Intramolecular Cycloadditions of α-Allyloxycarbonylnitrones: Stereoselective Synthesis of 3-Amino-2(5*H*)furanones

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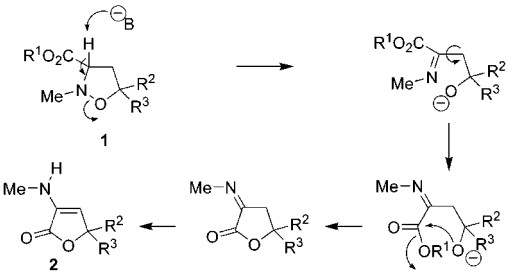
Abstract: Treatment of furoisoxazolidines with NaH leads to functionalized 3-amino-2(5*H*)-furanones through a new rearrangement pattern of the isoxazolidine nucleus. This process has been usefully exploited for the synthesis of enantiomerically pure (5*R*)-3-alkylamino-5-methyl-2(5*H*)-furanones.

Introduction

There has recently been a renewed interest in the synthesis of structurally simple 2(5*H*)-furanones or α-butenolides.[1] This ring system constitutes the central skeleton of a series of natural oxygenated heterocycles[2] and is widely present in secondary metabolites[3] that have specific physiological activities. In fact, most of the known compounds exhibit various biological properties, including antibiotic,[4] fungicidal,[5] anthelmintic,[6] and antitumoral activities.[7] Additionally, some of these are potent antiplatelet agents,[8] antifeedants,[9] or antagonists against opioid receptors.[10] In addition to their biological features, butenolides are useful intermediates in organic synthesis. For example, such compounds have been used to prepare peptide analogues or HIV-1 protease inhibitors.[11]

Scheme 1



However, since most substituted butenolides are too toxic for therapeutic utilization,[12] there is a need for new, nontoxic compounds containing this structural moiety. Procedures for the synthesis of α-butenolides have been reviewed, and in recent years, some new methods have been published.[13] The pericyclic reaction of suitable 1,3-dipoles to alkenes has also been usefully exploited,[14] especially as a synthetic approach toward this class of compounds. In this context, we previously reported[15] a new general route toward α-aminobutenolides that represent versatile synthons for obtaining *β*-lactams.[16] Our approach consists of a basic treatment of isoxazolidines suitably activated at position C_3 of the nucleus. Thus, isoxazolidines **1** (Scheme 1) undergo rearrangement to the corresponding 3-methylamino-2(5*H*)-furanones **2** after treatment with NaH at room temperature. By this approach, the lactone ring of compound **2**, otherwise obtainable after a multistep elaboration of lactone substrates, is smoothly formed by a ring opening of **1** followed by a straightforward intramolecular acyl nucleophilic substitution (Scheme 1).

Beginning with the suitable precursors, this reaction pathway could lead to highly functionalized butenolides. To accomplish this, we hoped to extend the reaction scheme to a series of bicyclic furoisoxazolidines, easily obtainable by an intramolecular cycloaddition reaction of α-allyloxycarbonyl-*N*-methylnitrones, to obtain func-

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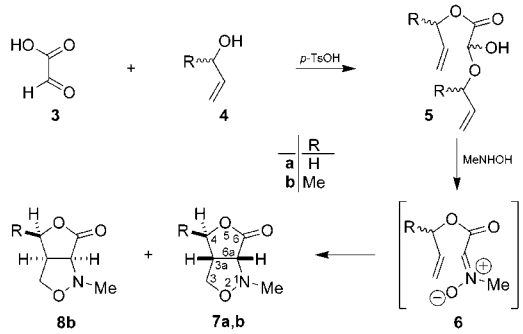
Scheme 2



tionalized 3-alkyl-substituted 2-aminobutenolides, which are useful synthons for the access to a series of nitrogen-containing functionalized γ-lactones. However, we realized that subsequent treatment of furoisoxazolidines with NaH opens a different reaction route that leads to 3-amino-2(5*H*)-furanones originating from a new rearrangement process of the isoxazolidine nucleus. This rearrangement process has been used to design an enantioselective approach to optically active α-aminolactones (5*R*)-(+)-5-methyl-3-methylamino-2(5*H*)-furanone and (5*R*)-(+)-3-benzylamino-5-methyl-2(5*H*)-furanone.

