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Concomitant C(α),C(β)-Asymmetric Induction in the Aza-Claisen Rearrangement of *N*-Allylketene *N,O*-Acetals

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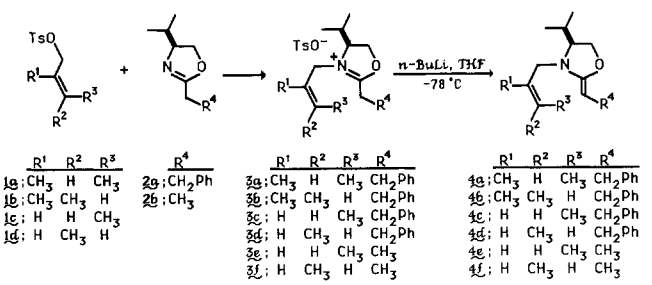
Asymmetric C–C bond formation via the diastereoselective aza-Claisen rearrangement of *N*-allylketene *N,O*-acetals **4** is described. The starting materials, allylic alkylating agent **1** and optically pure oxazoline **2**, are easily prepared and, in a one-pot procedure, generate rearranged oxazolines **5/7/9** in 97–98% enantiomeric excess and with 79–92% diastereoselectivity. The overall yields for this process (**2** → **5/7/9**) range from 73 to 87%. A combination of excellent *N,O*-acetal face selectivity, excellent (*Z*)-ketene *N,O*-acetal olefin selectivity, and moderate chair selectivity are shown to account for the observed diastereoselectivity.

The enantioselective construction of acyclic systems is a challenging goal of current interest in synthetic chemistry. Of the strategies which address this issue, often the most versatile are those which proceed with stereocontrolled C–C bond formation since chirality is established and the carbon skeleton is elaborated in one synthetic operation.[1] Due to the reliable stereoselectivity of sigmatropic rearrangements, this class of reactions has found numerous applications in acyclic stereocontrol, primarily in internal[2a] asymmetric induction[2] but also in relative[2a] asymmetric induction.[2] Of the latter, most are self-immolative[3] and stereogenicity is merely transmitted along the carbon chain. In complement to existing self-immolative Claisen protocols, we recently reported the enantioselective preparation of chiral C(α)- and C(β)-substituted pent-4-enoic acids by chiral auxillary-mediated aza-Claisen rearrangements of *N*-allylketene *N,O*-acetals.[4,5] In that work, stereoinduction at C(α) ranged from 92 to 94% enantiomeric excess (ee) and was shown to be the result of (*Z*)-ketene *N,O*-acetal olefin selectivity and oxazolidine C(α)-*si*-face selectivity.[4] For C(β)-induction, the critical transition-state parameters were shown to be oxazolidine face selectivity and chair/boat selectivity with stereoinduction ranging from 52 to 94% ee at C(β).[5] We now report that this aza-Claisen rearrangement can provide concomitant C(α),C(β)-asymmetric induction with excellent enantioselectivity. Moreover, the resulting Claisen products are masked C(α),C(β)-substituted pent-4-enoic acids, substrates which are not readily available enantioselectivly by other methods.[6]

Scheme I. *N*-Allylketene *N,O*-Acetal Preparation



These aza-Claisen rearrangements produce only two diastereomeric Claisen products in either C(α)- or C(β)-asymmetric induction.[4,5] In contrast, concomitant C(α),C(β)-induction can result in four Claisen products: two diastereomers with the C(α),C(β)-*l*-configuration[7] and two diastereomers with the C(α),C(β)-*u*-configuration.[7] However, *N*-allyl olefin geometry in **3** is the primary determinant of *l*/*u*-stereoselectivity in C(α),C(β) concomitant asymmetric induction. Therefore, selecting the appropriate

(1) For a recent review which illustrates this versatility for enolate–electrophile reactions, see: Evans, D. A. In *Asymmetric Synthesis*; Mosher, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, p 2.

