Diastereoselective Tandem Addition−Cyclization Reactions of Unsaturated Tertiary Amines Initiated by Photochemical Electron Transfer (PET)

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Polycyclic molecules and tetrahydroquinoleines were obtained in a tandem reaction involving the diastereoselective addition of α-aminoalkyl radicals to (5*R*)-5-menthyloxy-2[5*H*]-furanone **1**. The facial diastereoselectivity on **1** is ≥90%. The α-aminoalkyl radicals were produced from tertiary amines by photochemical-induced electron transfer. When *N*,*N*-dialkylanilines **19** were used as starting tertiary amines, a rearomatization step was involved and important side reactions of **1** were observed. A mechanistic study involving isotopic labeling of the starting amine indicated that the byproducts resulted from reduction of **1** during the rearomatization process. An efficient optimization of the reaction was obtained by simply adding acetone or cyclopentanone as mild oxidants to the reaction mixture. The side products resulting from reduction of the furanone **1** were completely suppressed under these conditions, and the yields of the tetrahydroquinolines **21a**−**i**, **22a**−**f**, and **26g**−**i** were doubled.

Introduction

Radical reactions have become an important tool in preparative organic chemistry,[1] but considerable efforts are still needed to improve their selectivity to become competitive with polar reactions.[2]

The radical addition of simple tertiary amines to alkenes has been known for a long time.[3] However, up to now, the yields of these reactions were low to moderate, independent of the initiation of the radical chain process. Various methods have been proposed to produce α-aminoalkyl radicals,[4] but only few reports describe their direct formation from tertiary amines. This type of nucleophilic radicals can be easily added to electron-deficient alkenes thus making available γ-aminobutyric acid derivatives and a large variety of biological active compounds. Among the initiation processes applied to the generation of α-aminoalkyl radicals, the photochemical electron transfer (PET)[5] has also been tested, and most frequently, ketones such as acetophenone and benzophenone were used as sensitizers. Unfortunately, the yields of these reactions were moderate and never exceeded 60% despite the fact that the sensitizers were used in stoichiometric amounts.[6] Furthermore, large quantities of reduction products, pinacols and other side products resulting from a degradation of the sensitizer or from a polymerization of the starting materials were also observed.

Recently, we reported that the radical addition of tertiary amines to electron-deficient alkenes became very efficient when aromatic ketones, having electron-donor substituents and T_1 states with $\pi\pi^*$ or charge-transfer character, were used as a sensitizer.[7−9] In contrast to their analogues acetophenone and benzophenone, which possess T_1 states with $n\pi^*$ character, the quantum yields of photoreduction or pinacolization of aromatic ketones having T_1 states with $\pi\pi^*$ or charge transfer character

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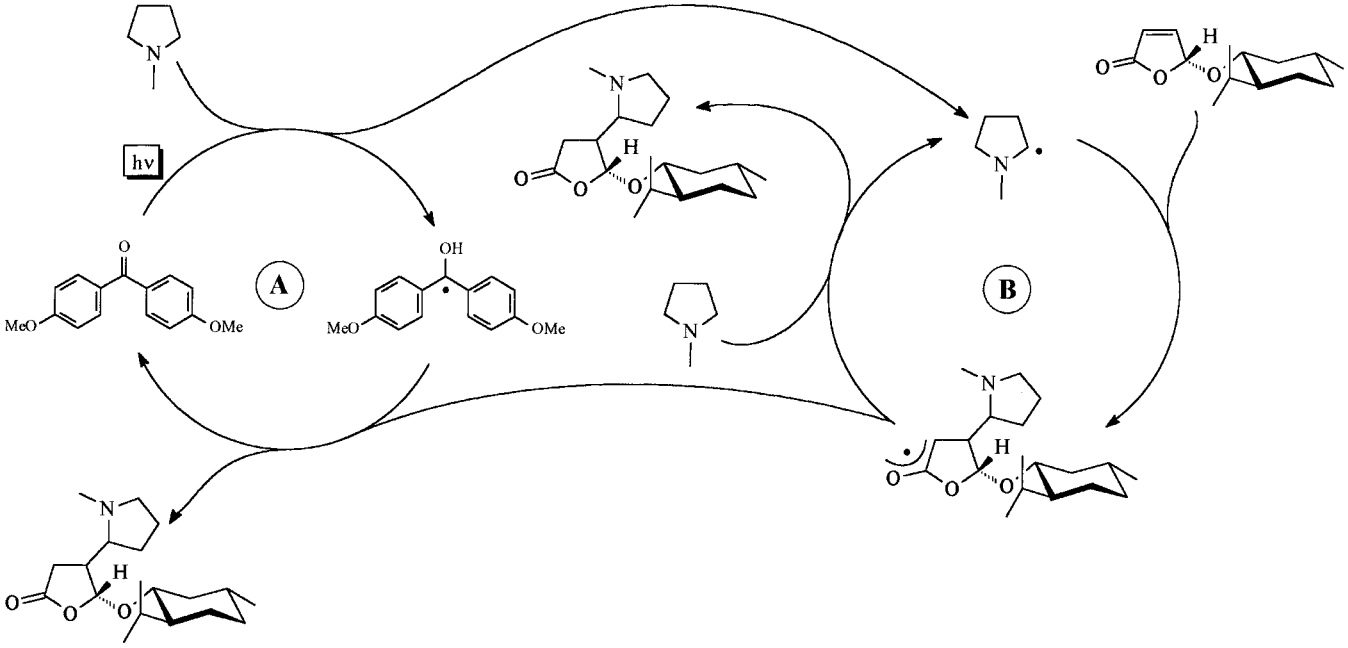
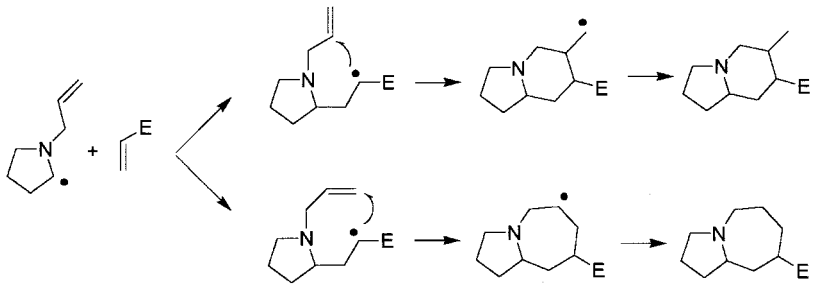
Scheme 1. Proposed Mechanism for the Efficient Stereoselective Radical Addition of Tertiary Amines to Electron-Deficient Alkenes



Scheme 2. Possible Pathways for Radical Tandem Reactions of Unsaturated Tertiary Amines with Electron-Deficient Alkenes



is only very small.[10] However, if 4,4′-bis-*N*,*N*-dimethylaminobenzophenone (Michler's ketone) is used in the presence of amines polymerization reactions can be initiated.[11] As a result of their lack of reactivity, aromatic ketones with electron-donating substituents have rarely been considered as efficient sensitizers in radical reactions induced by PET.[12,13] Nevertheless, we recently found that the initiation of a radical chain by a PET process between a tertiary amine and aromatic ketones such as 4,4′-dimethoxybenzophenone as a sensitizer can induce very efficient radical reactions. Interestingly, most of the sensitizer could be recovered after the reaction, despite the fact that it was used in very small quantities. These observations led us to conclude that the efficiency of the initiation process was due to the high delocalization and stability of the aromatic ketyl radicals and to the inefficient back electron transfer within the radical ion pair.[8] The efficient regeneration of the sensitizer was explained by a hydrogen transfer from the ketyl radical derived from the aromatic ketone to the oxoallyl radical involved in the radical chain of cycle A (Scheme 1). The chain process of cycle B was the result of a hydrogen abstraction from the tertiary amine by the same oxoallyl radical to regenerate the α-aminoalkyl radical and produce the final adduct. With *N*-alkyl pyrrolidines, the radical is preferentially formed on the pyrrolidine ring.

The preference for nucleophilic radical addition to electron-deficient alkenes led us to consider the reactivity of *N*-alkenylpyrrolidines and aniline derivatives. In the presence of electron-deficient alkenes in the reaction mixture, either an intramolecular cyclization or an intermolecular addition process could be possible with the α-aminoalkyl radical and tandem reactions might be expected. With *N*-allylpyrrolidines the intramolecular process should be less favorable for reasons of ring strain, and we anticipated that the intermolecular process might be possible for the nucleophilic α-aminoalkyl radical. After addition to the electron-deficient alkene, an electrophilic radical intermediate should be formed in the first step of a radical tandem process. In the second step, an intramolecular attack of the electrophilic radical on the electron-rich double bond should be realized by a 7-*endo* or 6-*exo trig* process. Finally, the products would result from a hydrogen abstraction by the cyclized radical intermediate as shown in Scheme 2.

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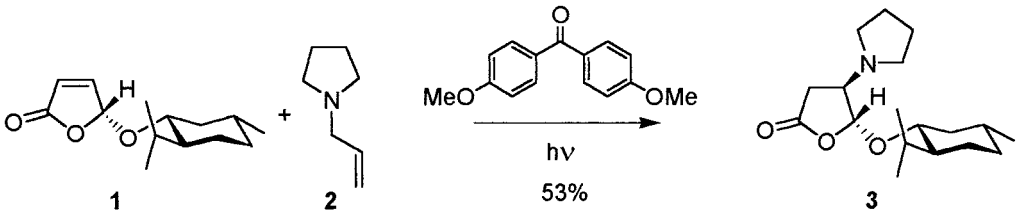
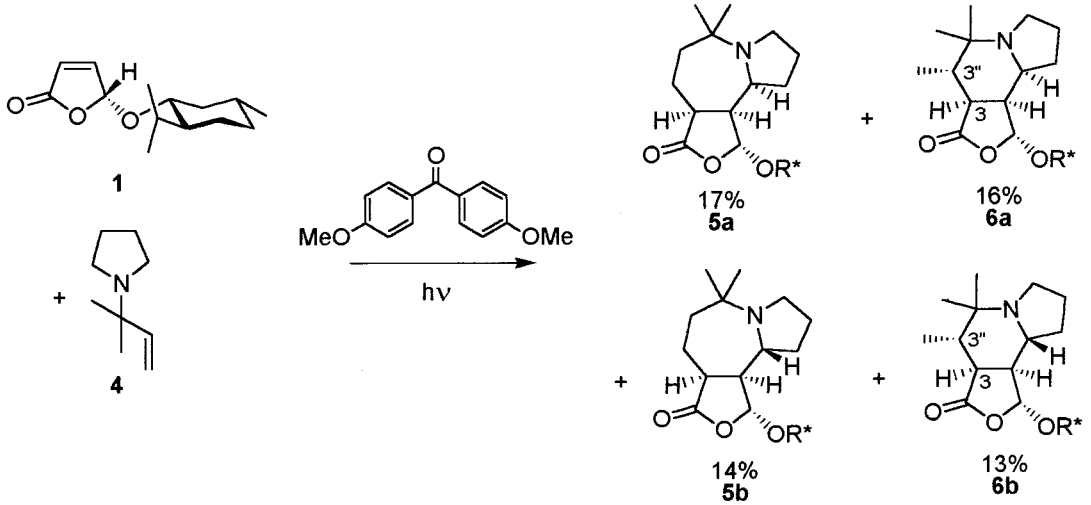
Scheme 3. Reaction of *N*-Allylpyrrolidine 2 with Furanone 1 under Photochemically Induced Electron Transfer Conditions



Scheme 4. Formation of Perhydroazaazulene and Indolizidine Derivatives in the Radical Tandem Reaction of the Unsaturated Tertiary Amine 4 with 1



We now report that the production of α-aminoalkyl radicals by a PET process can be applied to the stereoselective radical tandem reaction[14] of unsaturated tertiary amines with the electron-deficient alkene (5*R*)-5-menthyloxy-2[5*H*]-furanone **1**. This chiral synthon, which is readily available and frequently used in asymmetric synthesis,[15] has been recently applied to radical reactions.[7,8,16,17]

Results and Discussion

Addition of *N*-Allylpyrrolidine Derivatives to (5*R*)-5-Menthyloxy-2[5*H*]-furanone 1. We started our investigation by irradiating a solution of *N*-allylpyrrolidine **2**, (5*R*)-5-menthyloxy-2[5*H*]-furanone **1**, and catalytic amounts (5 mol %) of 4,4′-dimethoxybenzophenone as sensitizer. No radical addition of α-aminyl radicals to the furanone **1** could be observed in the reaction mixture. The only new product (**3**), which could be isolated, resulted from a Michael reaction (Scheme 3),[8] indicating that pyrrolidine had been liberated during the irradiation. This secondary amine, known to add rapidly to **1**,[18] might be initiated by hydrogen abstraction on the allyl side chain.

To avoid this complication, we replaced **2** by the dimethylated product **4**. Four new compounds **5a,b** and **6a,b** were isolated in almost equal amounts, resulting from a consecutive two-step radical process (Scheme 4). The products correspond to *endo trig* (**5a,b**) and *exo trig* (**6a,b**) cyclization. The configuration of all chiral centers created during the reaction has been controlled, except for the chiral center at the α position of the nitrogen atom. As expected, the attack of the α-aminoalkyl radical was highly stereoselective and *anti* with respect to the menthyloxy substituent on the furanone **1**.

When the alkyne derivative **7** was irradiated under the same conditions, a higher regioselectivity was observed (Scheme 5), with the formation of only *endo dig* products **8** (32%) and **9** (29%). Here again, the attack of the α-aminoalkyl radical was highly stereoselective and *anti* with respect to the menthyloxy substituent, while the configuration of the chiral center at the α position of the nitrogen atom was not controlled. Formation of the conjugated lactone **9** implied an isomerization process of the deconjugated intermediate **10**, which could not be characterized in the reaction mixture. Under the reaction conditions, a corresponding conjugated product is not formed from lactone **8**. Furthermore, when **8** was dissolved in triethylamine, no isomerization could be detected after 1 week at room temperature.