Results and Discussion

The preparation of the target α-allyloxycarbonylnitrones from allylic alcohols requires multiple steps,[17] and this becomes a significant drawback for the synthetic applications of the cycloaddition of the nitrones. In a first attempt, we exploited the synthetic approach outlined in Scheme 2. Allylic alcohols **4** were made to react with glyoxylic acid **3** in the presence of catalytic amounts of *p*-TsOH to afford hemiacetals **5**: compound **5b** has been obtained as an unseparable mixture of diastereoisomers.[18]

The structure of compounds **5** was confirmed by analytical and spectrometric data. In particular, the mass spectra show diagnostic fragmentations that are amenable to two reaction channels corresponding, respectively, to the acylium ion **A**, originated from the loss of the alkoxy radical, and to the fragment **B** originated from the loss of the alkoxycarbonyl radical (Figure 1).[18]

The reaction of **5** with *N*-methylhydroxylamine, performed at room temperature in anhydrous diethyl ether and in the presence of $CaCl_2$ and $NaHCO_3$, afforded directly, via the unisolated nitrone intermediates **6**, the furoisoxazolidines **7a** and **7b**, and **8b**, respectively, with a 40−50% overall yield starting from glyoxylic acid (Scheme 2). Compounds **7b** and **8b** have been obtained in a 1:1 ratio according to their integrals in the ^{1}H NMR spectrum of the crude reaction mixture.

The reactions show a complete regioselectivity, and no bridged adducts originating from a reverse regiochemistry have been detected in the crude reaction mixture. The structure of the obtained compounds was assigned on the basis of spectroscopic data (see the Experimental Section). The cis fusion of the two rings was ascertained from the value of the coupling constant between H_{6a} and H_{3a}, which was 8.1 Hz for compound **7a** and 7.9 and 9.7 Hz for compounds **7b** and **8b**, respectively.

The poor diastereoselection observed for this intramolecular cycloaddition is due to the high flexibility of nitrone intermediate **6b**, which generates two different

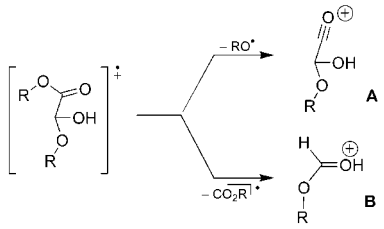


Figure 1. Mass spectra diagnostic fragmentation.

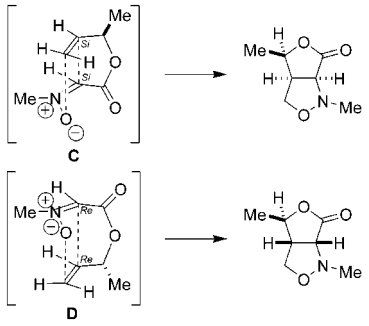
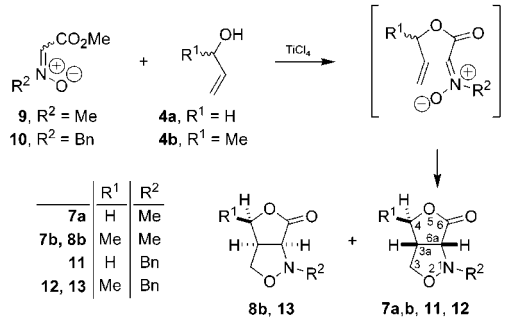


Figure 2. Transition states for intermediate nitrone **6b**.

Scheme 3



transition states **C** (*Si-Si* attack) and **D** (*Re-Re* attack)[19] that show no relevant steric interaction (Figure 2).

