b** by the partial reduction of **1**. Traces of compound **5** were also formed in a radical-coupling step. Several other inorganic semiconductors were also tested as sensitizers. ZnS and SiC (Table 1, Entries 2 and 3) are more reductive than TiO_2 while SnO_2 (Entry 4) is more oxidative.[21] The formation of the reduction product **4** was only marginally reduced when SnO_2 was used. In the case of the less oxidative semiconductors, ZnS and SiC, the yield

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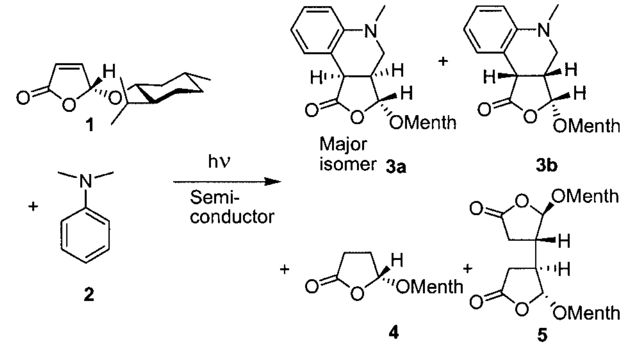
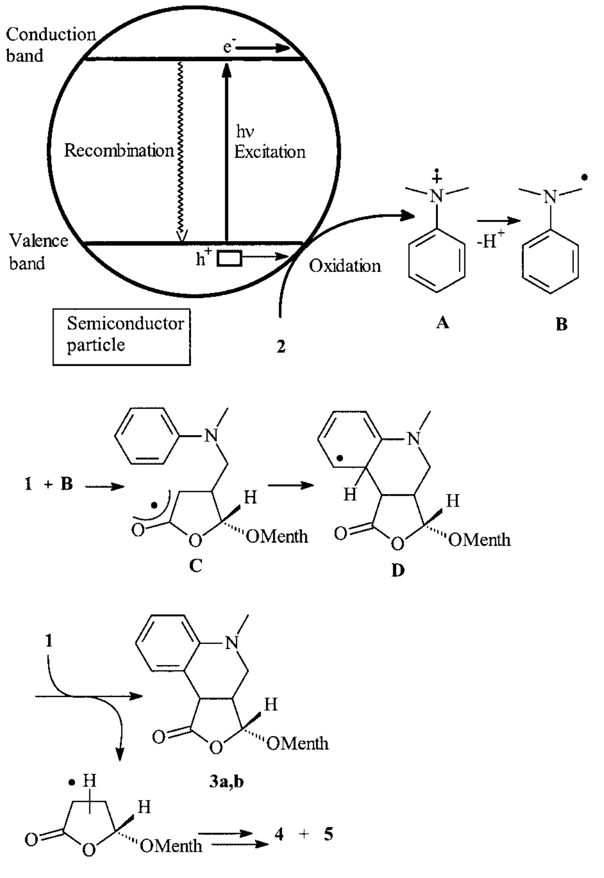


Scheme 1

Table 1. Tandem addition-cyclization of *N*,*N*-dimethylaniline (**2**) with (5*R*)-menthyloxyfuran-2(5*H*)-one (**1**) using different semiconductors as sensitizers (Scheme 1)

Entry	Semiconductor	Conversion[a] (%)	*de*[b] (%)	Yield (%)[c] 3a	3b	4	5
1	TiO_2	96	62	27	7	31	traces
2	ZnS	92	68	29	8	33	traces
3	SiC	95	50	31	9.5	31	traces
4	SnO_2	90	56	27	8	27	traces

[a] Conversion of **1**. [b] Determined from NMR spectra. [c] Yields of the isolated products with respect to the conversion of **1**.



Scheme 2

of the tetrahydroquinoline derivatives **3a**,**b** was slightly higher. Under the heterogeneous conditions described herein, the diastereoselectivity of **3a**,**b** was lower than that obtained under homogeneous conditions;[10] when the reaction was carried out in solution, **3a**,**b** were obtained with 92% diastereoselectivity. Furthermore, the facial diastereoselectivity depends on the semiconductor and varied between 50% in the case of SiC and 68% in the case of ZnS. These values were reproduced several times either by analyzing the resulting reaction mixtures or by separating and weighing the diastereoisomers. We attribute these differences in diastereoselectivity to orientation phenomena at the surface of the semiconductor. Probably, the conformational equilibrium is significantly influenced by the adsorption at the surface. Recently, we studied the effect of the conformational orientation of the menthyloxy substituent on the diastereoselectivity.[22]