The structure and the relative configuration of **5a,b**, **8**, and **9** have been determined by using NMR spectroscopy. The configuration of the asymmetric carbon created at the α position to the nitrogen was determined by NOE measurements (Scheme 6). The absence of the NOE on H4, when the irradiation was carried out on the acetal

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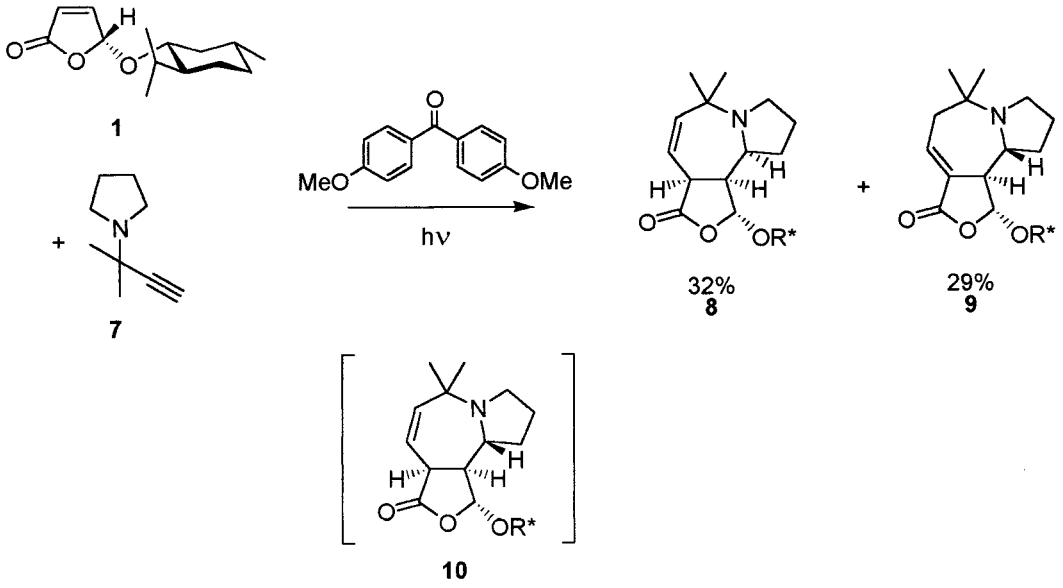
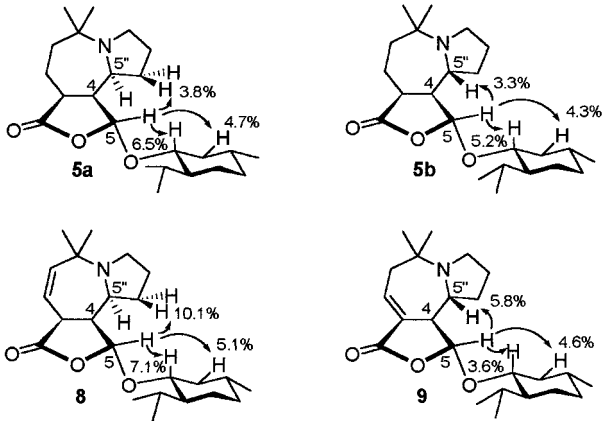
Scheme 5. Radical Tandem Reaction of *N*-(3,3-Dimethylpropin-3-yl)pyrrolidine 7 with 1



Scheme 6. Determination of the Configuration of Compounds 5a, 5b, 8, and 9 by NOE Measurements



proton H5, additionally confirmed the radical attack *anti* with respect to the menthyloxy substituent.

Compounds **6a,b** and **7a**, which possess NMR data very similar to the corresponding data of analogues **5a,b**, also result from an *anti* addition of the α-aminoalkyl radical on the lactone ring. Furthermore, the stereochemistry of the methyl group at 3″ appeared to be the same for **6a** and **6b**. The coupling constant $J_{(H3'',H3)} = 4.5$ Hz in both compounds indicated an *anti* orientation of the hydrogen atoms.[19]

To explain why the conjugation of the unsaturated lactone depends on the configuration at C5″ and why the corresponding enol intermediate led by tautomerization to the conjugated and compound **9**, we carried out a theoretical investigation. To save computational requirements, we replaced the menthyloxy substituent by a methoxy group and we optimized the structures of the corresponding deconjugated lactones **11** and **14** and their conjugated isomers **13** and **12**, respectively (Figure 1). Our investigation started with a conformational search.[20,21]

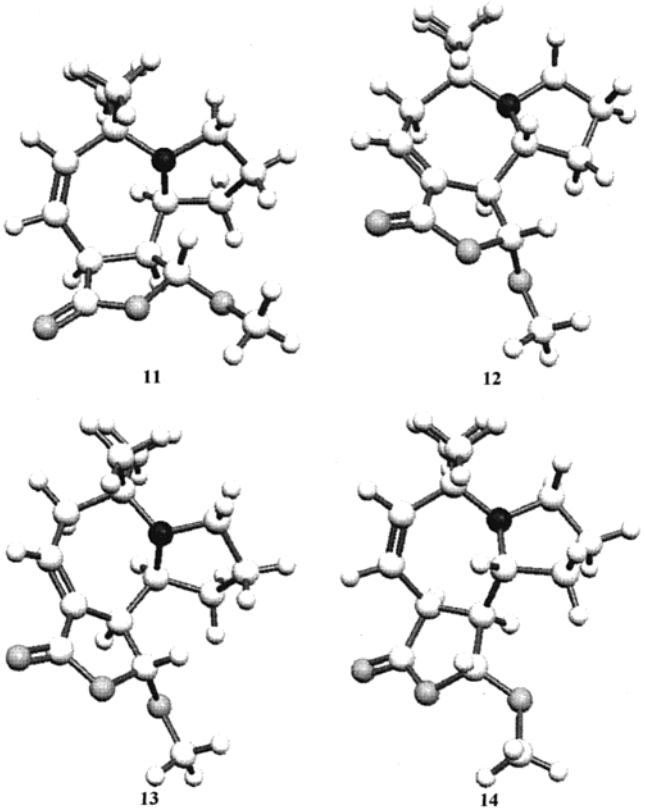


Figure 1. Shape of the isomers **11**−**14** as optimized at the B3LYP/6-31G level of calculation. The nitrogen atom is dark, and the oxygen atoms are gray.

The structures of lowest energy were reoptimized[22] at the Density Functional Theory level B3LYP/6-31G for a better comparison of the energies of the various compounds.

These results show that the compounds **12** and **13** possessing a conjugate C=C double bond are more stable than their isomers **11** and **14**. The energy gain by conjugation with the C=O bond is almost the same for both diastereoisomers **13** and **12** (Table 1). Therefore, thermodynamic stability cannot explain why the isomer

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(20) One thousand structures were requested to be processed. The lowest structures of each compound were found about 80 times.

(21) (a) Macromodel 6.0, Columbia University, **1997**. (b) Allinger, N. L.; Yuh, Y. H.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8552−8566.

Scheme 7. Radical Tandem Reaction of *N,N*-Dimethylaniline 19a and Furanone 1 under PET Conditions

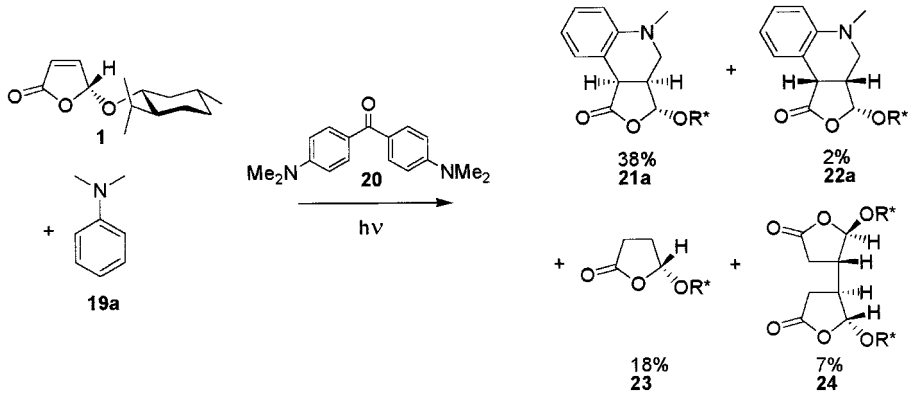

Table 1. Density Functionnal Theory (B3LYP) Computational Results Using the 6-31G Basis Set unless Otherwise Specified

	DFT B3LYP		
	absolute energy (au)	relative energy (kcal/mol)	
11	−826.27969	0.0	
13	−826.28777	−5.1	−5.1
14	−826.28173	−1.3	
12	−826.29096	−7.1	−5.8
15	−826.24279	+23.2	
16	−826.25006	+18.6	−4.6
17	−825.74151[a]		
18	−825.75403[a]		−7.9[a]

[a] 6-31+G basis set.

13 was not formed by tautomerization of **11** in basic conditions. To get some information on the kinetic control, we also performed calculations on the corresponding dienol (**15**, **16**) and dienolate (**17**, **18**) intermediates (Table 1, Figure 2). As required by the anionic character of the dienolates, diffuse functions were added to the basis set B3LYP/6-31+G. In the case of the dienolates the calculations show a significant energy difference between the two diastereoisomers **17** and **18** (7.9 kcal). That **17** is less stable is certainly due to the fact that the torsion angle between the C=C bond and the enolate moiety is about 153° (compared to 171° for **18**), which diminishes the conjugation. The difference between this torsion angle is even more important for the corresponding dienols **15** (140°) and **16** (167°).

From these calculations, we conclude that the absence of isomerization for **8** (Scheme 5) might be due to kinetic reasons and especially to the difficulty in obtaining the corresponding enol or enolate.

Addition of *N,N*-Dialkylaniline Derivatives to 1. To extend the scope of the radical tandem reactions, we became interested in reactions of aromatic tertiary amines under similar conditions. We first examined the addition of *N,N*-dimethylaniline **19a**. When a solution of **1** was irradiated in the presence of a large excess of *N,N*-dimethylaniline **19a** and a catalytic amount of Michler's ketone **20** as sensitizer, we obtained the tetrahydroquinolines **21a** and **22a** with a diastereomeric excess of 90%. (Scheme 7). Similar tandem reactions have already been reported to give low yields or to result from side reactions.[23,24] Unfortunately, in our preliminary experiments, the isolated yields were also low and the side products **23** and **24**, resulting from the reduction of **1**, were obtained in similar amounts. Normally, the efficiency of forming the reductive duplication product **24** should be sensitive to the relative concentration of the starting materials. Accordingly, when the concentration of **1** (5×10^{-3} mol L^{-1}) was decreased, the side product **24** disappeared from the reaction mixture, while the yield of the lactone **23** increased (23%). On the basis of the NMR data, we established that the adducts **21a** and **22a** contained a tetrahydroquinoline structure. The configuration of the major isomer **21a** was determined by X-ray analysis.[16]

On the basis of these observations, we concluded that the formation of the desired tetrahydroquinolines **21a** and **22a** and the formation of the side products **23** and **24** could be linked. As tetrahydroquinoline derivatives possess a great pharmaceutical interest,[25] we tried to optimize the reaction and reduce or eliminate the formation of byproducts. To improve the synthesis and to verify the origin of the side reactions of **1**, we carried out the reaction with the aniline derivatives **19a′** and **19a″** deuterated at the *ortho* and *para* position of the aromatic ring or at the *N*-methyl groups respectively (Scheme 8). In the presence of **19a′**, a deuterium transfer to the furanone **1** was observed at the α position of the lacton group of **23′** and at one of the corresponding positions of the bislactone **24′**. When the reaction was carried out with amine **19a″** possessing two CD_3 groups, deuterium transfer could be detected at the β position of the lactone **23″** and again at one of the α positions of the bislactone **24′**.

(22) *Gaussian 98*, Revision A.7; Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, Jr. J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A.; Gaussian, Inc.: Pittsburgh, PA, 1998.