Stereochemical assignments for compounds **7b** and **8b** are based on NOE measurements. Thus, irradiation of the proton at C_{6a} in **7b** (3.51 ppm) induces a positive NOE effect on H_{3a} (3.35 ppm) and on the methyl resonance at C_4, so indicating a cis relationship between these protons. Conversely, in compound **8b**, irradiation of the same resonance (3.86 ppm) resulted in a positive NOE effect for H_{3a} (3.56 ppm) and H_4 (4.74 ppm).

An alternative and more convenient access to furoisoxazolidines **7** and **8** has also been developed. Tamura et al. have recently reported[20] that α-methoxycarbonyl nitrones **9** and **10** cause tandem transesterification with allyl alcohols, *E*−*Z* isomerization, and intramolecular cycloadditions in the presence of titanium isopropoxide or $TiCl_4$ and 4 Å molecular sieves to give bicyclic furoisoxazolidines under mild conditions in one step.[19,20]

Consequently, as shown in Scheme 3, the reaction of **9** and **10** (1.6:1 *E*−*Z* equilibrating mixture in $CDCl_3$)[14a] with allyl alcohols **4** in the presence of titanium tetrachloride proceeded smoothly at room temperature to directly afford furoisoxazolidines **7a**,**b**, **8b**, and **11**−**13**.

The observed global yields are very satisfactory, in the range 75−85%, starting from nitrones **9** and **10**.

When isoxazolidines **7a**,**b**, **8b**, **11**−**13** were treated with NaH in anhydrous THF, 3-methylamino-2(5*H*)furanones

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(18) See the Supporting Information.

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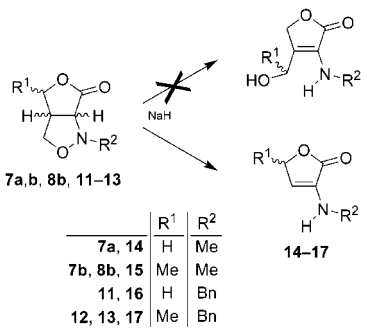
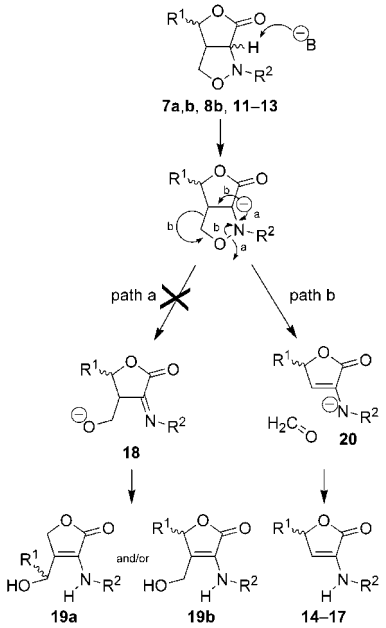
Scheme 4



	R^1	R^2
7a, 14	H	Me
7b, 8b, 15	Me	Me
11, 16	H	Bn
12, 13, 17	Me	Bn

Scheme 5



14−**17** have been obtained in yields ranging from 60 to 80% (Scheme 4).

Structural assignments have been performed on the basis of spectrometric data. The molecular formula of furanones follows from an exact mass determination; the IR absorptions of the carbonyl groups at 1720 cm^{-1} are in accord with the γ-lactones.

The ^1H NMR spectra of compounds **14-17** show the H_4 protons as doublets of doublets in the range 5.40−7.06 ppm, while the H_5 protons resonate at 4.57−5.04 ppm. Moreover, the *N*-methyl groups in compounds **14** and **16** resonate as doublets (J = 3.1 and 4.5 Hz) at 2.77 ppm.

With references to previously reported synthesis of aminofuranones,[14a] in the case of furoisoxazolidinones **7a**,**b**, **8b**, and **11**−**13**, the lactone ring created in the intramolecular cycloaddition processes is maintained and its functionalization described above is controlled by the fragmentation of the isoxazolidine nucleus. In fact, the chemical conversion of bicyclic compounds **7a**,**b**, **8b**, and **11**−**13** can be rationalized on the basis of the sequence steps shown in Scheme 5.