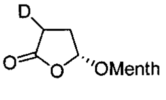
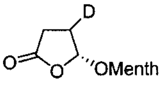
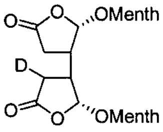
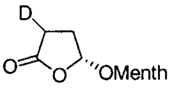
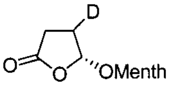
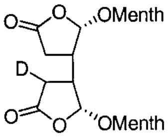
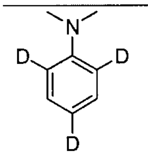
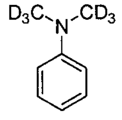
We propose the following mechanism for the radical tandem addition-cyclization reaction (Scheme 2). After photochemical excitation of the semiconductor particle and formation of an electron/hole pair, an electron is transferred from the aromatic tertiary amine to the hole in the valence band. The resulting radical cation **A** yields an α-aminoalkyl radical **B** by deprotonation. This nucleophilic radical readily adds to the electron-deficient alkene **1**. The resulting intermediate **C** possesses an electrophilic oxoallyl radical moiety which rapidly adds to the electron-rich aromatic ring in an intramolecular reaction. In order to obtain the final products, oxidative rearomatization must take place.

By using isotopic labeling, we have previously shown that under homogeneous conditions the intermediate **D** is capable of transferring a hydrogen atom to **1**.[10] Further steps lead to the formation of the reduction products **4** and **5**. We were able to completely suppress this side reaction by adding ketones like acetone to the reaction solution; ketones act as a mild oxidants replacing the menthyloxyfuranone **1** in the rearomatization step.

In order to gain an insight into the mechanism of the rearomatization step in the heterogeneous reaction, we have also performed the reaction with deuterated aniline derivatives. In this case, deuterium can be transferred to **1** and subsequently be detected in the side products **4** and **5**. This study was carried out using ZnS as the sensitizer. The results are shown in Table 2 and are compared with those obtained by homogeneous photocatalysis using aromatic ketones as sensitizers.

In the case of semiconductor photocatalysis and in contrast to homogeneous catalysis with Michler's ketone, no deuterium was transferred from the deuterated aniline derivative **2′** to **1**; lactones **4′**, **4′′** and **5′** were not formed, only undeuterated **4** and **5**. However, deuterium was transferred from **2′′** to **1**. In contrast to the corresponding reaction under homogeneous conditions, the deuterium was found exclusively at the α-position (**4′**). Similar to the homogeneous reaction, one deuterium atom was found at one of the α-positions of **5′**. However, the degree of deuteration was lower than in the homogeneous case. The reactions were also performed with TiO_2 as the sensitizer. In

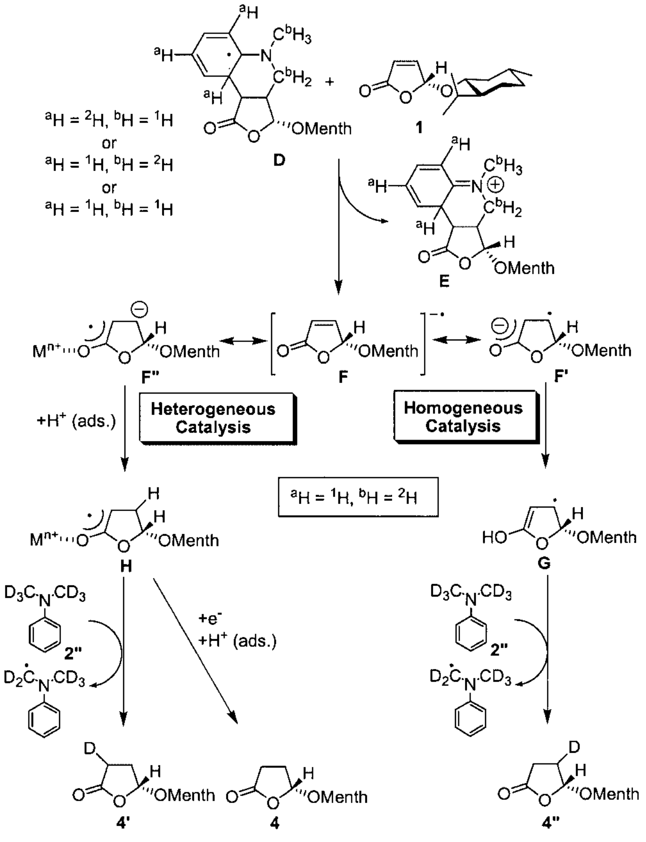
Table 2. Isotopic labeling experiments; transfer of deuterium from **2**′ or **2**′′ to **1** during the formation of **4** and **5**; yields (%) and percentage of single deuterium transfer (D_1); the percentage of deuterium in **3a**,**b** is > 95% (D_2 in the case of **2**′ and D_5 in the case of **2**")

	Heterogeneous catalysis						Homogeneous catalysis[10]					
												
	4'		**4"**		**5'**		**4'**		**4"**		**5'**	
		Yield		D_1	Yield	D_1		Yield		D_1	Yield	D_1
 **2'**		29[a]		0	5	0[b]	16		0	45	7	55
 **2"**	23		0	30	7	30[c]	0		15	55	7	55

[a] Incorporation of deuterium into **4** was not observed. [b] Conversion of 100% after 8 h of irradiation. [c] Conversion of 100% after 6.5 h of irradiation.

the case of **2**′, the reaction was slightly slower but the same results were obtained as for ZnS as far as the deuterium transfer was concerned. In the case of **2**′′, however, the reaction was significantly slower with TiO_2 and considerable degradation occurred during the prolonged irradiation time of 18 h (94% conversion). The kinetic isotope effect for the consumption of **1** was estimated to be 3.5.[23] Such effects were not observed in the homogeneous reaction.