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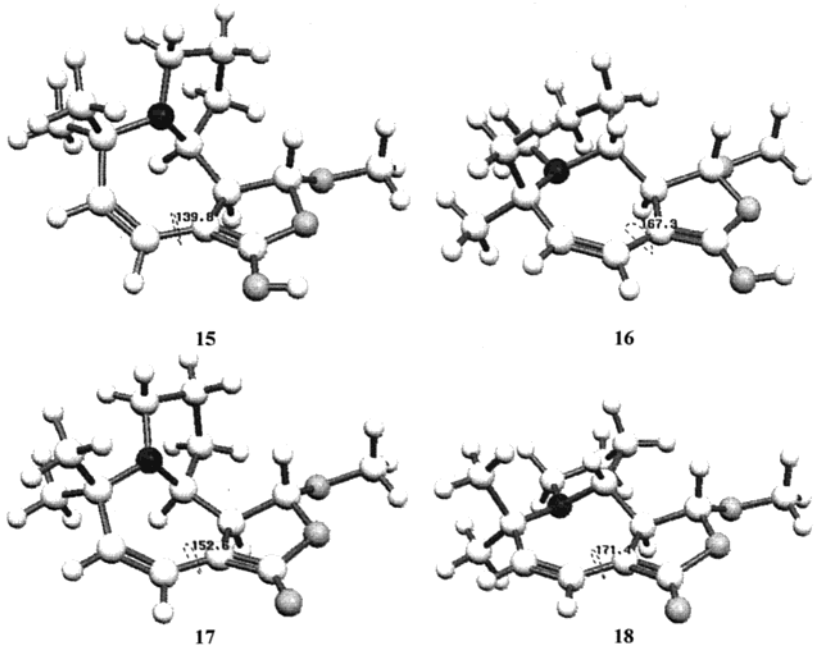
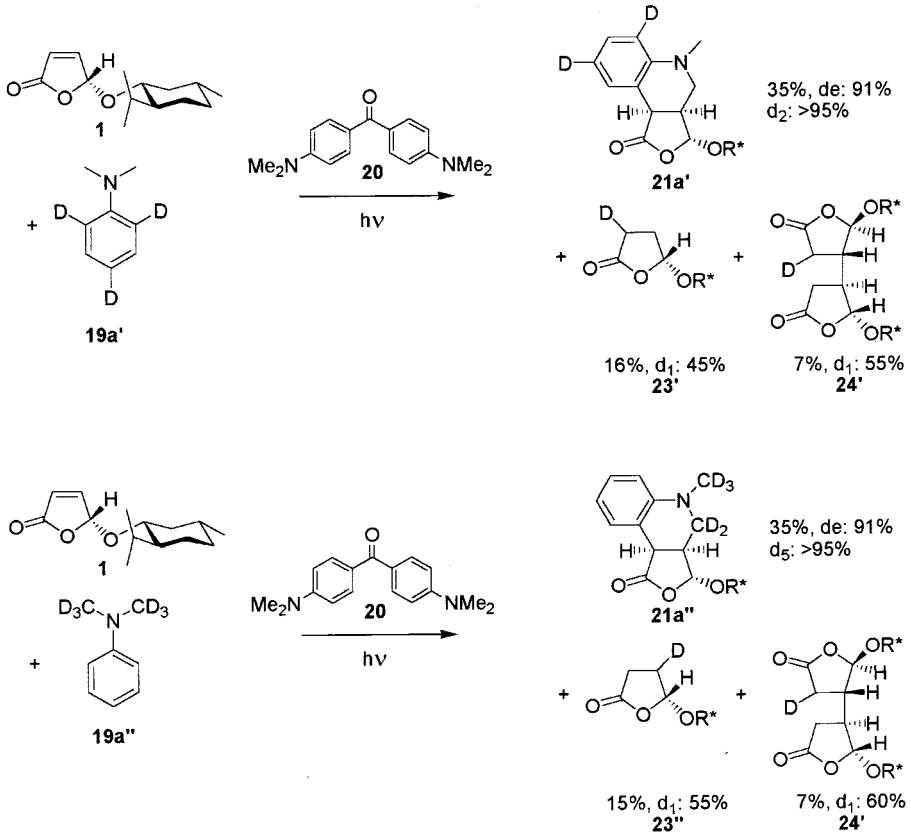


Figure 2. Shape of the enols **15** and **16** as optimized at the B3LYP/6-31G level of calculation. Shape of the enolates **17** and **18** as optimized at the B3LYP/6-31+G level of calculation. The nitrogen atom is dark, and the oxygen atoms are gray. The number in degrees indicates the dihedral angle between the double bonds.

Scheme 8. Radical Tandem Reaction of the Deuterated *N,N*-Dimethylanilines 19a′ and 19a″ and Furanone 1[a]

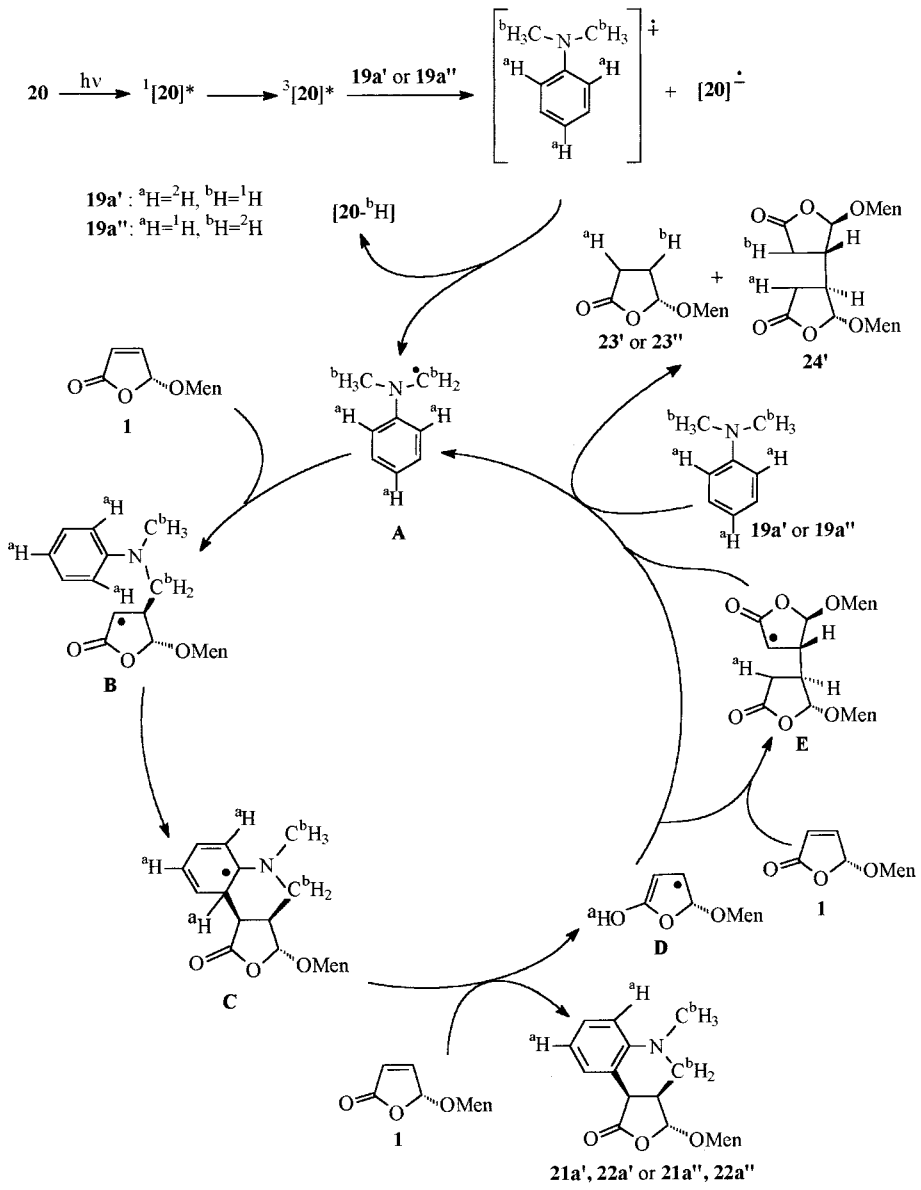


[a] The degree of deuteration in the products has been determined by signal integration of the corresponding protons in the ^{1}H NMR spectra.

The degree of deuteration was determined by integration of the corresponding signals of the ^{1}H NMR spectra. The intensity of the signals at 2.41 and 2.65 ppm for the protons at α position of lactone **23′** and at 2.28 ppm for the β protons of lactone **23″** were decreased with respect to the non deuterated analogues. The same effect was observed for the signal at 2.81 ppm for the one proton at the α position of the bis lactone **24′**.

The results of the isotopic labeling experiments can be explained by the mechanism depicted in Scheme 9.

Scheme 9. Mechanism of the Radical Tandem Reaction of the Deuterated *N,N*-Dimethylanilines 19a′ and 19a″ and Furanone 1



During the initiation step, nucleophilic α aminoalkyl radicals **A** are generated via a photochemical induced electron transfer.[5,26] After addition to **1**, the electrophilic oxoallyl radical **B** adds to the phenyl ring by an intramolecular reaction. A rearomatization process is needed to produce the final products **21a′** and **22a′**.

During the process, a deuterium is transferred from the former *ortho* position of the aromatic ring to **1**. Although such rearomatization processes are frequently observed in photochemical and radical reactions, little information is available on the nature of the oxidant and the mechanistic details.[24] After deuterium transfer to **1**, an O-deuterated oxyallyl radical **D** is produced. Then, **D** undergoes a hydrogen abstraction from the methyl group of **19a′**. After tautomerization, lactone **23′** is obtained possessing one deuterium at the α position.

The deuterium transfer from the methyl group of **19a″** to the *β* position of the lactone **23″** can be explained by the same mechanism. In this case, deuterium transfer from the CD_3 group of **19a″** to the *β* position of the hydroxyallyl radical **D** occurs.

To explain the incorporation of a deuterium atom at only one α position of compound **24′**, the addition of the O-deuterated oxyallyl intermediate **D** to **1**, followed by hydrogen abstraction from the *N*-methyl groups of **19a′**, has to be considered. When **19a″** was used, the deuterium transfer from the CD_3 group to the intermediate **E** occurs.

The labeling experiments indicate that a hydrogen atom has to be transferred to the oxygen atom of a carbonyl group. Such an unusual transfer might involve a two-step process. First, a single electron transfer

(26) (a) Peters, K. S.; Cashin, A.; Timbers, P. *J. Am. Chem. Soc.* **2000**, *122*, 107−113. (b) Dreyer, J.; Peters, K. S. *J. Phys. Chem.* **1996**, *100*, 19412−19416. (c) Zhang, X.; Yeh, S.-R.; Hong, S.; Freccero, M.; Albini, A.; Falvey, D. E.; Mariano, P. S. *J. Am. Chem. Soc.* **1994**, *116*, 4211−4220. (d) Pac, C.; Tosa, T.; Sakurai, H. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1169−1175. (e) Su, Z.; Falvey, D. E.; Yoon, U. C.; Mariano, P. S. *J. Am. Chem. Soc.* **1997**, *119*, 5261−5262. (f) Su, Z.; Mariano, P. S.; Falvey, D. E.; Yoon, U. C.; Oh, S. W. *J. Am. Chem. Soc.* **1998**, *120*, 10676−10686. (g) Arimitsu, S.; Masuhara, H.; Mataga, N.; Tsubomura, H. *J. Phys. Chem.* **1975**, *79*, 1255−1259. (h) Hendriks, B. M. P.; Walter, R. I.; Fischer, H. *J. Am. Chem. Soc.* **1979**, *101*, 2378−2383. (i) Bartholomew, R. F.; Davidson, R. S. *J. Chem. Soc. (C)* **1971**, 2342−2346. (j) Döpp, D.; Heufer, J. *Tetrahedron Lett.* **1982**, *23*, 1553−1556. (k) Lin, J. Ph.D. Thesis, Universität Gesamthochschule Duisburg, 1994.

Scheme 10. Rearomatization Step of the Formation of the Tetrahydroquinoline Derivatives 21a and 22a

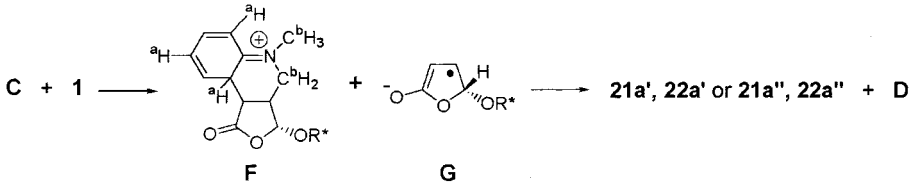


Table 2. Reaction of Furanone 1 with *N,N*-Dimethylaniline 19a in the Presence of Ketones as Mild Oxidants

ketone	quantity (equiv)	irradiation time[a] (min)	yield of **21a**, **22a** (%)
acetone	5	360	73
acetone	30	360	77
acetone	solv	420	71
cyclopentanone	5	360	78

[a] Michler's ketone 20 was used as sensitizer.

between the radical **C** and the carbonyl might produce a well stabilized carbenium ion **F** and an enolate anion **G** (Scheme 10). After consecutive proton (deuterium) transfer from **F** to **G**, a hydroxyallyl radical such as the intermediate **D** and the final products **21a** and **22a** would be formed.

As shown in Scheme 9, the furanone **1** can act as an electrophilic alkene as well as an oxidant in the rearomatization step of radical **C**. To avoid the formation of the side products **23** and **24** and to make the reaction more efficient and applicable in organic synthesis, **1** had to be replaced by a mild oxidant in the oxidation step. We considered that simple ketones might play this role. When acetone or cyclopentanone were added in excess to the reaction mixture, the formation of side products was completely suppressed while the yields of tetrahydroquinolines were doubled (Table 2). Under these reaction conditions, ketyl radicals **H** were also generated (Scheme 11). Such nucleophilic radicals are known to add efficiently to **1**.[17] When indeed acetone or cyclopentanone were introduced in the reaction mixture, we could detect traces of the corresponding product **25**.

We wondered if aliphatic ketones could replace aromatic ketones in the initiation of the radical process. When the irradiation of **1** and *N,N*-dimethylaniline was carried out at $\lambda = 300$ or 350 nm in the presence of a large excess of acetone but in the absence of the sensitizer **20**, only a slow and very unselective reaction was observed. The complex mixture obtained under these conditions is very similar to what is obtained for a radical addition of tertiary amines to alkenes when conventional sensitizers such as acetophenone or benzophenone are used to induce the electron transfer.[6−8]

Under optimized conditions, we next examined the reaction of **1** with several *N,N*-dimethylaniline derivatives (**19a**−**f**) (Scheme 12). In all cases, the tetrahydroquinoline derivatives (**21a**−**f** and **22a**−**f**) were obtained in high yield with 90% de. The reaction of the *meta* toluidine derivative **19e** yielded regioisomers **21e**, **22e** and **21′e**, **22′e**. The azasteroid like compounds **21f**, **22f** were obtained from the reaction of the tetrahydronaphthylamine derivative **19f**.

When the reaction was carried out with other *N,N*-dialkylated aniline derivatives, like *N,N*-diethylaniline **19g**, the radical attack occurred diastereospecifically *anti* with respect to the menthyloxy substituent of **1** (Scheme 13). However, the configuration of the chiral center at the α position of the amine nitrogen was not controlled. Similar results were already obtained for the radical addition of simple tertiary amines to electron-deficient alkenes such as **1**.[7,8] The reaction of **1** with *N*-phenylpyrrolidine **19h** and *N*-phenylpiperidine **19i** under the same conditions produced benzoindolizidine (**21h**, **26h**) and benzoquinolizidine derivatives (**21i**, **26i**), repectively. It has to be noted that the stereoselectivity was higher when phenylpiperidine **19i** was used as the tertiary amine.