The driving force for the transformations of **7a**,**b**, **8b**, and **11**−**13** into **14**−**17** is represented by the low critical energy required to induce a carbanionic center at position 6a of the furoisoxazolidinones **7a**,**b**, **8b**, and **11**−**13**. According to a previous report,[15] the intermediate alkoxy anion **18**, formed by the ring opening of the isoxazolidine ring nucleus (path a), could then evolve towards compound **19a** by intramolecular lactonization; alternatively, the cleavage of the N−O bond and the subsequent imino-amino isomerization could lead to compound **19b**. The population of a different reaction path with respect to the previously reported route, with formation of **14**−**17** (path b), is due to the electronic requirements that favor the formation of the endocyclic double bond of intermediate **20** over the exocyclic counterpart of intermediate **18**. In this case, a lower critical energy pathway is available whereby a formal retroaldol condensation reaction brings about the formation of the target α-enaminolactones with elimination of formaldehyde.

On the basis of the stereochemical features seen in the intramolecular cyclization of α-allyloxycarbonyl nitrones and the new rearrangement process of the isoxazolidine ring, we were able to exploit the overall process to enter enantioselective synthesis of 3-methylamino-2-(5*H*)-furanones in an optically pure form. In this context, the homochiral alcohol (*R*)-(−)-**4b** was reacted with nitrone **9** in the presence of $TiCl_4$ to yield enantiomerically pure (3a*R*,4*R*,6a*R*)-(+)-**7b** and (3a*S*,4*R*,6a*S*)-(+)-**8b**, which were separated by flash chromatography. Compounds **7b** (α = +38.2) and **8b** (α = +25.0) were obtained in a 1.5:1 ratio.

Finally, treatment with NaH of two separated diastereoisomers yielded the same (5*R*)-(+)-5-methyl-3-methylamino-2(5*H*)-furanone (**15**), in enantiomerically pure form (α = +8.6). The optical purity of the compound was confirmed by chiral HPLC and by the use of NMR chiral shift reagents.

To confirm the proposed reaction pathway, a mixture of enantiomerically pure **12** and **13** (1.5:1 ratio) was synthesized by reaction of nitrone **10** with the homochiral alcohol (*R*)-(−)-**4b**. Further treatment of this mixture with NaH furnished the compound (5*R*)-(+)-3-benzylamino-5-methyl-2(5*H*)-furanone (**17**) in enantiomerically pure form (α = +12.5).

This result confirms the hypothesis that the reaction proceeds with cleavage of the heterocyclic ring at the N−O bond, followed by a fragmentation reaction that involves the C_3-C_{3a} bond.

In conclusion, treatment of furoisoxazolidines with NaH affords a new rearrangement pattern of the isoxazolidine nucleus, and the present process has been extended to the synthesis of enantiomerically pure (5*R*)-3-alkylamino-5-methyl-2(5*H*)-furanones. Our process may also facilitate access to various stereochemically defined lactones.

Experimental Section

General Procedure for the Preparation of Bicyclic Isoxazolidines 7a,b, 8b, and 11−13. Method A. To a magnetically stirred suspension of *N*-methylhydroxylamine hydrochloride (2.09 g, 25 mmol) were added calcium chloride (3.88 g, 35 mmol) and sodium hydrogen carbonate (5.12 g, 61 mmol) in anhydrous diethyl ether (70 mL) in a two-neck round-bottom flask, equipped with a Dean−Stark trap and a dropping funnel, to which was added, in a dropwise fashion, a solution of **5** (17.5 mmol) in anhydrous diethyl ether (100 mL). The reaction mixture was stirred at room temperature for 24 h and then filtered. The solvent was removed under vacuum, and the residue was purified by column flash chromatography (hexane/EtOAc, 9:1). **Method B.** To a stirred suspension of allyl alcohol **4** (17.4 mmol) and 4 Å molecular sieves (900 mg) in 1,2-dichloroethane (30 mL) were successively added titanium tetrachloride (1 M solution in 1,2-dichloromethane, 3.5 mmol) and a solution of nitrone **9** or **10** (11.6 mmol) in 1,2-dichloroethane (10 mL) at room temperature. After the mixture was stirred for 20 h, a small amount of water was added and the mixture was again stirred for 1 h. The mixture was than filtered through a