The results clearly show significant differences between the heterogeneous and the homogeneous catalytic reactions in the rearomatization step. In order to explain these observations, we propose different mechanisms for the homogeneous and the heterogeneous catalyses (Scheme 3). As previously discussed, the rearomatization of **D** proceeds in two steps.[10,20] The radical anion **F** is obtained by electron transfer from **D** to **1**; cation **E**, which resembles the σ complex of an electrophilic substitution, is also produced. This step is followed by proton release from **E**. Two mesomeric structures of **F** preponderate depending on whether the intermediate is dissolved in the reaction mixture or adsorbed by the semiconductor via the carbonyl oxygen atom. (For references on complexation of carbonyl and carboxy functions, see refs.[19,24]) In the first case (**F**′), the negative charge is localized near the oxygen atom while in the second case (**F"**), this charge is displaced towards the β-carbon atom. The latter structure is favored in the heterogeneous system because the semiconductor particle is in a reductive environment (large excess of **2**) which makes the potential of the conduction band more negative. While it is irradiated, the particle acquires a negative charge by electron transfer from the tertiary amine to the hole in the valence band. This charge causes polarization of any adsorbed particles or molecules at the surface such that negative charge is pushed away from the surface. Hence, the negative charge of the adsorbed radical anion is pushed away from the surface. Despite the coulombic repulsion **F**′′ remains adsorbed on the semiconductor due to a strong specific metal−oxygen interaction.[13,24,25] Therefore, the radical

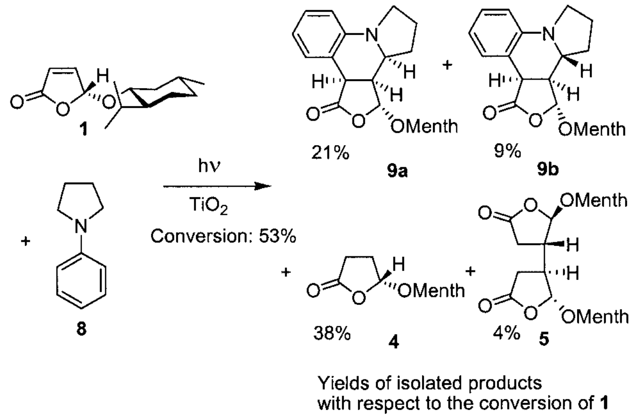


Scheme 3

anion **F''** is protonated at the β-position. In the case of homogeneous catalysis, however, protonation occurs at the enolate and after tautomerization, the proton or the deuterium (when **2'** is used) is localized at the α-position. Due to the fact that **F''** is adsorbed by the semiconductor, protonation preferentially takes place with protons that are on the surface (compare ref.[19,26]). This may explain why no deuterium is transferred when **2'** is used under heterogeneous reaction conditions. There is less deuterium on the semiconductor surface when the deuterium originates from the corresponding intermediate **E** ($^aH = {}^2H$, $^bH = {}^1H$), and therefore deuteration of **F''** is unlikely. The redox potential of **D** is sufficiently negative to reduce **1**, as is observed under homogeneous reaction conditions. The results presented here indicate that the rearomatization step is catalyzed by the semiconductor, but this must only be a surface effect since the reduction of **1** to **4** or **5** was not observed when aliphatic tertiary amines were added to **1** or similar electron-deficient alkenes under the same heterogeneous reaction conditions.[18,19] Therefore, it can be assumed that electron transfer from the conduction band to **1** does not occur. The isolation of tetrahydroquinoline derivatives **3a**,**b** in comparable yields to the reduction products **4** and **5** further supports the proposed mechanism.

When **2''** is used, the transfer of deuterium occurs one step later in the mechanism, as illustrated in Scheme 3. In the case of the homogeneous reaction, the hydroxyallyl intermediate **G** is deuterated leading to the menthyloxylactone **4''**. In the case of the heterogeneous reaction, the oxaallyl radical **H** is reduced either by electron transfer from the semiconductor particle followed by proton transfer leading to **4** or by deuterium transfer from **2''** leading to **4'**.[27] In contrast to the first hydrogen transfer, which almost only occurs from the semiconductor surface, the transfer from **2''** competes with that from the surface because the aromatic tertiary amine is applied in large excess. These effects also explain the results obtained for the deuteration of the second side product **5**. **F''** and **G** are nucleophilic in character and readily add to **1**. For the reasons indicated above, in this case again, deuterium is only transferred from **2''**.