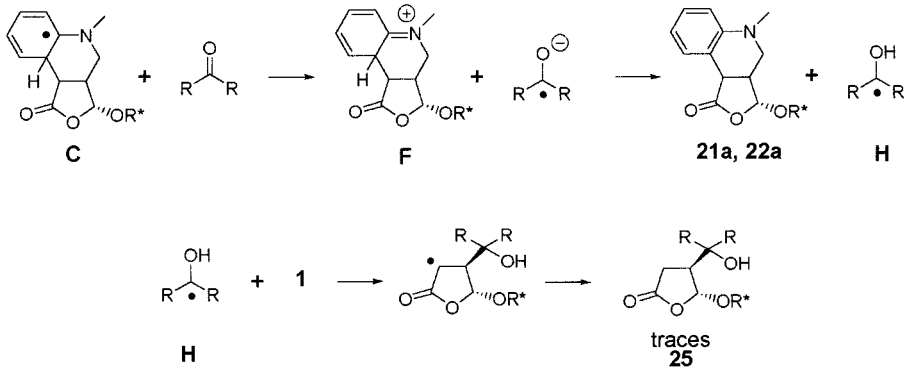
The relative configurations of **21g** and **26g** have been determined by NOE measurements (Scheme 14). The structure of **21h,i** and **26h,i** was assigned by comparison with **21g** and **26g**, which present analogue NMR data.

When radicals add to disubstituted sp^2 carbons, an important rate decrease is observed. To test the influence of two *ortho* substituents on the addition process, we next examined the reactivity of **27** with two protected *ortho* positions of the aromatic ring. In the reaction of *N*-mesitylpyrrolidine **27** with **1**, no tandem reaction could be detected in the reaction mixture. Two addition products **28** and **29** were formed in a faster reaction very similar to the radical reaction of *N*-alkylpyrrolidine derivatives to electron-deficient alkenes such as **1** (Scheme 15).[7,8] The high reactivity observed for **27** can be explained by a suppression of nitrogen lone pair conjugation with the aromatic π-system. As a result of steric hindrance of the *ortho* methyl groups, the aryl ring and the pyrrolidine ring are oriented in an orthogonal arrangement. Interestingly, the important steric hindrance of the mesityl substituent also causes an increase in the diastereoselectivity of the chiral center formed at the α position of the nitrogen atom. The diastereomeric ratio of 80:20 differs significantly from the ratio of 55:45 generally observed for the radical addition of *N*-alkylpyrrolidine derivatives.[8]

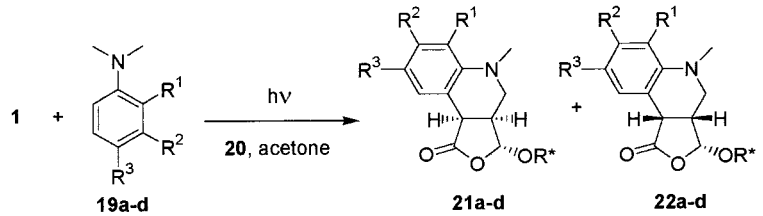
Conclusion

We have described an efficient and diastereoselective tandem addition reaction, involving a radical process, between (5*R*)-5-menthyloxy-2[5*H*]-furanone **1** with *N,N*-dialkylanilines and pyrrolidine derivatives possessing an unsaturated side chain on the nitrogen atom. Polycyclic molecules having a tetrahydroquinoline skeleton, indolizidine, benzoquinolizidine, and perhydroazaazulene derivatives, were obtained in this way. The radical chain process was initiated by a photochemically induced electron transfer. During the reaction of the *N,N*-dialkylanilines, considerable amounts of reduction products of **1** were formed in side reactions. A mechanistic study, based on isotopically labeled *N,N*-dimethylaniline, indicated that the furanone **1** was involved in a rearomatization step. When ketones such as acetone or cyclopentanone were added to the reaction mixture as hydrogen acceptors, the yield of the tetrahydroquinoline derivatives doubled and the formation of reduction side products was completely suppressed.

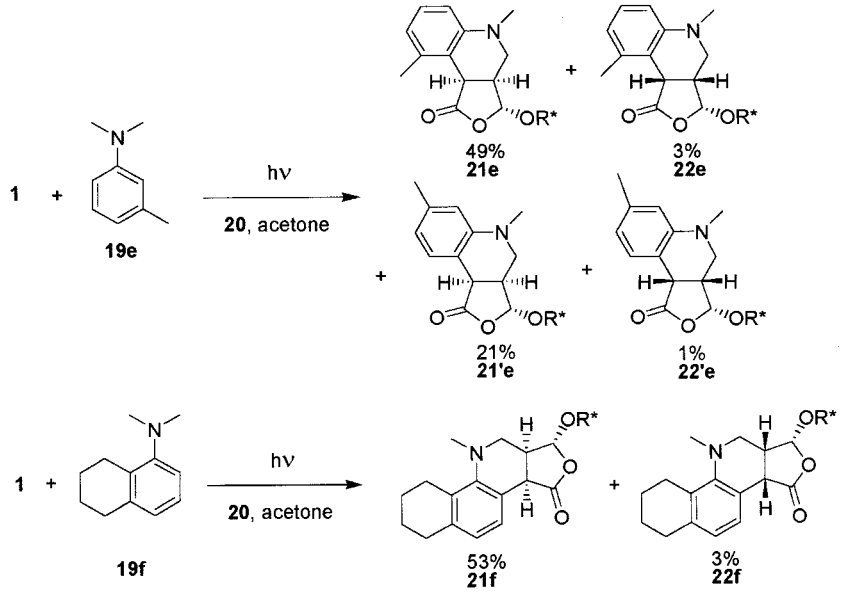
Scheme 11. Rearomatization Step of the Formation of the Tetrahydroquinoline Derivatives 21a and 22a in the Presence of Ketones as Mild Oxidants



Scheme 12. Asymmetric Synthesis of Tetrahydroquinoline and Azasteroid Derivatives by the Radical Tandem Addition of *N,N*-Dimethylaniline Derivatives with 1



19	R^1	R^2	R^3	21	22
a	H	H	H	74%	3%
b	Me	H	H	60%	2%
c	H	H	Me	78%	3%
d	Me	Me	H	64%	3%

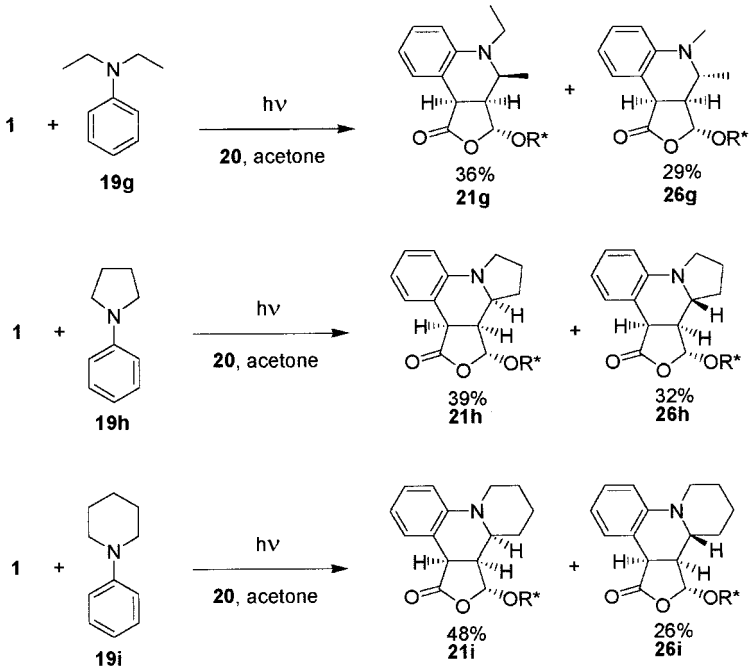


Experimental Section

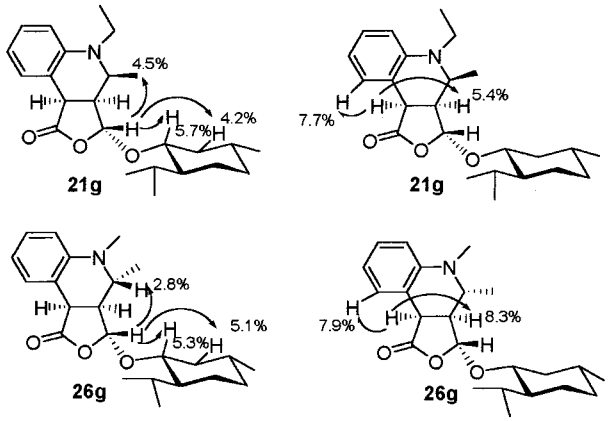
General Methods. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker AC 250 (250 MHz for ^{1}H and 62 MHz for ^{13}C) or Bruker DRX 500 (500 MHz for ^{1}H and 126 MHz for ^{13}C). Coupling constants are reported in hertz. Chemical shifts are given in ppm relative to tetramethylsilane as an internal standard. IR spectra were recorded with MIDAC Prospect IR (FTIR). MS spectra were recorded with JEOL D-300. Preparative chromatography was carried out with Merck 9385 Kieselgel 60. GC was carried out on a Hewlett-Packard 6890HP with a capillary column (HP-1). Specific rotation values were recorded in CH_2Cl_2 as solvent with a Perkin-Elmer 241 Polarimeter. Acetonitrile was dried with calcium hydride, then with magnesium sulfate before distillation. Starting amines were dried and distillated on calcium hydride. (5*R*)-5-Menthyloxy-2-[5*H*]-furanone **1** was prepared from furfural and (−)-menthol according to literature procedure.[15]

Irradiations of the solution were carried out in Pyrex tubes (Φ = 1 cm), at 350 nm, with a Rayonet apparatus (model RPR-100) from the Southern New England Ultraviolet Company. Solutions were degassed with argon before irradiation. HPLC chromatography was carried out on a SHIMADZU LC-10AS (detector, UV SPD-10A; column, Lichrosorb Si60 7 μm; length = 25 cm, i.d. = 9 mm, o.d. = 0.5 in.

Scheme 13. Asymmetric Synthesis of Nitrogen-Containing Polycyclic Compounds by Radical Tandem Addition of *N,N*-Dialkylaniline Derivatives 19g−i with 1



Scheme 14. Determination of the Configuration of Compounds 21g and 26g by NOE Measurements



Reaction of (5*R*)-5-Menthyloxy-2-[5*H*]-furanone 1 with *N*-(1,1-Dimethylallyl)pyrrolidine 4 and *N*-(1,1-Dimethylpropargyl)pyrrolidine 7. Preparation of Amine 4. Product **4** was synthesized according to a literature procedure.[27] A solution of vinylmagnesium chloride (23.7 mL, 40 mmol) was added dropwise to a solution of 2-methyl-2-pyrrolidinonitrile (5.5 g, 40 mmol) in THF (40 mL) that was cooled to 0 °C. The solution was then stirred at room temperature for 4 h. Diethyl ether (100 mL) was added. The resulting solution was washed with water. The aqueous phase was extracted twice with diethyl ether (50 mL). The combined organic phases were dried with $MgSO_4$. The solvent was evaporated, and the residue was distilled under reduced pressure. Yield: 3.12 g (56%). Bp_{20}: 58 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.11 (s, 6H), 1.57 (m, 4H), 2.53 (m, 4H), 4.95 (d, J = 6.2, 1H), 5.02 (d, J = 0.8, 1H), 5.87 (dd, J = 6.2, 0.8, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 23.7, 24.2, 46.0, 56.0, 112.5, 143.7.

Preparation of Amine 7.[28] A mixture of 1,1-dimethylpropargylamine (16.6 g, 200 mmol) and K_2CO_3 (13.8 g, 100 mmol) in 20 mL of ethanol was added to 1,4-dibromobutane. The mixture was then stirred at 60 °C for 72 h. A solution of K_2CO_3 (10%) and 100 mL ether was added. The organic phase was washed with brine and dried over $MgSO_4$. The solvent was evaporated, and the residue was recrystallized from ethyl acetate/petroleum ether. Yield: 24.11 g (88%). Mp: 75 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.41 (s, 6H), 1.80 (m, 4H), 2.23 (s, 1H), 2.72 (m, 4H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 23.6, 29.4, 47.9, 53.6, 71.1, 85.4. IR (KBr): ν 3135, 2970, 2810, 2080, 1455, 1365, 1190, 1015.

A solution of (5*R*)-5-menthyloxy-2[5*H*]-furanone **1** (950 mg, 4 mmol), the pyrrolidine derivative **4** or **7** (16 mmol), and 4,4′dimethoxybenzophenone (45 mg, 0.2 mmol) in acetonitrile (80 mL) was irradiated at 350 nm for 4 h. In the case of the reaction of **4**, the solvent and the excess of the unsaturated amine were evaporated and the residue was subjected to flash chromathography (eluent, ethyl acetate/petroleum ether 1/5). In the case of the reaction of **7**, most of the solvent was evaporated. The residue (mixture of crystals of **7** and reaction products) was washed with petroleum ether. The solvent of the washing solution was evaporated and the residue residue was subjected to flash chromathography (eluent, ethyl acetate/petroleum ether 1/5).