(20) (a) Tamura, O.; Yamaguchi, T.; Okabe, T.; Sakamoto, M. *Synlett* **1994**, 620. (b) Tamura, O.; Yamaguchi, T.; Noe, K.; Sakamoto, M. *Tetrahedon Lett.* **1993**, *34*, 4009. (c) Tamura, O.; Okabe, T.; Yamaguchi, T.; Gotanda, K.; Noe, K.; Sakamoto, M. *Tetrahedron* **1995**, *51*, 107. (d) Tamura, O.; Okabe, T.; Yamaguchi, T.; Kotani, J.; Gotanda, K.; Sakamoto, M. *Tetrahedron* **1995**, *51*, 119.

pad of Celite, and the filtrate was then diluted with water, extracted with dichlorometane, and dried over $MgSO_4$. After filtration, the filtrate was concentrated in a vacuum and the residue was purified by column flash chromatography as described in method A.

(3a*SR*,6a*RS*)-1-Methyltetrahydro-3*H*,6*H*-furo[3,4-*c*]isoxazol-6-one (7a). Following **method A**, **5a** (3.01 g) afforded **7a** (1.80 g, 72%) as pale yellow solid: mp 74−75 °C; IR (KBr) 3529, 2980, 1778, 1447, 1199, 1194 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.75 (s, 3H, *N*-CH_3), 3.60 (m, 1H, H_{3a}), 3.85 (dd, 1H, J = 3.0, 9.1 Hz, $H_{3'}$), 3.92 (d, 1H, J = 8.1 Hz, H_{6a}), 4.25 (dd, 1H, J = 7.5, 10.0 Hz, $H_{4'}$), 4.30 (dd, 1H, J = 3.3, 9.1 Hz, $H_{3''}$), 4.53 (dd, 1H, J = 8.1, 10.0 Hz $H_{4''}$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.9, 47.8, 66.5, 68.3, 71.2, 168.9; MS (70 eV) 143 (M^+, 65), 143 (25), 99 (30), 42 (100); HRMS (EI) calcd for [M^+] $C_6H_9NO_3$ 143.0582, found 143.0580. Anal. Calcd for $C_6H_9NO_3$: C, 50.33; H, 6.34; N, 9.79. Found: C, 50.24; H, 6.32; N, 9.82.

Following **method B**, **4a** (1.01 g) and **9** (1.36 g) afforded **7a** (1.08 g, 65%).

(3a*RS*,4*RS*,6a*RS*)-1,4-Dimethyltetrahydro-3*H*,6*H*-furo[3,4-*c*]isoxazol-6-one (7b). Following **method A**, **5b** (3.50 g) afforded **7b** (848 mg, 31%) as light yellow oil: first eluted product; IR (neat) 3453, 2980, 1771, 1560, 1460, 1390 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.40 (d, 3H, J = 6.6 Hz), 2.76 (s, 3H, *N*-CH_3), 3.35 (dddd, 1H, J = 3.9, 6.0, 7.9, 8.3, H_{3a}), 3.51 (d, 1H, J = 7.9 Hz, H_{6a}), 4.09 (dq, 1H, J = 6.0, 6.6 Hz, H_4), 4.25 (dd, 1H, J = 3.9, 9.8 Hz, $H_{3'}$), 4.45 (dd, 1H, J = 8.3, 9.8 Hz, $H_{3''}$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.3, 46.1, 50.4, 71.0, 75.4, 81.0, 168.7; MS (70 eV) 157 (M^+, 20), 113 (100); HRMS (EI) calcd for [M^+] $C_7H_{11}NO_3$ 157.0739, found 157.0736. Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.28; H, 7.06; N, 8.94.