(2) Reviews: (a) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 1. (b) Murray, A. W. *Org. React. Mech.* **1980**, 517. (c) Hill, R. K. In *Asymmetric Synthesis*; Mosher, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, p 503. (d) Bennett, G. B. *Synthesis* **1977**, 589. (e) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227. (f) Rhoads, S. J.; Raulins, N. R. *Org. React. (N.Y.)* **1975**, *22*, 1.

(3) Mislow, K. *Introduction to Stereochemistry*; Benjamin: New York, 1965; p 131.

(4) Kurth, M. J. Decker, O. H. W.; Hope, H.; Yanuck, M. D. *J. Am. Chem. Soc.* **1985**, *107*, 443.

(5) Kurth, M. J.; Decker, O. H. W. *J. Org. Chem.* **1985**, *50*, 5769.

(6) For a recent review of the highly enantioselective C(α)-alkylation or C(β)-conjugate addition protocols developed by Meyers, see: Lutomski, K. A.; Meyers, A. I. In *Asymmetric Synthesis*; Mosher, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, p 213.

(7) Seebach, D.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654.

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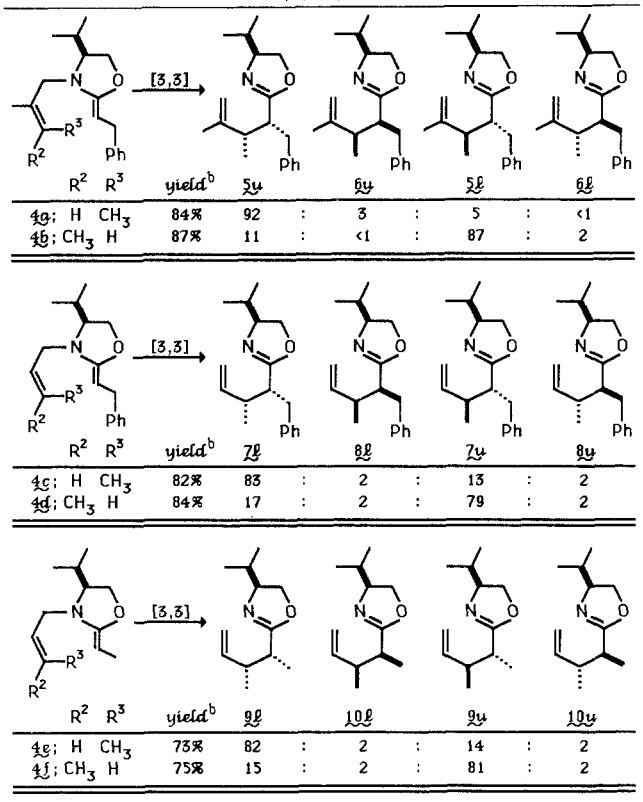
Table I. Concomitant C(α),C(β)-Asymmetric Induction[a]



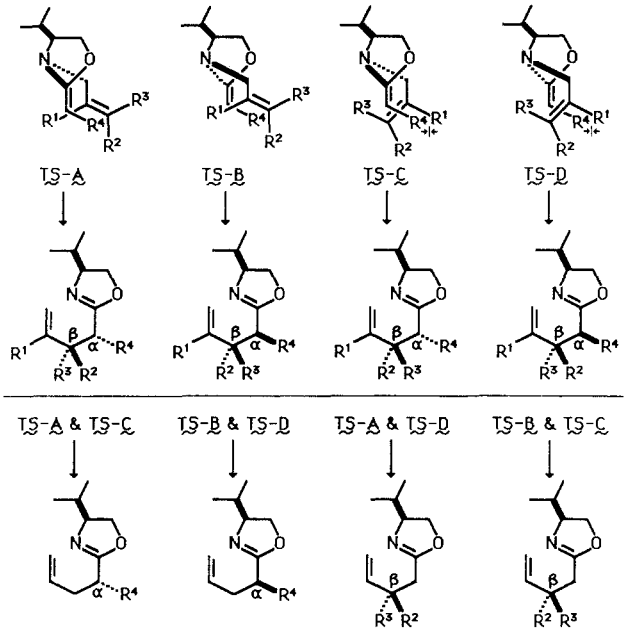
[a] Ratios determined by integration of base-line resolved ^{1}H NMR resonances of the corresponding *N*-methyloxazolinium salts (see Experimental Section). [b] Combined yield of the four oxazolines after purification by chromatography.