When higher *N*-substituted aniline derivatives like *N*-phenylpyrrolidine (**8**) react with **1** under homogeneous catalysis conditions, secondary α-aminoalkyl radicals were formed as intermediates. Their addition to **1** occurred with complete facial diastereoselectivity. However, the configuration at the α-position to the nitrogen atom could not be controlled and two diastereoisomers **9a**,**b** were obtained in almost equal amounts.[10] We wondered whether this selectivity could be influenced by performing the reaction under heterogeneous conditions using TiO_2 as the sensitizer. Under the reaction conditions described above **8** was added to **1** (Scheme 4). The reaction rate was lower. After 8 h of irradiation, the conversion reached 53%. Once again the side products **4** and **5** were isolated. As was previously observed under the homogeneous reaction conditions, the products **9a**,**b** were obtained with complete facial stereoselectivity. However, compared with the homogeneous reaction, the stereoselectivity at the chiral center at the α-position to the nitrogen atom was significantly increased and the isomers **9a** and **9b** were formed in a ratio of about 2:1.



Scheme 4

Conclusions

We have shown that the diastereoselective tandem addition-cyclization reaction of *N*,*N*-dimethylaniline (**2**) with the menthyloxyfuranone **1** can be performed by photochemically induced electron transfer using inorganic semiconductors as sensitizers. In this way, the concept of heterogeneous catalysis was applied which simplified product isolation. The whole reaction occurred at the surface of the semiconductor particle. Two types of catalysis can be distinguished. On the one hand, steps involving electron transfer to the valence band (oxidation of the amine) or from the conduction band (reduction of the oxaallyl radicals) are observed. Of course, these steps can only occur with adsorbed molecules. On the other hand, steps involving only the surface of the semiconductor particles are detected (e.g. electron transfer from **D** to **1**). Significant differences in the rearomatization step of the homogeneous and heterogeneous reactions have been detected by isotopic labeling experiments. These differences result from polarization effects at the surface of the semiconductor. Based on these mechanistic results, we are currently trying to optimize the reaction and in particular to reduce the quantity of the reduction side products.

Experimental Section

General Methods: NMR spectra were recorded with a Bruker AC 250 (250 MHz for ^1H and 62 MHz for ^{13}C) or Bruker DRX 500 spectrometer (500 MHz for ^1H and 126 MHz for ^{13}C). Chemical shifts are given in ppm relative to tetramethylsilane as an internal standard. MS spectra were recorded with a JEOL D-300 spectrometer. [α] values were recorded with a Perkin−Elmer 241 polarimeter. Preparative chromatography was carried out with Merck art 9385 Kieselgel 60. Commercial TiO_2 (99% anatase, from AGROS), SnO_2 (from AGROS), ZnS (Prolabo) and SiC (Aldrich) were used as sensitizers.

Radical Tandem Reaction of Menthyloxyfuranone 1 with *N*,*N*-Dimethylaniline (2): After being degassed with argon, a well-stirred suspension of the semiconductor (0.1 mol-equiv. with respect to **1**) in a solution of (5*R*)-menthyloxyfuran-2(5*H*)-one (**1**) (500 mg, 2.1 mmol) and *N*,*N*-dimethylaniline (**2**) (6 mL) in acetonitrile (40 mL) was irradiated in a pyrex tube (diameter: 2 cm) at 350 nm (Rayonet reactor) for 5 h. The reaction mixture was filtered through Celite before evaporation of **2** and the solvent. The residue was purified and separated by flash chromatography on silica gel (eluent: ethyl acetate/petroleum ether).

Tetrahydroquinoline 3a: M.p. 116 °C. $[\alpha]_D^{21} = -206.9$ (c = 0.98, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ = 0.82 (d, J = 6.9 Hz, 3 H), 0.92 (d, J = 7.6 Hz, 3 H), 0.94 (d, J = 6.9 Hz, 3 H), 0.79−1.07 (m, 3 H), 1.21−1.47 (m, 2 H), 1.58−1.72 (m, 2 H), 2.07−2.17 (m, 2 H), 2.76−2.91 (m, 2 H), 2.85 (s, 3 H), 3.21 (m, 1 H), 3.57 (td, J = 10.7, 4.2 Hz, 1 H), 3.84 (d, J = 6.9 Hz, 1 H), 5.49 (d, J = 1.5 Hz, 1 H), 6.68 (d, J = 8.4 Hz, 1 H), 6.82 (td, J = 7.2, 1.1 Hz, 1 H), 7.17 (td, J = 8.4, 1.1 Hz, 1 H), 7.46 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.7, 20.8, 22.2, 23.2, 25.5, 31.3, 34.3, 39.4, 39.9, 40.4, 41.1, 47.7, 49.9, 77.2, 101.5, 112.0, 116.9, 118.4, 128.3, 130.5, 146.8, 175.5 ppm. $C_{22}H_{31}NO_3$ (357.23): calcd. C 73.90, H 8.99, N 3.92; found C 73.62, H 8.99, N 3.80. For further characterizations see ref.[10]