Following **method B**, **4b** (1.25 g) and **9** (1.36 g) afforded **7b** (711 mg, 39%). Following **method B**, (*R*)-(−)-**4b** afforded (3a*R*,4*R*,6a*R*)-**7b**: $[\alpha]^{25}_D$ = +38.2 (*c* 1.15, $CHCl_3$).

(3a*SR*,4*RS*,6a*SR*)-1,4-Dimethyltetrahydro-3*H*,6*H*-furo[3,4-*c*]isoxazol-6-one (8b). Following **method A**, **5b** (3.50 g) afforded **8b** (821 mg, 30%) as light yellow oil: further eluted product; IR (neat) 3429, 2970, 1778, 1447, 1399 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.44 (d, 3H, J = 6.6 Hz), 2.74 (s, 3H, *N*-CH_3), 3.56 (dddd, 1H, J = 3.4, 3.5, 3.8, 9.7, H_{3a}), 3.86 (d, 1H, J = 9.7 Hz, H_{6a}), 3.90 (dd, 1H, J = 3.4, 9.6 Hz, $H_{3'}$), 3.95 (dd, 1H, J = 3.5, 9.6 Hz, $H_{3''}$), 4.74 (dq, 1H, J = 3.8, 6.6 Hz, H_4); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.4, 46.1, 51.5, 64.9, 70.1, 76.6, 168.5; MS (70 eV) 157 (M^+, 25), 142 (10), 113 (100); HRMS (EI) calcd for [M^+] $C_7H_{11}NO_3$ 157.0739, found 157.0737. Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.35; H, 7.04; N, 8.93.

Following **method B**, **4b** (1.25 g) and **9** (1.36 g) afforded **8b** (674 mg, 37%). Following **method B**, (*R*)-(−)-**4b** afforded (3a*S*,4*R*,6a*S*)-**8b**: $[\alpha]^{25}_D$ = +25.0 (*c* 1.07, $CHCl_3$).

(3a*SR*,6a*RS*)-1-Benzyltetrahydro-3*H*,6*H*-furo[3,4-*c*]isoxazol-6-one (11). Following **method B**, **4a** (1.01 g) and **10** (2.24 g) afforded **11** (1.52 g, 60%) as white needles: mp 163−164 °C; IR (KBr) 3539, 2960, 1782, 1221, 1210 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.55 (ddddd, 1H, J = 3.0, 3.3, 7.6, 8.4, 8.6, H_{3a}), 3.92 (dd, 1H, J = 3.0, 10.2 Hz, $H_{3'}$), 4.00 (dd, 1H, J = 8,6, 10.2 Hz, $H_{3''}$), 4.05 (d, 1H, J = 13.2 Hz, PhC*H*), 4,17 (d, 1H, J = 13.2 Hz, PhC*H*), 4.27 (dd, 1H, J = 3.3, 9.6 Hz, $H_{4'}$), 4.31 (d, 1H, J = 8.4 Hz, H_{6a}), 4.50 (dd, 1H, J = 7.6, 9.6 $H_{4''}$), 7.26−7.44 (m, 5H, aromatic protons); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 30.9, 42.7, 64.5, 71.6, 72.6, 127.8, 128.5, 128.9, 135.9, 169.4; MS (70 eV) 219 (M^+, 19), 92 (10), 91 (100); HRMS (EI) calcd for [M^+] $C_{12}H_{13}NO_3$ 219.0895, found 219.0896. Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.81; H, 5.99; N, 6.40.