(*E*)- or (*Z*)-allyl tosylate (**1a–d**) ultimately provides stereocontrolled access to either the *l*- or the *u*-2,3-disubstituted pent-4-enoic acid.

A one-pot elaboration of starting oxazoline **2** to rearranged C(α),C(β)-chiral oxazolines **5–10** was accomplished by using reagents and conditions analogous to those developed for rearrangements producing C(α)- or C(β)-chiral oxazolines. Thus, as outlined in Scheme I, neat oxazoline **2** (**a**,**b**) was alkylated with the appropriate tosylate ester **1** (**a–d**) to yield oxazolinium salt **3** (**a–f**). Subsequent trituration with ether followed by neutralization with *n*-butyllithium in THF gave the desired *N*-allylketene *N*,*O*-acetal **4** (**a–f**) which, without isolation, was heated at 180 °C in decalin for 4 h to effect the aza-Claisen rearrangement. The substrates, overall yields [**2** → (**5–10**)], and product ratios for this one-pot procedure are presented in Table I.

It is important to recognize that four stereochemical factors operate in C(α),C(β)-induction: (i) (*E*/*Z*)-*N*-allyl olefin geometry (determined by tosylate selection),[4] (ii) (*Z*)-ketene *N*,*O*-acetal olefin selectivity (>97% (*Z*)-selectivity),[5] (iii) oxazolidine face selectivity (relative asymmetric induction),[4] and (iv) chair/boat selectivity (internal asymmetric induction). These parameters represent a summation of those shown to control separate C(α)- and C(β)-induction. Moreover, while transition-states TS-A and TS-C (or TS-B and TS-D) cannot be differentiated in C(α)-induction, they are clearly differentiated in concomitant C(α),C(β)-induction.[8] Likewise, transition-states

Scheme II. Transition-State Topographies for C(α),C(β)-Induction



TS-A and TS-D (or TS-B and TS-C) cannot be differentiated in C(β)-induction but are clearly differentiated in concomitant C(α),C(β)-induction. Thus, the C(α),C(β) diastereomer ratios obtained in the present study indicate that all four transition-state topographies depicted in Scheme II are operative in C(α)-, C(β)-, and C(α),C(β)-induction. Analysis of the data in Table I illustrates the pivotal role of *N*-allyl olefin geometry in this protocol. For example, comparison of the Claisen products obtained from **4c** vs. those obtained form **4d** illustrates that the relative configuration at C(α),C(β) in the major product is indeed reversed by variation of the olefin geometry in tosylate ester **1**. Thus, (*Z*)-crotyl tosylate (**1c**) leads to **4c** which undergoes *ul*-addition to **7*l*** whereas (*E*)-crotyl tosylate (**1d**) leads to **4d** which undergoes *lk*-addition to **7u**. Analogous diastereocontrol is manifest in the preparation of oxazolines **5** and **9**. Stereochemical assignments for these aza-Claisen products follow directly from correlation with the absolute stereoinductions previously established for separate C(α)- and C(β)-studies where stereochemistry was established by either X-ray diffraction analysis or by conversion to compounds of known absolute configuration.[4,5]

Inspection of Table I reveals that each optically pure *N*-allylketene *N*,*O*-acetal (**4a–f**) generates all four of the possible diastereomeric aza-Claisen products. Fortunately, however, the major Claisen product of each rearrangement is produced in 97–98% ee, thus signifying excellent relative asymmetric induction for this enantioselective protocol (cf. **5u** vs. **6u** from **4a**).[9] Incomplete internal asymmetric induction (incomplete chair/boat selectivity) accounts for the observed 85:15 *l*/*u* product ratios and, in large part, determines the 79–92% ds[10] of these rearrangements. It is interesting to note that **4a** rearranges with significantly increased chair selectivity (95:5 chair/boat) relative to **4c–f** (≤85:15 chair/boat) and suggests that when $R^1 = R^4 =$

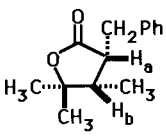
(8) While the relative conformer reactivities may vary as a consequence of dissimilar nonbonding interactions in C(α),C(β)-vs. C(α)-induction, the present results do clarify the extent to which the 97% ds realized in C(α)-induction is the summed consequence of two transition-states conformations: C(α)-*si*-face/chair and C(α)-*si*-face/boat.