Tetrahydroquinoline 3b: $[\alpha]_D^{21} = -52.4$ (c = 0.42, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ = 0.71 (d, J = 6.9 Hz, 3 H), 0.82 (d, J = 7.6 Hz, 3 H), 0.89 (d, J = 6.9 Hz, 3 H), 0.79−1.07 (m, 3 H), 1.18−1.39 (m, 2 H), 1.52−1.65 (m, 2 H), 2.01−2.14 (m, 2 H), 2.81−2.94 (m, 2 H), 2.83 (s, 3 H), 3.21 (dd, J = 12.0, 4.7 Hz, 1 H), 3.56 (td, J = 10.7, 4.2 Hz, 1 H), 3.64 (d, J = 7.1 Hz, 1 H), 5.80 (d, J = 4.4 Hz, 1 H), 6.61 (d, J = 8.0 Hz, 1 H), 6.73 (td, J = 7.4, 1.0 Hz, 1 H), 7.11 (td, J = 8.5, 1.4 Hz, 1 H), 7.33 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.9, 20.9, 22.2, 23.2, 25.6, 31.4, 34.3, 38.0, 39.6, 39.8, 43.1, 47.4, 47.8, 78.6, 100.2, 111.8, 116.3, 117.8, 128.5, 130.7, 146.9, 173.9 ppm. $C_{22}H_{31}NO_3$ (357.23): calcd. C 73.90, H 8.99, N 3.92; found C 73.66, H 8.96, N 3.78. For further characterizations see ref.[10]

Lactone 4: M.p. 58 °C. $[\alpha]_D^{21} = -141.3$ (c = 0.86, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ = 0.78 (d, J = 6.9 Hz, 3 H), 0.88 (d, J = 7.1 Hz, 3 H), 0.93 (d, J = 6.6 Hz, 3 H), 0.65−1.07 (m, 3 H), 1.15−1.28 (m, 1 H), 1.30−1.45 (m, 1 H), 1.60−1.71 (m, 2 H), 2.03−2.15 (m, 3 H), 2.33 (m, 1 H), 2.43 (ddd, J = 18.1, 9.5, 3.4 Hz, 1 H), 2.67 (td, J = 17.6, 9.5 Hz, 1 H), 3.52 (td, J = 10.7, 4.2 Hz, 1 H), 5.72 (dd, J = 5.3, 1.9 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.5, 20.8, 22.2, 23.0, 25.4, 27.0, 29.1, 31.3, 34.2, 39.7, 47.7, 76.5, 100.3, 176.7 ppm. $C_{14}H_{24}O_3$ (240.17): calcd. C 69.95, H 10.07; found C 69.71, H 9.79. For further characterizations see ref.[10]

The reaction of **1** with deuterated aniline derivatives **2′** and **2′′** was carried out with ZnS and TiO_2 under the same conditions as described above. The irradiation times are indicated in Table 2. For the synthesis of **2′** see refs.[10,28] and for the synthesis of **2′′** see refs.[10,23e,29] The position and the amount of deuterium incorporated into **4′**, **4′′** and **5′** was determined by ^1H and ^{13}C NMR spectroscopy.

Coupling Product 5: $[\alpha]_D^{21} = -195.4$ (c = 0.84, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ = 0.78 (d, J = 7.3 Hz, 6 H), 0.88 (d, J = 7.3 Hz, 6 H), 0.96 (d, J = 6.5 Hz, 6 H), 0.72−1.12 (m, 6 H), 1.21−1.55 (m, 4 H), 1.62−1.84 (m, 4 H), 2.04−2.27 (m, 6 H), 2.50 (m, 2 H), 2.41 (dd, J = 17.8, 8.5 Hz, 2 H), 3.52 (td, J = 10.7, 4.2 Hz, 2 H), 5.53 (d, J = 2.3 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.8, 20.8, 22.3, 23.1, 25.5, 31.4, 32.1, 34.3, 39.7, 43.4, 47.8, 77.0, 102.0, 173.7 ppm. MS (EI, 70 eV): m/z (%) = 478 (54) [M^+], 373 (26), 335 (15), 229 (46), 216 (100), 139 (84). $C_{28}H_{46}O_6$ (478.66): calcd. C 70.54, H 9.31; found C 70.30, H 9.19. For further characterizations see ref.[10]

Radical Tandem Reaction of Menthyloxyfuranone 1 with *N*-Phenylpyrrolidine (8): After being degassed with argon, a well-stirred suspension of TiO_2 (12 mg, 0.15 mmol, 0.1 mol-equiv. with respect to **1**) in a solution of (5*R*)-menthyloxyfuran-2(5*H*)-one (**1**) (375 mg, 1.6 mmol) and *N*-phenylpyrrolidine (**8**) (5.5 g) in acetonitrile (30 mL) was irradiated in a pyrex tube (diameter: 2 cm) at 350 nm (Rayonet reactor) for 8 h. The reaction mixture was filtered through Celite before evaporation of **8** and the solvent. The residue was purified and separated by flash chromatography on silica gel (eluent: ethyl acetate/petroleum ether). After 8 h of irradiation the conversion was 53%.