(3a*RS*,4*RS*,6a*RS*)-1-Benzyl-4-methyltetrahydro-3*H*,6*H*-furo[3,4-*c*]isoxazol-6-one (12). Following **method B**, **4b** (1.25 g) and **10** (2.24 g) afforded **12** (1.08 g, 40%) as a white solid: mp 150−152 °C; first eluted product; IR (KBr) 3425, 2980, 1802, 1250, 1210 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.46 (d, 3H, J = 6.6 Hz), 3.48 (m, 1H, H_{3a}), 3.97 (d, 1H, J = 6.8 Hz, H_{6a}), 4.05 (m, 2H, H_3), 4.12 (d, 1H, J = 12.8 Hz, PhC*H*), 4,18 (d, 1H, J = 12.8 Hz, PhC*H*), 4.73 (dq, 1H, J = 5.4, 6.6 Hz, H_4), 7.30−7.44 (m, 5H, aromatic protons); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.3, 46.0, 50.4, 65.9, 75.2, 80.9, 128.5, 128.9, 129.0, 135.7, 168.8; MS (70 eV) 233 (M^+, 20), 142 (15), 98 (60), 91 (100); HRMS (EI) calcd for [M^+] $C_{13}H_{15}NO_3$ 233.1052, found 233.1055. Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.87; H, 6.47; N, 5.98.

Following **method B** with (*R*)-(−)-**4b** (1.25 g) afforded (3a*R*,4*R*,6a*R*)-**12**: $[\alpha]^{25}_D$ = +10.0 (*c* 1.35, $CHCl_3$).

(3a*SR*,4*RS*,6a*SR*)-1-Benzyl-4-methyltetrahydro-3*H*,6*H*-furo[3,4-*c*]isoxazol-6-one (13). Following **method B** with **4b** (1.25 g) and **10** (2.24 g) afforded **13** (1.05 g, 39%) as white solid: mp 161−162 °C; first eluted product; IR (KBr) 3453, 2980, 1771, 1560, 1460, 1390 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.42 (d, 3H, J = 6.3 Hz), 3.17 (m, 1H, H_{3a}), 3.97 (m, 1H, $H_{3'}$), 4.02 (m, 1H, $H_{3''}$), 4.07 (d, 1H, J = 4.8 Hz, H_{6a}), 4.10 (d, 1H, J = 12.8 Hz, PhC*H*), 4.12 (d, 1H, J = 12.8 Hz, PhC*H*), 4.75 (dq, 1H, J = 3.6, 6.3 Hz, H_4), 7.29−7.44 (m, 5H, aromatic protons); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.5, 46.3, 65.5, 70.2, 75.3, 80.9, 127.8, 128.92, 128.98, 135.7, 168.9; MS (70 eV) 233 (M^+, 18), 98 (40) 91 (100). HRMS (EI) calcd for [M^+] $C_{13}H_{15}NO_3$ 233.1052, found 233.1050. Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.79; H, 6.49; N, 6.03.

Following **method B** with (*R*)-(−)-**4b** (1.25 g) afforded (3a*S*,4*R*,6a*S*)-**13**: $[\alpha]^{25}_D$ = +30.5 (*c* 1.20, $CHCl_3$).

General Procedure for the Preparation of 3-Alkylamino-2(5*H*)furanones 14−17. To a solution of furoisoxazolidine **7**, **8**, or **11**−**13** (2.0 mmol) in dry THF (10 mL) was added NaH (48 mg, 2.0 mmol), and the mixture was stirred for 5 h at room temperature, until the TLC showed the disappearance of the starting material. The reaction mixture was then charged with water, extracted with chloroform, and the combined organic phases, dried over Na_2SO_4, evaporated under reduced pressure. The residue was then purified by column flash chromatography (hexane/EtOAc, 9:1).