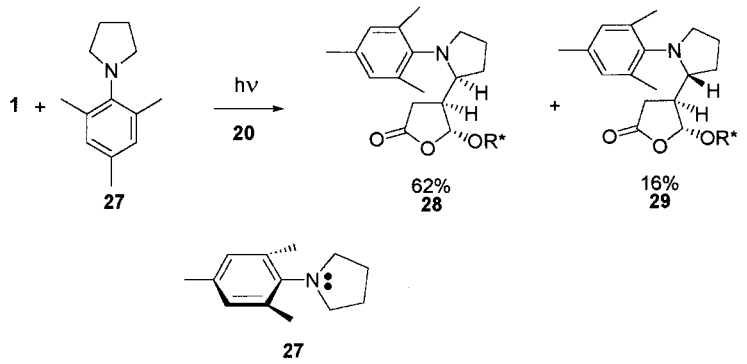
Perhydroazaazulene Derivative 5a. Yield: 257 mg (17%). Mp: 112 °C. $[\alpha]^{21}_D$: −96.7. $[\alpha]^{21}_{578}$: −99.5. $[\alpha]^{21}_{546}$: −103.4. $[\alpha]^{21}_{436}$: −188.6. $[\alpha]^{21}_{365}$: −210.3 (c = 1.68). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.77 (d, J = 6.9, 3H), 0.85 (d, J = 6.9, 3H), 0.91 (d, J = 7.6, 3H), 0.92 (s, 3H), 0.68−1.02 (m, 3H), 1.04 (s, 3H), 1.08−1.47 (m, 4H), 1.52−1.68 (m, 4H), 1.69−2.14 (m, 6H), 2.37 (ddd, J = 9.8, 4.6, 2.2, 1H), 2.61−2.82 (m, 2H,) 2.92 (m, 1H), 3.21 (ddd, J = 10.3, 4.6, 2.3, 1H), 3.57 (td, J = 10.7, 4.2, 1H), 5.82 (d, J = 4.6,1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.7, 15.8, 20.9, 22.3, 23.0, 23.1, 24.6, 25.3, 30.8, 31.3, 31.8, 34.3, 39.9, 41.5, 43.7, 47.8, 49.5, 50.3, 53.9, 54.2, 76.9, 101.7, 178.6. IR (KBr): ν 2955, 2915, 2865, 1785, 1260, 1145, 945. MS m/z (relative intensity): 377 (M^+, 3.7), 362 (100), 318 (27), 238 (12), 224 (11), 194 (21), 150 (5), 112 (16). Anal.Calcd for $C_{23}H_{39}NO_3$: C, 73.10; H, 10.34; N, 3.71. Found: C, 73.03; H, 10.00; N, 3.65.

Perhydroazaazulene Derivative 5b. Yield: 211 mg (14%). Mp: 121 °C. $[\alpha]^{21}_D$: −81.4. $[\alpha]^{21}_{578}$: −85.0. $[\alpha]^{21}_{546}$: −96.3. $[\alpha]^{21}_{436}$: −161.6. $[\alpha]^{21}_{365}$: −191.3 (c = 0.88). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.73 (d, J = 6.9, 3H), 0.82 (d, J = 6.9; 3H), 0.83 (s, 3H), 0.91 (d, .J = 6, 3H), 0.68−1.06 (m, 3H), 1.04 (s, 3H), 1.12−1.42 (m, 4H), 1.45−1.87 (m, 7H), 1.92−2.17 (m, 3H), 2.62 (dd,

(27) Trost, B. M.; Spagnol, M. D. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2083−2096.

(28) (a) Hennion, G. F.; Nelson, K. W. *J. Am. Chem. Soc.* **1957**, *79*, 2142−2145. (b) Hennion, G. F.; Perrino, A. C. *J. Org. Chem.* **1961**, *26*, 1073−1079.

Scheme 15. Radical Addition of *N*-Mesitylpyrrolidine 27 to 1



J = 7.2, 4.6,1H), 2.61−2.91 (m, 3H), 2.98 (ddd, J = 8.2, 4.6, 2.2, 1H), 3.43 (td, J = 10.7, 4.2, 1H), 5.28 (s, 1H).^{13}C NMR (62 MHz, $CDCl_3$): δ 15.6, 19.1, 20.4, 20.8, 22.3, 23.1, 24.0, 25.5, 28.1, 31.3, 31.4, 34.3, 39.6, 40.1, 41.9, 47.7, 47.8, 52.9, 54.1, 54.2, 76.1, 101.3, 179.3. IR (KBr): ν 2960, 2920, 2870, 1780, 1455, 1365, 1105, 955. MS *m*/*z* (relative intensity): 377 (M^+, 3.7), 362 (27), 318 (12), 238 (100), 224 (16), 194 (8), 150 (7), 112 (11). Anal. Calcd for $C_{23}H_{39}NO_3$: C, 73.10; H, 10.34; N, 3.71. Found: C, 72.78; H, 10.19; N, 3.59.

Quinolizidine Derivative 6a. Yield: 241 mg (16%). Mp: 89 °C. $[\alpha]^{21}_D$: −102.3. $[\alpha]^{21}_{578}$: −107.6. $[\alpha]^{21}_{546}$: −123.53. $[\alpha]^{21}_{436}$:−162.5. $[\alpha]^{21}_{365}$: −209.3 (c = 0.96). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.71 (d, J = 6.9, 3H), 0.80 (d, J = 6.9,3H), 0.83 (d, J = 6.2, 3H), 0.85 (s, 3H), 0.93 (d, J = 7.6, 3H), 0.68−1.02 (m, 3H), 1.12 (s, 3H), 1.12−1.42 (m, 4H), 1.47−1.82 (m, 5H), 1.96−2.42 (m, 4H), 2.59−2.71 (m, 2H), 2.98 (ddd, J = 9.3, 4.1, 2.2, 1H), 3.55 (td, J = 10.7, 4.2, 1H), 5.80 (d, J = 6.1, 1H).^{13}C NMR (62 MHz, $CDCl_3$): δ 13.4, 15.8, 20.9, 22.3, 22.9, 23.1, 24.2, 25.2, 27.1, 27.1, 31.4, 34.3,40.3, 41.3, 43.9, 46.0, 47.7, 48.0, 52.2, 55.4, 78.2, 100.8, 176.4. IR (KBr): ν 2960, 2875, 1780, 1450, 1355, 955. MS *m*/*z* (relative intensity): 377 (M^+, 3.7), 362 (100), 318 (27), 238 (12), 224 (11), 194 (21), 150 (5), 112 (16). Anal. Calcd for $C_{23}H_{39}NO_3$: C, 73.10; H, 10.34; N, 3.71. Found: C, 72.82; H, 10.06; N, 3.55.

Quinolizidine Derivative 6b. Yield: 196 mg (13%). Mp: 119 °C. $[\alpha]^{21}_D$: −117.3. $[\alpha]^{21}_{578}$: −120.9. $[\alpha]^{21}_{546}$: −136.5. $[\alpha]^{21}_{436}$:−177.3. $[\alpha]^{21}_{365}$: −231.1 (c = 1.00). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.75 (d, J = 6.9, 3H), 0.80 (d, J = 6.9, 3H), 0.83 (s, 3H), 0.86 (d, J = 6.2, 3H), 0.87 (d, J = 7.6, 3H), 0.58−1.01 (m, 3H), 1.09 (s, 3H), 1.08−1.42 (m, 4H), 1.45−1.82 (m, 5H), 1.87−2.17 (m, 2H), 2.42−2.70 (m, 3H), 2.80 (m, 1H), 2.87 (m, 1H), 3.42 (td, J = 10.7, 4.2, 1H), 5.18 (s, 1H).^{13}C NMR (62 MHz, $CDCl_3$): δ 15.4, 15.8, 18.4, 18.9, 20.7, 22.1, 22.9, 23.1, 23.8, 25.3, 31.1, 34.1, 39.8, 40.7, 41.7, 47.5, 47.7, 49.7, 54.8, 58.2, 76.0, 101.1, 179.1. IR (KBr): ν 2970, 2920, 1775, 1455, 1355, 1110, 955. MS *m*/*z* (relative intensity): 377 (M^+, 3), 362 (100), 318 (23), 224 (23), 194 (16), 112 (31). Anal. Calcd for $C_{23}H_{39}NO_3$: C, 73.10; H, 10.34; N, 3.71. Found: C, 73.02; H, 10.12; N, 3.58.

Azaazulene Derivative 8. Yield: 481 mg (32%). Mp: 111 °C. $[\alpha]^{21}_D$: −67.4. $[\alpha]^{21}_{578}$: −69.8. $[\alpha]^{21}_{546}$: −78.6. $[\alpha]^{21}_{436}$: −123.2. $[\alpha]^{21}_{365}$: −129.3 (c = 1.00). ^{1}H NMR (250 MHz, C_6D_6): δ 0.48 (m, 1H), 0.69 (s, 3H), 0.83 (d, J = 6.9, 3H), 0.95 (d, J = 6.9, 3H), 0.98 (d, J = 7.6, 3H), 0.68−1.02 (m, 2H), 1.20 (s, 3H), 1.20−1.68 (m, 8H), 2.10 (m, 1H), 2.25 (dd, J = 7.2, 5.0, 1H), 2.36 (dsept, J = 6.7, 2.3, 1H), 2.32 (m, 1H), 2.79 (m, 1H), 3.02 (m, 1H), 3.32 (dd, J = 9.2,7.2, 1H), 3.51 (td, J = 10.7, 4.2, 1H), 5.27 (d, J = 11.0, 1H), 5.36 (dd, J = 11.0, 9.2, 1H), 5.59 (s, 1H). ^{13}C NMR (62 MHz, C_6D_6): δ 15.4, 17.2, 20.9, 22.2, 22.9, 25.4, 26.1, 26.7, 28.6, 31.3, 34.3, 39.7, 39.9, 46.5, 47.8, 52.1, 55.6, 60.4, 75.8, 99.2, 116.9, 144.1, 176.9. IR (KBr): ν 2960, 2920, 1795, 1465, 1090, 930. MS *m*/*z* (relative intensity): 375 (M^+, 17), 360 (100), 316 (43), 236 (82), 220 (23), 178 (51), 148 (82), 124 (61). Anal. Calcd for $C_{23}H_{37}NO_3$: C, 73.56; H, 9.93; N, 3.73. Found: C, 73.32; H, 9.76; N, 3.50.

Azaazulene Derivative 9. Yield: 436 mg (29%). Mp: 98 °C. $[\alpha]^{21}_D$: −82.0. $[\alpha]^{21}_{578}$: −84.0. $[\alpha]^{21}_{546}$: −95.0. $[\alpha]^{21}_{436}$: −142.4. $[\alpha]^{21}_{365}$: −141.7 (c = 1.02). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.72 (d, J = 6.9, 3H), 0.80 (d, J = 7.6, 3H), 0.87 (d, J = 6.9, 3H), 0.92 (s, 3H), 0.67−1.02 (m, 3H), 1.10−1.42 (m, 2H), 1.20 (s, 3H), 1.53−2.11 (m, 8H), 2.18 (dd, J = 14.9, 9.2, 1H), 2.53 (m, 1H), 2.61 (m, 1H), 2.63 (dd, J = 14.9, 7.2, 1H), 2.80 (m, 1H), 3.07 (m, 1H), 3.51 (td, J = 10.7, 4.2, 1H), 5.33 (d, J = 3.8, 1H), 6.89 (ddd, J = 9.2, 7.2, 3.0, 1H).^{13}C NMR (62 MHz, $CDCl_3$): δ 15.8, 15.9, 20.3, 20.8, 22.3, 23.1, 25.3, 29.4, 31.3, 32.1, 34.3, 39.4, 42.5, 47.8, 48.5, 51.9, 55.8, 56.4, 77.3, 100.8, 132.3, 139.4, 168.5. IR (KBr): ν 2960, 2925, 1770, 1465, 1115, 940. MS *m*/*z* (relative intensity): 375 (M^+, 9), 360 (37), 236 (23), 219 (10), 178 (8), 148 (14), 136 (29), 111 (100). Anal. Calcd for $C_{23}H_{37}NO_3$: C, 73.56; H, 9.93; N, 3.73. Found: C, 73.33; H, 9.82; N, 3.48.

Reaction of (5*R*)-5-Menthyloxy-2-[5*H*]-furanone 1 with *N*,*N*-Dimethylaniline 19a. A solution of (5*R*)-5-menthyloxy-2[5*H*]-furanone **1** (300 mg, 1.26 mmol), *N*,*N*-dimethylaniline (2.42 g, 20 mmol), and Michler's ketone **20** (30 mg, 0.1 mmol) in acetonitrile (10 mL) was irradiated at 350 nm for 7 h. The solvent was evaporated, and the residue was subjected to flash chromathography (eluent, ethyl acetate/petroleum ether 1/5). The tetrahydroquinoline derivatives **21a** and **22a** were separated by HPLC.

Tetrahydroquinoline Derivative 21a. Yield: 171 mg (38%). Mp: 116 °C. $[\alpha]^{21}_D$: −206.9. $[\alpha]^{21}_{578}$: −212.1. $[\alpha]^{21}_{546}$: −241.4. $[\alpha]^{21}_{436}$: −382.7. $[\alpha]^{21}_{365}$: −441.3 (c = 0.98). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.82 (d, J = 6.9, 3H), 0.92 (d, J = 7.6, 3H), 0.94 (d, J = 6.9, 3H), 0.79−1.07 (m, 3H), 1.21−1.47 (m, 2H), 1.58−1.72 (m, 2H), 2.07−2.17 (m, 2H), 2.76−2.91 (m, 2H), 2.85 (s, 3H), 3.21 (m, 1H), 3.57 (td, J = 10.7, 4.2, 3H), 3.84 (d, J = 6.9, 1H), 5.49 (d, J = 1.5, 1H), 6.68 (d, J = 8.4, 1H), 6.82 (td, J = 7.2, 1.1, 1H), 7.17 (td, J = 8.4, 1.1, 1H), 7.46 (d, J = 7.2, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): 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. IR (KBr): ν 2950, 2920, 1765, 1505, 1310, 1140, 970, 930, 750. MS *m*/*z* (relative intensity): 357 (M^+, 70), 313 (32), 254 (7), 174 (100), 157 (19), 146 (92), 144 (89). HRMS Calcd for $C_{22}H_{31}NO_3$: 357.2296. Found: 357.2304. Anal. Calcd for $C_{22}H_{31}NO_3$: C, 73.90; H, 8.99; N, 3.92. Found: C, 73.62; H, 8.99; N, 3.80.