Benzoindolizidine Derivative 9a: M.p. 130 °C. $[\alpha]_D^{21} = -115.2$ (c = 1.00, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ = 0.74 (d, J = 6.9 Hz, 3 H), 0.84 (d, J = 6.9 Hz, 3 H), 0.88 (d, J = 7.6 Hz, 3 H), 0.70−1.00 (m, 3 H), 1.03−1.38 (m, 2 H), 1.53−1.72 (m, 4 H), 1.83−2.14 (m, 3 H), 2.22 (dsept, J = 6.9, 2.7 Hz, 1 H), 2.30 (dd, J = 11.0, 7.2 Hz, 1 H), 2.68 (ddd, J = 11.0, 10.0, 5.7 Hz, 1 H), 3.05 (ddd, J = 14.8, 9.1, 4.6 Hz, 1 H), 3.36 (dd, J = 14.8, 8.8 Hz, 1 H), 3.51 (td, J = 10.7, 4.2 Hz, 1 H), 3.80 (d, J = 7.2 Hz, 1 H), 5.47 (s, 1 H), 6.45 (d, J = 8.0 Hz, 1 H), 6.69 (dd, J = 7.6, 7.2 Hz, 1 H), 7.08 (dd, J = 7.6, 7.2 Hz, 1 H), 7.39 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.7, 20.9, 22.2, 22.7, 23.2, 25.7, 30.8, 31.4, 34.3, 39.7, 40.0, 45.6, 46.6, 47.7, 55.9, 77.5, 100.3, 111.7, 115.5, 117.3, 128.3, 130.7, 144.3, 176.1 ppm. $C_{24}H_{33}NO_3$ (383.26): calcd. C 75.14, H 9.20, N 3.65; found C 74.99, H 8.96, N 3.56. For further characterizations see ref.[10]

Benzoindolizidine Derivative 9b: M.p. 124 °C. $[\alpha]_D^{21} = -109.9$ (c = 1.00, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ = 0.74 (d, J = 6.9 Hz, 3 H), 0.83 (d, J = 6.9 Hz, 3 H), 0.93 (d, J = 7.6 Hz, 3 H), 0.69−0.97 (m, 3 H), 1.10−1.34 (m, 2 H), 1.51−1.67 (m, 4 H), 1.81−2.09 (m, 3 H), 2.16 (dsept, J = 6.9, 2.7 Hz, 1 H), 2.83−2.99 (m, 2 H), 3.18 (ddd, J = 11.8, 6.9, 3.4 Hz, 1 H), 3.40−3.55 (m, 2 H), 3.89 (d, J = 9.5 Hz, 1 H), 5.63 (d, J = 6.5 Hz, 1 H), 6.48 (dd, J = 8.4, 0.8 Hz, 1 H), 6.68 (dt, J = 7.2, 0.8 Hz, 1 H), 7.07 (dt, J = 8.4, 0.8 Hz, 1 H), 7.42 (dd, J = 7.2, 0.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.9, 21.0, 22.3, 22.7, 23.1, 25.3, 27.3, 31.4, 34.3, 40.0, 43.7, 45.6, 47.1, 48.0, 55.8, 78.2, 101.0, 112.3, 116.8, 118.0, 128.4, 129.2, 146.1, 174.4 ppm. $C_{24}H_{33}NO_3$ (383.26): calcd. C 75.14, H 9.20, N 3.65; found C 74.93, H 8.91, N 3.59. For further characterizations see ref.[10]

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[1] [1a] J. Fossey, D. Lefort, J. Sorba, *Free Radicals in Organic Chemistry*, Wiley, Chichester, **1995**. [1b] B. Giese, *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon Press, Oxford, **1986**. [1c] D. P. Curran, *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming, M. F. Semmelhack), Pergamon Press, Oxford, **1991**, vol. 4, pp. 715−777 and 779−831.

[2] *Radicals in Organic Synthesis* (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**.

[3] D. P. Curran, N. A. Porter, B. Giese, *Stereochemistry of Radical Reactions*, Wiley-VCH, Weinheim, **1996**.

[4] [4a] W. H. Urry, O. O. Juveland, *J. Am. Chem. Soc.* **1958**, *80*,

3322−3328. [4b] R. C. Cookson, J. Hudec, N. A. Mirza, *J. Chem. Soc., Chem. Commun.* **1968**, 180. [4c] E. S. de Alvarenga, J. Mann, *J. Chem. Soc., Perkin Trans. 1* **1993**, 2141−2142. [4d] E. Farrand, J. Mann, *J. Chem. Soc., Perkin Trans. 1* **1997**, 1083−1084.