(9) (a) When the remote stereogenic center (e.g., that due the transient[9b] chiral auxillary) is exclused from the analysis, the enantiomeric excess of the major Claisen product from **4a** is **5*u*** vs. **6*u***; **4b** is **5*l*** vs. **6*l***; **4c** is **7*l*** vs. **8*l***; **4d** is **7*u*** vs. **8*u***; **4e** is **9*l*** vs. **10*l***; **4f** is **9*u*** vs. **10*u***. (b) Goodwin, T. E. *Chem. Eng. News* **1985**, January 14, 4.

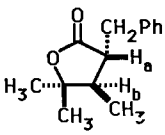
(10) Refer to ref 13 of: Thaisrivongs, S.; Seebach, D. *J. Am. Chem. Soc.* **1983**, *105*, 7407.

alkyl, a pivotal nonbonding interaction destabilizes TS-C and TS-D relative to TS-A and TS-B (Scheme II).

As a further confirmation of diastereoselectivity, the relative stereochemical assignments at C(α) and C(β) for the major Claisen products from **4a** and **4b** were verified independently by nuclear Overhauser enhancement difference (NOED) spectroscopy.[11] Hydrolysis of the Claisen products from **4a** with 10% aqueous HCl at 100 °C gave, in one step, γ-butyrolactone **11** as the major product while similar hydrolysis of the Claisen products from **4b** gave γ-butyrolactone **12** as the major product. Irradiation of H_b in these two diastereomeric γ-butyrolactones proved particularly informative in that a positive NOE was observed for H_a in **11** but not in **12**.[12] The consensus of these NOED results verifies the **4a** → **5u** and **4b** → **5l** stereochemical assignments made in Table I.



11



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Aza-Claisen rearrangement of each *N*-allylketene *N,O*-acetal (**4a–f**) generates four diastereomeric oxazolines but direct determination of their ratios by HPLC or ^{1}H NMR proved intractable. Fortunately however, our *N*-methyloxazolinium salt NMR technique[13] does provide a reliable method for product ratio determination. Thus, each aza-Claisen rearrangement mixture was treated with dimethyl sulfate to give a quantitative yield of the corresponding *N*-methyloxazolinium salts. These crude salts were then directly analyzed by 360-MHz ^{1}H NMR and the relative integrals of base-line resolved diastereomer resonances are reported as oxazoline ratios in Table I. Comparison samples containing mixtures of all four oxazoline diastereomers were prepared by one of two procedures. For example, a nearly 1:1 mixture of **5u** and **6l** was prepared by C(α)-benzylation of (4*S*,2′*S*)-2-(2,3-dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole, in turn prepared by C(β)-enantioselective aza-Claisen rearrangement.[5] Likewise, a nearly 1:1 mixture of **5l** and **6u** was prepared from (4*S*,2′*R*)-2-(2,3-dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole. For oxazolines **7–10**, acid-catalyzed C(α)-epimerization of the aza-Claisen mixture produced oxazoline mixture enriched in the minor isomers (e.g., **4c** → **7*l*** and under acid catalysis **7*l*** → **7*l*** + **8u**). These experiments, together with the C(α)[4] and C(β)[5] studies, corroborate the absolute stereochemical assignments for oxazolines **5** through **10**.

We are currently studying extensions of this work to heterosubstituted systems as well as applications of this aza-Claisen protocol in synthesis.