Tetrahydroquinoline Derivative 22a. Yield: 8 mg (1.7%). $[\alpha]^{21}_D$: −52.4. $[\alpha]^{21}_{578}$: −60.7. $[\alpha]^{21}_{546}$: −132.9. $[\alpha]^{21}_{436}$: −53.5. $[\alpha]^{21}_{365}$: −114.6 (c = 0.42). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.71 (d, J = 6.9, 3H), 0.82 (d, J = 7.6, 3H), 0.89 (d, J = 6.9, 3H), 0.79−1.07 (m,3H), 1.18−1.39 (m, 2H), 1.52−1.65 (m, 2H), 2.01−2.14 (m, 2H), 2.81−2.94 (m, 2H), 2.83 (s, 3H), 3.21 (dd, J = 12.0, 4.7, 1H), 3.56 (td, J = 10.7, 4.2, 3H), 3.64 (d, J = 7.1, 1H), 5.80 (d, J = 4.4, 1H), 6.61 (d, J = 8.0, 1H), 6.73 (td, J = 7.4, 1.0, 1H), 7.11 (td, J = 8.5, 1.4, 1H), 7.33 (d, J = 7.4, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): 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. IR (KBr): ν 2950, 2920, 1765, 1505, 1310, 1140, 970, 930, 750. MS *m*/*z* (relative intensity): 357 (M^+, 100), 313 (34), 254 (7), 174 (100), 157 (25), 146 (94), 144 (100). Anal. Calcd for $C_{22}H_{31}NO_3$: C, 73.90; H, 8.99; N, 3.92. Found: C, 73.66; H, 8.96; N, 3.78.

Lactone 23. Yield: 55 mg (18%). Mp: 58 °C. $[\alpha]^{21}_D$: −141.3. $[\alpha]^{21}_{578}$: −146.0. $[\alpha]^{21}_{546}$: −166.9. $[\alpha]^{21}_{436}$: −276.4. $[\alpha]^{21}_{365}$: −278.0 (c = 0.86). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.78 (d, J = 7.3, 3H), 0.88 (d, J = 7.3, 3H), 0.93 (d, J = 6.5, 3H), 0.65−1.12 (m,

3H), 1.17−1.48 (m, 2H), 1.58−1.72 (m, 2H), 2.00−2.17 (m, 3H), 2.28 (m, 1H), 2.41 (ddd, J = 18.1, 9.5, 3.4, 1H), 2.65 (m, 1H), 3.52 (td, J = 10.7, 4.2, 1H), 5.71 (dd, J = 5.3, 1.9, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.6, 20.8, 22.2, 23.1, 25.5, 27.0, 29.1, 31.3, 34.3, 39.8, 47.8, 76.5, 100.3, 170.8. IR (KBr): ν 2950, 2925, 2870, 1790, 1460, 1360, 1155, 975, 950. MS (NH_3) m/z (relative intensity): 258 ($M^+ + 18$, 85), 241 ($M^+ + 1$, 100), 223 (24), 178 (10), 156 (92), 150 (35), 139 (98), 120 (50). Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.95; H, 10.07. Found: C, 69.71; H, 9.79.

Bislactone 24. Yield: 42 mg (7%). $[\alpha]^{21}_D$: −195.4. $[\alpha]^{21}_{578}$: −205.4. $[\alpha]^{21}_{546}$: −233.5. $[\alpha]^{21}_{436}$: −388.0. $[\alpha]^{21}_{365}$: −579.8 (c = 0.84). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.78 (d, J = 7.3, 6H), 0.88 (d, J = 7.3, 6H), 0.96 (d, J = 6.5, 6H), 0.72−1.12 (m, 6H), 1.21−1.55 (m, 4H), 1.62−1.83 (m, 4H), 2.04−2.27 (m, 6H), 2.50 (m, 2H), 2.81 (dd, J = 17.8, 8.5, 2H), 3.56 (td, J = 10.7, 4.2, 2H), 5.53 (d, J = 2.3, 2H). ^{13}C NMR (62 MHz, $CDCl_3$): 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. IR (KBr): ν 2955, 2925, 2870, 1785, 1510, 1345, 1165, 945. MS (NH_3) m/z (relative intensity): 478 (M^+, 54), 373 (26), 335 (15), 229 (46), 216 (100), 139 (84). Anal. Calcd for $C_{28}H_{46}O_6$: C, 70.54; H, 9.31. Found: C, 70.30; H, 9.19.

Isotopic Labeling Experiments. **Preparation of *N,N*-Dimethyl-2,4,6-trideuterioaniline 19a′.**[29] *N,N*-Dimethyl-2,4,6-tribromoaniline[30] was synthesized according to the literature.[31] The reduction was also carried out according to a literature procedure.[32] Under an argon atmosphere, sodium (5 g, 218 mmol) was added slowly to mercury (100 g, 500 mmol). After the mixture cooled to room temperature, deuteriomethanol (40 mL) was added. The mixture was then heated to reflux until the complete fusion of the amalgam. A solution of *N,N*-dimethyl-2,4,6-tribromoaniline (7.15 g, 20 mmol) in deuteriomethanol (10 mL) was added, and the resulting mixture was heated under reflux for 6 h. Water (100 mL) was added, and the mixture was extracted two times with ether. The organic phase was washed with brine and dried over $MgSO_4$. After evaporation, the residue was distilled. Yield: 2.06 g (83%). Bp_{20}: 86 °C, ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.01 (s, 6H) 7.32 (s, 2H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 40.3, 112.2, 116.2 (t, J = 23.9), 128.6 (t, J = 23.9), 150.3. IR (film): ν 2935, 2860, 2795, 1590, 1490, 1430. MS m/z (relative intensity): 124 (M^+, 68), 123 (100).

Preparation of *N,N*-Bis(trideuteriomethyl)aniline 19a″.[33,26d] Trideuterioiodomethane was prepared according to a literature procedure.[34] The *N*-alkylation was carried out according to a modified literature procedure.[35] Trideuteriodomethan (62.3 g, 430 mmol) was added dropwise to a mixture of aniline (15 g, 161 mmol), Na_2CO_3 (18 g, 217 mmol), and ethanol (25 mL). The reaction mixture was heated under reflux for 10 h. After the mixture cooled to room temperature an aqueous solution of dimethylamine (140 mL, 40%) was added. The resulting mixture was heated on a water bath for 3 h. NaOH (10 mL, 2 N) was then added, and the solution was extracted with ether. The organic phase was dried with $MgSO_4$. The ether was evaporated and the residue was distilled. Yield: 12.2 g (60%). Bp_{10}: 78 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.83 (m, 3H), 7.35 (s, 2H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 39.6 (sep, J = 20.5), 112.5, 116.5, 129.0, 150.6. IR (film): ν 3060, 2055, 1605, 1505, 1340. MS m/z (relative intensity): 127 (M^+, 63), 125 (100).

Reaction of (5*R*)-5-Menthyloxy-2-[5*H*]-furanone 1 with Deuterated *N,N*-Dimethylaniline Derivatives 19a′, 19a″. The reactions were carried out under the same conditions as described for **19a**. The degree of deuteration (Scheme 8) was determined by integration of the ^{1}H NMR spectra.

Tetrahydroquinoline Derivative 21a′. Yield: 158 mg (35%). Mp: 116 °C. $[\alpha]^{21}_D$: −197.4. $[\alpha]^{21}_{578}$: −203.5. $[\alpha]^{21}_{546}$: −229.9. $[\alpha]^{21}_{436}$: −363.9. $[\alpha]^{21}_{365}$: −439.6 (c = 0.94). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.82 (d, J = 6.9, 3H), 0.92 (d, J = 7.6, 3H), 0.94 (d, J = 6.9, 3H), 0.79−1.07 (m, 3H), 1.21−1.47 (m, 2H), 1.58−1.72 (m, 2H), 2.07−2.17 (m, 2H), 2.76−2.91 (m, 2H), 2.87 (s, 3H), 3.21 (dd, J = 16.9, 9.2, 1H), 3.57 (td, J = 10.7, 4.2, 3H), 3.87 (d, J = 6.9, 1H), 5.49 (d, J = 1.5, 1H), 7.19 (s, 1H), 7.48 (s, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): 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 (t, J = 23.2), 116.9, 118.4 (t, J = 23.0), 128.3, 130.5, 146.8, 175.5. IR (KBr): ν 2950, 2920, 2865, 1770, 1595, 1490, 1450, 1315, 1150, 1135, 970, 930. MS m/z (relative intensity): 359 (M^+, 35), 315 (17), 176 (100), 159 (13), 148 (91), 142 (71). Anal. Calcd for $C_{22}H_{29}D_2NO_3$: C, 73.49; H/D, 9.25; N, 3.91. Found: C, 73.58; H/D, 9.25; N, 4.02.

Tetrahydroquinoline Derivative 21a″. Yield: 160 mg (35%). Mp: 114 °C. $[\alpha]^{21}_D$: −156.2. $[\alpha]^{21}_{578}$: −160.0. $[\alpha]^{21}_{546}$: −180.6. $[\alpha]^{21}_{436}$: −297.9. $[\alpha]^{21}_{365}$: −381.1 (c = 1.00). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.82 (d, J = 6.9, 3H), 0.92 (d, J = 7.6, 3H), 0.94 (d, J = 6.9, 3H), 0.79−1.07 (m, 3H), 1.21−1.47 (m, 2H), 1.58−1.72 (m, 2H), 2.07−2.17 (m, 2H), 2.86 (dd, J = 8.0, 2.3, 1H, H4), 3.57 (td, J = 10.7, 4.2, 3H), 3.87 (d, J = 8.0, 1H), 5.49 (d, J = 2.3, 1H), 6.68 (dd, J = 8.4, 1.1, 1H), 6.82 (td, J = 7.2, 1.1, 1H), 7.17 (td, J = 8.4, 1.1, 1H), 7.46 (d, J = 7.2, 1H). ^{13}C NMR (62 MHz, C_6D_6): δ 16.0, 21.2, 22.4, 23.4, 25.9, 31.4, 34.6, 38.3 (sept, J = 21.5), 40.3, 40.5, 41.3, 48.2, 48.9 (qt, J = 22.3), 77.0, 101.2, 112.3, 113.0, 118.8, 129.5, 131.2, 147.2, 174.9. IR (KBr): ν 2950, 2925, 2820, 1770, 1580, 1490, 1455, 1325, 1155, 1140. MS m/z (relative intensity): 362 (M^+, 38), 318 (23), 181 (100), 161 (19), 151 (93), 147 (73). Anal. Calcd for $C_{22}H_{26}D_5NO_3$: C, 72.82; H/D, 9.93; N, 3.86. Found: C, 72.49; H/D, 9.64; N, 3.71.

Preparation of Tertiary Aniline Derivatives 19d and 19f.[31] A solution of the 2,3-dimethylaniline or 5,6,7,8-tetrahydronaphthalen-1-ylamine (27 mmol) and sodium borohydride (6 g, 159 mmol) in THF was added dropwise to a solution of formaline (37%, 8.3 mL, 110 mmol) and sulfuric acid (7 mL, 128 mmol) in 50 mL of THF. The mixture was rapidly stirred for 1 h. Water (50 mL) was then added dropwise, and solid KOH (21.5 g) was added to adjust the pH at about 10. After filtration the solution was extracted with ether (2 × 50 mL). The organic phases were washed with brine and dried with $MgSO_4$. After evaporation of the solvent, the residue was distilled.

Aniline derivative 19d.[31] Yield: 3.27 g (81%). Bp_{20}: 97 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.49 (s, 3H), 2.50 (s, 3H), 2.79 (s, 6H), 7.00 (d, J = 7.3, 1H), 7.05 (d, J = 7.3, 1H), 7.18 (t, J = 7.3, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 14.2, 20.5, 44.6, 116.1, 124.5, 125.6, 130.9, 137.8, 152.9.

Aniline Derivative 19f.[36] Yield: 4.08 g (86%). Bp_{20}: 138 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.87 (m, 4H), 2.73 (s, 6H), 2.86 (m, 4H), 6.88 (d, J = 8.1, 1H), 6.96 (d, J = 8.1, 1H), 7.14 (t, J = 8.1, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 23.0, 23.2, 25.4, 29.7, 44.4, 115.7, 124.0, 125.6, 132.2, 138.1,154.3.

Reaction of (5*R*)-5-Menthyloxy-2-[5*H*]-furanone 1 with *N,N*-Dimethylaniline 19a in the Presence of Ketones. (Table 2, Schemes 12 and 13) A solution of (5*R*)-5-menthyloxy-2-[5*H*]-furanone **1** (200 mg, 0.84 mmol), *N,N*-dimethylaniline **19a** (1.21 g, 20 mmol), bis(dimethylamino)benzophenone **20**, and acetone or cyclopentanone in acetonitrile (15 mL) or acetone was irradiated according to Table 2. For the reactions described in Schemes 13 and 14, acetone (1 mL) was added to the reaction mixture. The solution was evaporated, and the residue was subjected to flash chromatography (ethyl acetate/petroleum ether 1/5). The diastereomeric excess was then determined by NMR spectroscopy (integration of the signal of H5 in the ^{1}H NMR spectrum). After recrystallization from petroleum ether, the major isomers were completely characterized.