[5] [5a] S. Bertrand, N. Hoffmann, J. P. Pete, *Eur. J. Org. Chem.* **2000**, 2227−2238. [5b] S. Bertrand, C. Glapski, N. Hoffmann, J. P. Pete, *Tetrahedron Lett.* **1999**, *40*, 3169−3172. [5c] S. Bertrand, N. Hoffmann, J. P. Pete, *Tetrahedron Lett.* **1999**, *40*, 3173−3174.

[6] [6a] G. J. Kavarnos, *Fundamentals of Photoinduced Electron Transfer*, VCH, New York, **1993**. [6b] J. Mattay, *Synthesis* **1989**, 233−252. [6c] J. Mattay, M. Vondenhof, *Top. Curr. Chem.* **1991**, *159*, 219−255. [6d] A. Albini, E. Fasani, M. Mella, *Top. Curr. Chem.* **1993**, *168*, 143−173. [6e] G. Pandey, *Top. Curr. Chem.* **1993**, *168*, 175−221. [6f] F. Lewis, *Adv. Electron Transfer Chem.* **1996**, *5*, 1−39. [6g] J. Cossy, J. P. Pete, *Adv. Electron Transfer Chem.* **1996**, *5*, 141−195. [6h] U. C. Yoon, P. S. Mariano, R. S. Givens, B. W. Atwater III, *Adv. Electron Transfer Chem.* **1994**, *4*, 117−205. [6i] S. K. Khim, E. Cederstrom, D. C. Ferri, P. S. Mariano, *Tetrahedron* **1996**, *52*, 3195−3222. [6j] *Photoinduced Electron Transfer* (Eds.: M. A. Fox, M. Chanon), Elsevier, Amsterdam, **1988**, parts A−D. [6k] M. Julliard, M. Chanon, *Chem. Rev.* **1983**, *83*, 425−506. [6l] G. Pandey, *Synlett* **1992**, 546−552. [6m] J. Cossy, *Radicals in Organic Synthesis* (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**, vol. 1, p. 229−249.

[7] [7a] P. Renaud, L. Giraud, *Synthesis* **1996**, 913−926. [7b] M. Schmittel, A. Burghart, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2550−2589. [7c] T. Linker, M. Schmittel, *Radikale und Radikalionen in der Organischen Synthese*, Wiley-VCH, Weinheim, **1998**. [7d]E. Meggers, E. Steckhan, S. Blechert, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2137−2139. For structure and stability, see: [7e] D. D. M. Wayner, K. B. Clark, A. Rauk, D. Yu, D. A. Armstrong, *J. Am. Chem. Soc.* **1997**, *119*, 8925−8932. [7f] G. W. Dombrowski, J. P. Dinnocenzo, S. Farid, J. L. Goodman, I. R. Gould, *J. Org. Chem.* **1999**, *64*, 427−431.

[8] For the influence of polarity effects on the reactivity of radicals, see: [8a] B. Giese, W. Mehl, *Tetrahedron Lett.* **1991**, *32*, 4275−4278. [8b] D. Lefort, J. Fossey, J. Sorba, *New J. Chem.* **1992**, *16*, 219−232. [8c] J. M. Tedder, *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 401−410. [8d] H. Fischer, L. Radom, *Angew. Chem. Int. Ed.* **2001**, *40*, 1340−1371. [8e] A. R. Cherkasov, M. Jonsson, V. I. Galkin, R. A. Cerkasov, *Russ. Chem. Rev.* **2001**, *70*, 1−22.

[9] For the competive addition of ketyl radicals and α-aminoalkyl radicals, see: C. Brulé, N. Hoffmann, *Tetrahedron Lett.* **2002**, *43*, 69−72.

[10] S. Bertrand, N. Hoffmann, S. Humbel, J. P. Pete, *J. Org. Chem.* **2000**, *65*, 8690−8703.

[11] T. R. Rheault, M. P. Sibi, *Synthesis* **2003**, 803−819.

[12] O. Legrini, E. Oliveros, A. M. Braun, *Chem. Rev.* **1993**, *93*, 671−698.

[13] M. A. Fox, M. T. Dulay, *Chem. Rev.* **1993**, *93*, 341−357.

[14] M. A. Fox, *Electron Transfer in Chemistry* (Ed.: V. Balzani), vol. 5, part 3 (Ed.: I. R. Gould), Wiley-VCH, Weinheim, **2001**, pp. 271−311.

[15] M. Grätzel, J. E. Moser, *Electron Transfer in Chemistry* (Ed.: V. Balzani), vol. 5, part 3 (Ed.: I. R. Gould), Wiley-VCH, Weinheim, **2001**, pp. 589−644.