3-Methylamino-2(5*H*)furanone (14). Compound **7a** (286 mg) gave **14** (115 mg, 51%) as a light yellow oil: IR (neat) 3380, 2934, 2880, 1750, 1660, 1140, 1037 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.77 (d, 3H, J = 3.1 Hz, *N*-CH_3), 3.90 (bs, 1H, N*H*), 4.85 (d, 2H, J = 2.9 Hz, H_5), 6.93 (t, 1H, J = 5.0 Hz, H_4); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 32.8, 67.5, 122.1, 136.6, 172.3; MS (70 eV) 113 (M^+, 43), 85 (40), 69 (100); HRMS (EI) calcd for [M^+] $C_5H_7NO_2$ 113.0476, found 113.0472. Anal. Calcd for $C_5H_7NO_2$: C, 53.09; H, 6.24; N, 12.38. Found: C, 52.91; H, 6.22; N, 12.40.

(5*RS*)-5-Methyl-3-methylamino-2(5*H*)furanone (15). Compounds **7b** and **8b** (314 mg) gave **15** (130 mg, 51%) as a light yellow oil: IR (neat) 3370, 2900, 1750, 1650, 1140, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.40 (d, 3H, J = 6.6 Hz, CH_3), 2.77 (d, 3H, J = 4.8, *N*-CH_3), 3.90 (bs, 1H, N*H*), 5.04 (dq, 1H, J = 6.6 and 2.0 Hz, H_5), 5.55 (d, 1H, J = 2.0, H_4); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.9, 31.1, 75.9, 111.1, 144.7, 172.5; MS (70 eV) 127 (M^+, 33), 99 (15), 83 (100); HRMS (EI) calcd for [M^+] $C_6H_9NO_2$ 127.0633, found 127.0631. Anal. Calcd for $C_6H_9NO_2$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.59; H, 7.13; N, 11.00. Compounds (3a*R*,4*R*,6a*R*)-**7b** and (3a*S*,4*R*,6a*S*)-**8b** afforded (5*R*)-**15**; $[\alpha]^{25}_D$ = +8.6 (*c* 0.58, $CHCl_3$).

3-Benzylamino-2(5*H*)furanone (16). Compound **11** (438 mg) gave **16** (193 mg, 51%) as a light yellow oil: IR (neat) 3350, 2834, 1760, 1630, 1180, 1120, 1057 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.34 (s, 2H, PhCH_2), 4.72 (d, 2H, J = 3.0, H_5), 7.06 (t, 1H, J = 3.0 Hz, H_4), 7.22−7.63 (m, 5H, aromatic protons), 8.57 (bs, 1H, N*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.3, 67.9, 126.6, 127.5, 129.3, 129.6, 133.9, 135.0, 173.4; MS (70 eV) 189 (M^+, 33), 161 (28), 145 (40), 91 (100); HRMS (EI) calcd for [M^+] $C_{11}H_{11}NO_2$ 189.0789, found 189.0791. Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.91; H, 5.87; N, 7.38.

(5*RS*)-3-Benzylamino-5-methyl-2(5*H*)furanone (17). Compounds **12** and **13** (466 mg) gave **17** (223 mg, 55%) as a light yellow oil: IR (neat) 3350, 2900, 2830, 1760, 1140, 1017 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.28 (d, 3H, J = 6.8 Hz, CH_3), 4.34 (d, 2H, J = 13.5, PhCH_2), 4.57 (dq, 1H, J = 2.7 and 6.8 Hz, H_5), 6.80 (t, 1H, J = 2.7 H_4), 7.22−7.63 (m, 5H, aromatic protons), 8.44 (bs, 1H, N*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.4, 44.3, 75.2, 126.6, 129.3, 129.6, 133.5, 134.9, 150.7, 172.6; MS (70 eV) 203 (M^+, 25), 175 (15), 159 (50), 91 (100); HRMS (EI) calcd for [M^+] $C_{12}H_{13}NO_2$ 203.0946, found 203.0948. Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 71.11; H, 6.50; N, 6.87. Compounds (3a*R*,4*R*,6a*R*)-**12** and (3a*S*,4*R*,6a*S*)-**13** afforded (5*R*)-**17**: $[\alpha]^{25}_D$ = +12.5 (*c* 0.75, $CHCl_3$).

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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