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Tetrahydroquinoline Derivative 21b. Yield: 232 mg (62%). Mp: 126 °C. $[\alpha]^{21}_{D}$: −103.2. $[\alpha]^{21}_{578}$: −107.4. $[\alpha]^{21}_{546}$: −123.2. $[\alpha]^{21}_{436}$: −197.9. $[\alpha]^{21}_{365}$: −266.3 (c = 0.96). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.82 (d, J = 6.9, 3H), 0.93 (d, J = 7.6, 3H), 0.95 (d, J = 6.9, 3H), 0.79−1.07 (m, 3H), 1.19−1.46 (m, 2H), 1.58−1.74 (m, 2H), 2.04−2.15 (m, 2H), 2.28 (s, 3H), 2.76 (s, 3H), 2.80−2.95 (m, 2H), 3.17 (m, 1H), 3.61 (td, J = 10.7, 4.2, 1H), 3.88 (d, J = 7.6, 1H), 5.53 (s, 1H), 7.08 (d, J = 7.6, 1H), 7.17 (t, J = 8.2, 1H), 7.43 (d, J = 7.6, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.7, 18.0, 20.9, 22.2, 23.3, 25.7, 31.4, 33.9, 34.4, 39.6,40.2, 42.0, 47.9, 50.8, 76.5, 100.3, 121.8, 122.9, 126.7, 128.7, 130.2, 146.0,175.9. IR (KBr): ν 2960, 2870, 2795, 1795, 1590, 1480, 1365, 1115, 930, 765. MS m/z (relative intensity): 372 (M^+ + 1, 47), 327 (15), 234 (32), 188 (16), 158 (3), 135 (18), 134 (100). Anal. Calcd for $C_{23}H_{33}NO_3$: C, 74.34; H, 8.96; N, 3.77. Found: C, 74.13; H, 8.93; N, 3.54.

Tetrahydroquinoline Derivative 22b. ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.96 (d, J = 4.6, 1H).

Tetrahydroquinoline Derivative 21c. Yield: 300 mg (81%). Mp: 142 °C. $[\alpha]^{21}_{D}$: −182.3. $[\alpha]^{21}_{578}$: −186.1. $[\alpha]^{21}_{546}$: −210.8. $[\alpha]^{21}_{436}$: −343.1. $[\alpha]^{21}_{365}$: −438.4 (c = 1.00). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.82 (d, J = 6.9, 3H), 0.92 (d, J = 7.6, 3H), 0.94 (d, J = 6.9, 3H), 0.79−1.07 (m, 3H), 1.21−1.47 (m, 2H), 1.58−1.72 (m, 2H), 2.07−2.17 (m, 2H), 2.26 (s, 3H), 2.76−2.91 (m, 2H), 2.83 (s, 3H), 3.17 (m, 1H), 3.57 (td, J = 10.7, 4.2, 1H), 3.82 (d, J = 7.6, 1H), 5.51 (d, J = 1.5, 1H), 6.60 (d, J = 8.4, 1H), 6.98 (dd, J = 7.6, 1.2, 1H), 7.29 (d, J = 1.1, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.5, 20.0, 20.6, 22.0, 23.0, 25.3, 31.1, 34.1, 39.4, 39.7, 40.3, 41.2, 47.5, 50.0, 76.8, 101.4, 112.0, 116.7, 127.5, 128.8, 130.7, 144.5, 175.4. IR (KBr): ν 2860, 1770, 1515, 1365, 1280, 1090, 925, 800. MS m/z (relative intensity): 371 (M^+, 100), 327 (60), 189 (53), 188 (97), 171 (35), 161 (32), 160 (97), 158 (100), 144 (32). Anal. Calcd for $C_{23}H_{33}NO_3$: C, 74.34; H, 8.96; N, 3.77. Found: C, 74.94; H, 8.85; N, 3.61.

Tetrahydroquinoline Derivative 22c. ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.83 (d, J = 4.6, 1H).

Tetrahydroquinoline Derivative 21d. Yield: 258 mg (67%). Mp: 158 °C. $[\alpha]^{21}_{D}$: −104.0. $[\alpha]^{21}_{578}$: −104.6. $[\alpha]^{21}_{546}$: −120.0. $[\alpha]^{21}_{436}$: −182.6. $[\alpha]^{21}_{365}$: −231.2 (c = 1.00). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.82 (d, J = 6.9, 3H), 0.91 (d, J = 7.6, 3H), 0.96 (d; J = 6.9, 3H), 0.82−1.10 (m, 3H), 1.22−1.51 (m, 2H), 1.61−1.75 (m, 2H), 2.06−2.20 (m, 2H), 2.20 (s, 3H), 2.26 (s, 3H), 2.67 (s, 3H), 2.76 (dd, J = 12.2, 6.5, 1H), 2.90 (ddd, J = 7.2, 6.5, 4.2, 1H), 3.30 (dd, J = 12.2, 4.2, 1H), 3.60 (td, J = 10.7, 4.2, 1H), 3.81 (d, J = 7.2, 1H), 5.37 (s, 1H), 6.95 (d, J = 7.6, 1H), 7.38 (d, J = 7.6, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 14.2, 15.6, 20.4, 20.9, 22.5, 23.1, 25.6, 31.4, 33.4, 34.3, 39.7, 39.9, 42.5, 47.8, 50.7, 76.4, 100.3, 119.4, 125.0, 127.9, 130.5, 137.1, 146.1, 176.2. IR (KBr): ν 2920, 2860, 1780, 1455, 1255, 1105, 1030, 915. MS m/z (relative intensity): 385 (M^+, 69), 341 (58), 230 (14), 202 (100), 172 (79), 158 (32). Anal. Calcd for $C_{24}H_{35}NO_3$: C, 74.75; H, 9.16; N, 3.63. Found: C, 74.76; H, 9.11; N, 3.45.

Tetrahydroquinoline Derivative 22d. ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.84 (d, J = 4.5, 1H).

Tetrahydroquinoline Derivative 21e. Yield: 192 mg (52%). Mp: 123 °C. $[\alpha]^{21}_{D}$: −206.6. $[\alpha]^{21}_{578}$: −218.0. $[\alpha]^{21}_{546}$: −249.2. $[\alpha]^{21}_{436}$: −418.0. $[\alpha]^{21}_{365}$: −596.4 (c = 0.24). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.83 (d, J = 6.9, 3H), 0.89 (d, J = 7.6, 3H), 0.95 (d, J = 6.9, 3H), 0.80−1.07 (m, 3H), 1.19−1.45 (m, 2H), 1.58−1.72 (m, 2H), 2.07−2.17 (m, 2H), 2.43 (s, 3H), 2.84 (s, 3H), 2.74−2.96 (m, 2H), 3.18 (m, 1H), 3.60 (td, J = 10.7, 4.2, 1H), 4.12 (d, J = 7.6, 1H), 5.44 (s, 1H), 6.56 (d, J = 8.0, 1H), 6.71 (d, J = 8.0, 1H), 7.09 (t, J = 8.0,1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.8, 19.9, 20.9, 22.2, 22.6, 25.9, 29.5, 34.3, 38.6, 39.8, 39.9, 40.9, 47.8, 50.9, 76.7, 101.9, 109.9, 116.3, 121.0, 128.0, 139.1, 154.7, 175.9. IR (KBr): ν 2950, 2365, 1785, 1610, 1485, 1095, 920. MS m/z (relative intensity): 371 (M^+, 70), 327 (23), 188 (100), 160 (84), 158 (76). Anal. Calcd for $C_{23}H_{33}NO_3$: C, 74.34; H, 8.96; N, 3.77. Found: C, 74.11; H, 9.13; N, 3.86.

Tetrahydroquinoline Derivative 22e. ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.93 (d, J = 4.6, 1H).

Tetrahydroquinoline Derivative 21′e. Yield: 82 mg (22%). Mp: 131 °C. $[\alpha]^{21}_{D}$: −153.9. $[\alpha]^{21}_{578}$: −157.9. $[\alpha]^{21}_{546}$: −178.0. $[\alpha]^{21}_{436}$: −277.9. $[\alpha]^{21}_{365}$: −357.7 (c = 1.00). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.81 (d, J = 6.9, 3H), 0.91 (d, J = 7.6, 3H), 0.95 (d, J = 6.9, 3H), 0.81−1.11 (m, 3H), 1.21−1.48 (m, 2H), 1.60−1.74 (m, 2H), 2.04−2.20 (m, 2H), 2.47 (s, 3H), 2.87 (s, 3H), 2.67−3.00 (m, 2H), 3.21 (m, 1H), 3.57 (td, J = 10.7, 4.2, 1H), 3.83 (d, J = 8.2, 1H), 5.51 (d, J = 1.9, 1H), 6.52 (s, 1H), 6.68 (d, J = 8.0, 1H), 7.47 (d, J = 8.0, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.7, 20.9, 21.7, 22.2, 23.1, 25.5, 31.4, 34.3, 39.5, 39.9, 40.2, 41.1, 47.7, 50.0, 77.2,101.6, 109.5, 112.8, 119.4, 130.4, 138.2, 147.1, 176.3. IR (KBr): ν 2945, 2870, 1775, 1640, 1455, 1110, 930. MS m/z (relative intensity): 371 (M^+, 70), 327 (23), 188 (100), 160 (84), 158 (76). Anal. Calcd for $C_{23}H_{33}NO_3$: C, 74.34; H, 8.96; N, 3.77. Found: C, 74.08; H, 9.07; N, 3.83.

Tetrahydroquinoline Derivative 22′e. ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.93 (d, J = 4.5, 1H).

Azastereoid 21f. Yield: 230 mg (56%). Mp: 158 °C. $[\alpha]^{21}_{D}$: −159.0. $[\alpha]^{21}_{578}$: −163.6. $[\alpha]^{21}_{546}$: −185.4. $[\alpha]^{21}_{436}$: −283.5. $[\alpha]^{21}_{365}$: −358.9 (c = 1.02). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.83 (d, J = 7.6, 3H), 0.92 (d, J = 6.9, 3H), 0.96 (d, J = 6.9, 3H), 0.80−1.07 (m, 3H), 1.21−2.03 (m, 8H), 2.04−2.23 (m, 1H), 2.37−2.53 (m, 1H), 2.68 (s, 3H), 2.72−2.82 (m, 3H), 2.83−2.96 (m, 3H), 3.27 (dd, J = 14.2, 4.2, 1H), 3.61 (td, J = 10.7, 4.2, 1H), 3.85 (d, J = 7.2, 1H), 5.34 (s, 1H), 6.88 (d, J = 7.6, 1H), 7.38 (d, J = 7.6, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.7, 20.9, 22.2, 23.0, 23.1, 23.2, 25.4, 25.7, 29.5, 31.4, 33.7, 34.4, 39.6, 39.8, 41.7, 47.9, 51.0, 77.0, 100.4, 118.8, 124.4, 127.8, 131.6, 137.4, 147.9, 176.2. IR (KBr): ν 2950, 2860, 1770, 1455, 1365, 1105, 915. MS m/z (relative intensity): 411 (M^+, 18), 367 (14), 228 (16), 188 (100). Anal. Calcd for $C_{26}H_{37}NO_3$: C, 75.86; H, 9.67; N, 3.40. Found: C, 75.75; H, 9.57; N, 3.46.

Azasteroid 22f. ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.83 (d, J = 4.5, 1H).

Tetrahydroquinoline Derivative 21g. Yield: 138 mg (36%). Mp: 133 °C. $[\alpha]^{21}_{D}$: −128.9. $[\alpha]^{21}_{578}$: −133.3. $[\alpha]^{21}_{546}$: −150.0. $[\alpha]^{21}_{436}$: −232.8. $[\alpha]^{21}_{365}$: −276.1 (c = 0.92). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.75 (d, J = 6.9, 3H), 0.80 (d, J = 6.5, 3H), 0.83 (d, J = 6.9, 3H), 0.86 (d, J = 7.6, 3H), 0.72−0.95 (m, 3H), 0.97−1.26 (m, 2H), 1.13 (t, J = 7.2, 3H), 1.54−1.67 (m, 2H), 2.02−2.16 (m, 2H), 2.81 (dd, J = 8.4, 5.0, 1H), 3.06 (dq, J = 14.5, 7.2, 1H), 3.21−3.58 (m, 3H), 3.74 (d, J = 8.4, 1H), 5.44 (s, 1H), 6.61 (d, J = 8.9, 1H), 6.71 (t, J = 7.4, 1H), 7.08 (t, J = 9.0, 1H), 7.52 (d, J = 7.6, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 13.0, 13.1, 15.7, 20.9, 22.2, 23.1, 25.6, 31.3, 34.3, 37.6, 39.7, 43.7, 44.3, 47.7, 50.8, 76.6, 100.3, 112.4, 115.7, 117.3, 128.3, 130.5, 143.5, 176.1. IR (KBr): ν 2940, 2870, 1780, 1600, 1500, 1455, 1360, 1265, 1110, 930. MS m/z (relative intensity): 385 (M^+, 74), 341 (23), 326 (18), 202 (100), 188 (45), 174 (34), 158 (90), 144 (15), 130 (31). Anal. Calcd for $C_{24}H_{35}NO_3$: C, 74.75; H, 9.16; N, 3.64. Found: C, 74.84; H, 8.89; N, 3.76.