[16] [16a] Y. Li, *Organic Photochemistry* (Eds.: V. Ramamurthy, K. S. Schanze), Marcel Dekker, Inc., New York, **1997**, pp. 295−323. [16b] P. Pichat, *Catal. Today* **1994**, *19*, 313−334. [16c] L. Cermenati, C. Richter, A. Albini, *Chem. Commun.* **1998**, 805−806. [16d] L. Cermenati, M. Mella, A. Albini, *Tetrahedron* **1998**, *54*, 2575−2582. [16e] L. Cermenati, D. Dondi, M. Fagoni, A. Albini, *Tetrahedron* **2003**, *59*, 6409−6414.

[17] H. Kisch, M. Hopfner, *Electron Transfer in Chemistry* (Ed.: V. Balzani), vol. 4, part 1 (Ed.: S. Fukuzumi), Wiley-VCH, Weinheim, **2001**, pp. 232−275.

[18] S. Marinković, N. Hoffmann, *Chem. Commun.* **2001**, 1576−1578.

[19] S. Marinković, N. Hoffmann, *Int. J. Photoenergy* **2003**, *5*, 175−182.

[20] S. Bertrand, N. Hoffmann, J. P. Pete, V. Bulach, *Chem. Commun.* **1999**, 2291−2292.

[21] More oxidative semiconductors possess energetically low valance and conduction band-edges. In contrast, more reductive semiconductors possess energetically high valence and conduction band-edges. For tables and diagrams see refs.[17,24,25a] and: D. Wöhrle, M. W. Tausch, W.-D. Stohrer, *Photochemie*, Wiley-VCH, Weinheim, **1998**; T. Yamamoto, *Synlett* **2003**, 425−450; R. Memming, *Semiconductor Electrochemistry*, Wiley-VCH, Weinheim, **2001**; M. Grätzel, *Photocatalysis* (Eds.: N. Serpone, E. Pelizetti), Wiley, New York, **1989**, pp. 123−157. Oxidative or reductive character can also be induced by doping; see ref.[25e] and: N. S. Lewis, M. L. Rosenbluth, *Photocatalysis* (Eds.: N. Serpone, E. Pelizetti), Wiley, New York, **1989**, pp. 45−98.

[22] S. Marinković, C. Brulé, N. Hoffmann, E. Prost, J. M. Nuzillard, V. Bulach, *J. Org. Chem.* **2004**, *69*, 1646−1651.

[23] For isotope effects in SET reactions of *N*,*N*-dimethyleaniline (**2**), see: [23a] J. Dreyer, K. S. Peters, *J. Phys. Chem.* **1996**, *100*, 19412−19416. [23b] D. Döpp, J. Heufer, *Tetrahedron Lett.* **1982**, *23*, 1553−1556. [23c] J. Lin, Dissertation, Gerhard-Mercator-Universität-Gesamthochschule Duisburg, **1994**. [23d]M. Hata, Y. Hirano, M. Tsuda, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 1577−1583. [23e] J. P. Dinnocenzo, S. B. Karki, J. P. Jones, *J. Am. Chem. Soc.* **1993**, *115*, 7111−7116. [23f] E. Baciocchi, O. Lanzalunga, A. Lapi, L. Manduchi, *J. Am. Chem. Soc.* **1998**, *120*, 5783−5787. [23g] M. Bronstrup, D. Schröder, H. Schwarz, *Can. J. Chem.* **1999**, *77*, 774−780.

[24] A. L. Linsebigler, G. Lu, J. T. Yates Jr., *Chem. Rev.* **1995**, *95*, 735−758.

[25] [25a] A. Hagfeldt, M. Grätzel, *Chem. Rev.* **1995**, *95*, 49−68. [25b] F. Seker, K. Meeker, T. F. Kuech, A. B. Ellis, *Chem. Rev.* **2000**, *100*, 2505−2536. [25c] C. A. Koval, J. N. Howard, *Chem. Rev.* **1992**, *92*, 411−433. [25d] J. Eriksen, *Photoinduced Electron Transfer* (Eds.: M. A. Fox, M. Chanon), Elsevier, **1988**, part A, chapter 1.10. [25e] J. A. Turner, *J. Chem. Educ.* **1983**, *60*, 327−329.

[26] M. R. Hoffmann, S. T. Martin, W. Choi, D. W. Bahnemann, *Chem. Rev.* **1995**, *95*, 69−96.

[27] This reduction can also occur in two steps. Electron transfer from $\mathbf{2}''$ to the electrophilic oxaallyl radical **H** is followed by proton transfer.

[28] [28a] G. H. Prenner, J. M. Polson, S. I. Daleman, K. Reid, *Can. J. Chem.* **1993**, *71*, 417−426. [28b] Y. Miura, H. Oka, E. Yamano, M. M. Musiani, P. Rossi, *Synthesis* **1980**, 743−746.

[29] [29a] C. Pac, T. Tosa, H. Sakurai, *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1169−1175. [29b] J. Thesing, *Chem. Ber.* **1954**, *87*, 692−699.

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