Tetrahydroquinoline Derivative 26g. Yield: 112 mg (29%). Mp: 116 °C. $[\alpha]^{21}_{D}$: −110.9. $[\alpha]^{21}_{578}$: −107.3. $[\alpha]^{21}_{546}$: −115.5. $[\alpha]^{21}_{436}$: −116.4. $[\alpha]^{21}_{365}$: −179.1 (c = 1.00). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.81 (d, J = 6.9, 3H), 0.91 (d, J = 7.6, 3H), 0.93 (d, J = 6.9, 3H), 0.79−1.10 (m, 3H), 1.08 (d, J = 6.5, 3H), 1.17−1.46 (m, 2H), 1.23 (t, J = 7.1, 3H), 1.50−1.71 (m, 2H), 2.04 (m, 1H), 2.11 (dst, J = 6.9, 2.5, 1H), 2.51 (ddd, J = 9.2, 6.5, 2.7, 1H), 3.12 (dq, J = 14.5, 7.2, 1H), 3.42 (m, 2H), 3.51 (td, J = 10.7, 4.2, 1H), 3.84 (d, J = 9.2, 1H), 5.61 (d, J = 6.5, 1H), 6.63 (d, J = 8.4, 1H), 6.71 (td, J = 7.2, 0.8, 1H), 7.14 (td, J = 7.2, 0.8, 1H), 7.47 (dd, J = 7.2, 0.8, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 13.4, 15.8, 16.5, 20.9, 22.2, 23.1, 25.4, 31.3, 34.2, 40.3, 40.4, 43.8, 47.8, 48.7, 50.2, 78.6, 103.5, 112.1, 115.2, 117.3, 128.7, 129.5, 143.1, 174.4. IR (KBr): ν 2935, 2855, 1765, 1600, 1500, 1330, 1135, 930. MS m/z (relative intensity): 385 (M^+, 40), 341 (19), 326 (51), 230 (12), 202 (100), 188 (23), 174 (28), 158 (68), 130 (18). Anal. Calcd for $C_{24}H_{35}NO_3$: C, 74.75; H, 9.16; N, 3.64. Found: C, 74.82; H, 8.84; N, 3.79.

Benzoindolizidine Derivative 21h. Yield: 150 mg (39%). Mp: 130 °C. $[\alpha]^{21}_{D}$: −115.2. $[\alpha]^{21}_{578}$: −119.7. $[\alpha]^{21}_{546}$: −135.0. $[\alpha]^{21}_{436}$: −211.5. $[\alpha]^{21}_{365}$: −226.5 (c = 1.00). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.76 (d, J = 6.9, 3H), 0.84 (d, J = 6.9, 3H), 0.88 (d, J = 7.6, 3H), 0.70−1.00 (m, 3H), 1.03−1.38 (m, 2H), 1.53−1.72 (m, 4H), 1.83−2.14 (m, 3H), 2.22 (dst, J = 6.9, 2.7, 1H), 2.30 (dd, J = 11.0, 7.2, 1H), 2.68 (ddd, J = 11.0, 10.0, 5.7, 1H),

3.05 (ddd, J = 14.8, 9.1, 4.6, 1H), 3.36 (dd, J = 14.8, 8.8, 1H), 3.51 (td, J = 10.7, 4.2, 1H), 3.80 (d, J = 7.2, 1H), 5.47 (s, 1H), 6.45 (d, J = 8.0, 1H), 6.69 (dd, J = 7.6, 7.2, 1H), 7.08 (dd, J = 7.6, 7.2, 1H), 7.39 (d, J = 7.2, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.7, 20.9, 22.2, 22.7, 23.2 (C3′) 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. IR (KBr): ν 2955, 2855, 1775, 1460, 1260, 1095, 1035. MS m/z (relative intensity): 383 (M^+, 63), 200 (100), 170 (81), 146 (60). Anal. Calcd for $C_{24}H_{33}NO_3$: C, 75.14; H, 9.20; N, 3.65. Found: C, 74.99; H, 8.96; N, 3.56.

Benzoindolizidine Derivative 26h. Yield: 122 mg (32%). Mp: 124 °C. $[\alpha]^{21}_D$: −109.9. $[\alpha]^{21}_{578}$: −111.3. $[\alpha]^{21}_{546}$: −117.2. $[\alpha]^{21}_{436}$: −104.0. $[\alpha]^{21}_{365}$: +274.0 (c = 1.00). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.74 (d, J = 6.9, 3H), 0.83 (d, J = 6.9, 3H), 0.93 (d, J = 7.6, 3H), 0.69−0.97 (m, 3H), 1.10−1.34 (m, 2H), 1.51−1.67 (m, 4H), 1.81−2.09 (m, 3H), 2.16 (dst, J = 6.9, 2.7, 1H), 2.83−2.99 (m, 2H), 3.18 (ddd, J = 11.8, 6.9, 3.4, 1H), 3.40−3.55 (m, 2H), 3.89 (d, J = 9.5, 1H), 5.63 (d, J = 6.5, 1H), 6.48 (dd, J = 8.4, 0.8, 1H), 6.68 (td, J = 7.2−0.8, 1H), 7.07 (td, J = 8.4, 0.8, 1H), 7.42 (dd, J = 7.6, 0.8, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): 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. IR (KBr): ν 2920, 2845, 1770, 1605, 1505, 1455, 1115, 955. MS m/z (relative intensity): 383 ($M^{+\bullet}$, 70), 200 (21), 169 (33), 146 (100), 119 (16). Anal. Calcd for $C_{24}H_{33}NO_3$: C, 75.14; H, 9.20; N, 3.65. Found: C, 74.93; H, 8.91; N, 3.59.

Benzoquinolizidine Derivative 21i. Yield: 191 mg (48%). Mp: 129 °C. $[\alpha]^{21}_D$: −133.2. $[\alpha]^{21}_{578}$: −137.5. $[\alpha]^{21}_{546}$: −154.6. $[\alpha]^{21}_{436}$: −222.8. $[\alpha]^{21}_{365}$: −256.1 (c = 1.00). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.81 (d, J = 6.9, 3H), 0.91 (d, J = 7.6, 3H), 0.95 (d, J = 6.9, 3H), 0.78−1.12 (m, 3H), 1.21−1.48 (m, 2H), 1.52−1.92 (m, 9H), 2.18 (dst, J = 6.9, 2.7, 1H), 2.61 (td, J = 12.2, 3.0, 1H), 2.78 (ddd, J = 9.5, 7.6, 4.6, 1H), 3.02−3.18 (m, 2H), 3.58 (td, J = 10.7, 4.2, 1H), 3.88 (d, J = 9.5, 1H), 5.80 (d, J = 4.6, 1H), 6.82 (dd, J = 8.4, 7.6, 1H), 6.86 (d, J = 8.4, 1H), 7.18 (td, J = 8.4, 1.5, 1H), 7.42 (d, J = 7.6, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.8, 21.0, 22.3, 23.2, 24.0, 24.4, 25.4, 28.3, 31.4, 34.3, 39.9, 41.6, 45.9, 47.9, 48.4, 54.4, 77.8, 101.3, 113.5, 119.0, 127.1, 128.5, 130.1, 146.7, 175.0. IR (KBr): ν 2930, 2850, 1780, 1625, 1460, 1365, 1270, 1155, 945. MS m/z (relative intensity): 397 (M^+, 71), 353 (23), 214 (100), 186 (77), 149 (53), 129 (22), 120 (83). Anal. Calcd for $C_{25}H_{37}NO_3$: C, 75.52; H, 8.88; N, 3.52. Found: C, 75.41; H, 9.01; N, 3.47.

Benzoquinolizidine Derivative 26i. Yield: 102 mg (26%). Mp: 142 °C. $[\alpha]^{21}_D$: −125.2. $[\alpha]^{21}_{578}$: −127.0. $[\alpha]^{21}_{546}$: −144.3. $[\alpha]^{21}_{436}$: −217.9. $[\alpha]^{21}_{365}$: −239.9 (c = 0.98). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.82 (d, J = 6.9, 3H), 0.92 (d, J = 7.6, 3H), 0.95 (d, J = 6.9, 3H), 0.80−1.12 (m, 3H), 1.21−1.56 (m, 2H), 1.57−1.76 (m, 6H), 1.78−1.95 (m, 3H), 2.15 (dst, J = 6.9, 2.7, 1H), 2.52 (ddd, J = 8.0, 3.4, 3.1, 1H), 2.69−2.82 (m, 2H), 3.57 (td, J = 10.7, 4.2, 1H), 3.82 (d, J = 8.0, 1H), 3.96 (m 1H), 5.61 (d, J = 3.1, 1H), 6.82 (dd, J = 8.0, 7.6, 1H), 6.87 (d, J = 8.0, 1H), 7.18 (t, J = 8.0, 1H), 7.39 (d, J = 7.6, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.7, 20.9, 22.2, 23.1, 23.7, 24.1, 25.7, 30.2, 31.4, 34.3, 39.4, 40.0, 46.8, 47.7, 48.1, 54.2, 77.7, 101.5, 113.2, 116.3, 118.4, 128.6, 130.4, 145.1, 175.4. IR (KBr): ν 2935, 2860, 1770, 1590, 1455, 1365, 1270, 1125,925. MS m/z (relative intensity): 397 (M^+, 78), 353 (44), 214 (100), 186 (93), 149 (45), 129 (48), 120 (96). Anal. Calcd for $C_{25}H_{37}NO_3$: C, 75.52; H, 8.88; N, 3.52. Found: C, 75.46; H, 9.07; N, 3.67.

Preparation of *N*-Mesitylpyrrolidine 27.[37] 1,4-Dibromobutane (21.6 g, 100 mmol) was added to a solution of 2,4,6-trimethylaniline (13.52, 100 mmol) in 10 mL of ethanol. The solution was maintained at 60 °C for 72 h. After addition of an aqueous KOH solution (10%, 50 mL), the mixture was extracted with ether. The organic phase was washed with brine and dried with $MgSO_4$. After evaporation of the solvent, a yellow oil was obtained that was dissolved in 20 mL of CH_2Cl_2 and filtered over silica. After evaporation, an uncolored oil was obtained. Yield: 15.9 g (84%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.15 (m, 4H), 2.22 (s, 6H), 2.26 (s, 3H), 3.15 (m, 4H), 6.82 (s, 2H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 18.5, 20.7, 26.5, 50.1, 129.2, 134.4, 138.1, 142.7.

Reaction of (5*R*)-5-Menthyloxy-2-[5*H*]-furanone 1 with *N*-Mesitylpyrrolidine 27. A solution of (5*R*)-5-menthyloxy-2-[5*H*]-furanone **1** (120 mg, 0.5 mmol), *N*-mesitylpyrrolidine **27** (1.89 g, 10 mmol), and 4,4′-dimethoxybenzophenone (12 mg, 0.05 mmol) was irradiated at 350 nm for 7 min. After evaporation of the excess of solvent and amine, the residue was subjected to flash chromatography (eluent, ethyl acetate/petroleum ether 1/2).

Amine Adduct 28. Yield: 132 mg (62%). $[\alpha]^{21}_D$: −57.6. $[\alpha]^{21}_{578}$: −59.2. $[\alpha]^{21}_{546}$: −63.7. $[\alpha]^{21}_{436}$: −66.8. $[\alpha]^{21}_{365}$: −67.4 (c = 0.98). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.62 (d, J = 6.9, 3H) 0.78 (d, J = 7.6, 3H) 0.82 (d, J = 6.9, 3H) 0.52−0.96 (m, 3H) 0.98−1.32 (m, 4H) 1.40−1.78 (m, 4H) 1.80−2.22 (m, 2H) 2.11 (s, 3H) 2.18 (s, 3H) 2.19 (s, 3H) 2.36 (dd, J = 18.3, 8.0, 1H) 2.58 (dd, J = 18.3, 8.7, 1H) 2.91 (ddd, J = 15.8, 7.3, 6.9, 1H) 3.38 (m, 3H) 3.60 (dd, J = 7.3, 6.1, 1H) 5.09 (s, 1H) 6.72 (s, 1H) 6.74 (s, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.3, 19.0, 19.2, 20.7, 20.8, 22.1, 24.5, 25.0, 25.4, 29.2, 30.4, 31.1, 34.2, 39.0, 47.3, 47.7, 52.5, 60.0, 75.4, 101.8, 129.3, 130.6, 134.8, 135.6, 135.8, 141.8, 176.4. IR (KBr): ν 2960, 2870, 1780, 1455, 1360, 1245, 1155, 940. MS m/z (relative intensity): 427 (M^+, 7), 288 (11), 188 (100), 146 (5). Anal. Calcd for $C_{27}H_{41}NO_3$: C, 75.82; H, 9.67; N, 3.28. Found: C, 75.60; H, 9.39; N, 3.06.

Amine Adduct 29. Yield: 34 mg (16%). $[\alpha]^{21}_D$: −97.1. $[\alpha]^{21}_{578}$: −101.8. $[\alpha]^{21}_{546}$: −118.2. $[\alpha]^{21}_{436}$: −121.3. $[\alpha]^{21}_{365}$: −133.2 (c = 0.98). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.66 (d, J = 6.9, 3H), 0.78 (d, J = 7.6, 3H), 0.80 (d, J = 6.9, 3H), 0.50−0.98 (m, 3H), 1.00−1.32 (m, 4H), 1.43−1.72 (m, 4H), 1.80−2.27 (m, 2H), 2.13 (s, 3H), 2.16 (s, 3H), 2.18 (s, 3H), 2.42 (dd, J = 18.0, 7.2, 1H), 2.47 (dd, J = 18.0, 9.3, 1H), 2.91 (ddd, J = 16.0, 8.4, 7.2, 1H), 3.28 (m, 3H), 3.63 (ddd, J = 8.4, 7.3, 4.2, 1H), 5.22 (d, J = 4.2, 1H), 6.74 (s, 1H) 6.78 (s, 1H). ^{13}C NMR (62 MHz, $CDCl_3$): δ 15.6, 18.6, 19.2, 20.6, 20.7, 22.1, 22.8, 25.0, 25.4, 29.2, 30.3, 30.8, 34.2, 36.2, 47.3, 48.8, 53.1, 57.9, 73.6, 98.6, 128.3, 130.4, 134.6, 136.8, 137.9, 142.3, 176.3. IR (KBr): ν 2955, 2865, 1785, 1450, 1375, 1245, 1145, 930. MS m/z (relative intensity): 427 (M^+, 7), 288 (7), 188 (100), 146 (8), 119 (8). Anal. Calcd for $C_{27}H_{41}NO_3$: C, 75.82; H, 9.67; N, 3.28. Found: C, 75.63; H, 9.42; N, 3.01.

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Supporting Information Available: Table with NMR data for the determination of structures **6a,b** by comparison with corresponding data of **5a,b**. Tables with energies and XYZ coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

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