Experimental Section

General Methods. Proton magnetic resonance spectra were obtained in deuteriochloroform on Varian EM 390 (90-MHz), Nicolet NTCFT-1180 (360-MHz), and Nicolet NMCFT-1280 (500-MHz) spectrometers and are reported in ppm (δ units) downfield of internal tetramethylsilane (Me_4Si). Infrared spectra were recorded on a Beckman IR-8 spectrophotometer. Mass spectra were determined on a Dupont 21-492 B instrument (electron impact, EI) through the Facility for Advanced Instrumentation, University of California, Davis. Elemental analyses were performed by the University of California, Berkeley, analytical laboratories. MPLC refers to chromatography done at 10–50 psi through EM Lobar columns packed with LiChroprep Si60 (40–63 μm) with hexane/EtOAc eluent and monitored by refractive index detection.

[4*S*,(*Z*)]-4,5-Dihydro-3-(2-methyl-2-butenyl)-4-(1-methylethyl)-2-(2-phenylethyl)oxazolium 4-Methylbenzenesulfonate (3a). A mixture of oxazoline **2a** (4.08 g, 18.7 mmol) and tosylate ester **1a** (5.41 g, 22.5 mmol) was stirred for 48 h at 25 °C. Trituration with anhydrous Et_2O (3 × 40 ml) at 0 °C and evacuation at 1 torr gave **3a** as a white solid (8.58 g, 18.7 mmol, quantitative): $[\alpha^{25}]_D$ −33.9° (*c* 2.19, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.66 (d, *J* = 6.7 Hz, 3 H), 0.89 (d, *J* = 7.0 Hz, 3 H), 1.57 (br s, 3 H), 1.72 (d, *J* = 6.7 Hz, 3 H), 2.15 (qqd, *J* = 7.0, 6.7, 2.1 Hz, 1 H), 2.33 (s, 3 H), 2.97–3.08 (m, 1 H), 3.08–3.20 (m, 2 H), 3.45–3.57 (m, 1 H), 4.44 (d, *J* = 15.5 Hz, 1 H), 4.50 (d, *J* = 15.5 Hz, 1 H), 4.60–4.69 (m, 2 H), 5.32 (ddd, *J* = 13.0, 7.8, 5.2 Hz, 1 H), 5.59 (q, *J* = 6.7 Hz, 1 H), 7.13 (d, *J* = 8.0 Hz, 2 H), 7.16–7.33 (m, 5 H), 7.78 (d, *J* = 8.0 Hz, 2 H); IR ($CHCl_3$) 3040, 2990, 1630, 1480, 1450, 1395, 1375, 1215, 1175, 1120, 1030, 1005, 810, 680 cm^{-1}. Anal. Calcd for $C_{26}H_{35}NO_4S$ (crude salt): C, 68.24; H, 7.71; N, 3.06. Found C, 66.99; H, 7.69; N, 3.02.

[4*S*,(*E*)]-4,5-Dihydro-3-(2-methyl-2-butenyl)-4-(1-methylethyl)-2-(2-phenylethyl)oxazolium 4-Methylbenzenesulfonate (3b). A mixture of oxazoline **2a** (4.02 g, 18.48 mmol) and tosylate ester **1b** (5.33 g, 22.18 mmol) was stirred for 20 h at 25 °C. Trituration with anhydrous Et_2O (3 × 60 ml) at 0 °C and evacuation at 1 torr gave **3b** as a white solid (8.01 g, 17.5 mmol, 95%): $[\alpha]^{25}_D$ −9.6° (*c* 5.2, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.67 (d, *J* = 6.7 Hz, 3 H), 0.89 (d, *J* = 7.0 Hz, 3 H), 1.54 (br s, 3 H), 1.59 (d, *J* = 6.7 Hz, 3 H), 2.13 (qqd, *J* = 7.0, 6.7, 2.9 Hz, 1 H), 2.33 (s, 3 H), 2.98–3.19 (m, 3 H), 3.46–3.58 (m, 1 H), 4.25 (d, *J* = 16.0 Hz, 1 H), 4.37 (d, *J* = 16.0 Hz, 1 H), 4.62 (dd, *J* = 8.2, 6.4 Hz, 1 H), 4.67 (ddd, *J* = 9.2, 6.4, 2.9 Hz, 1 H), 5.36 (dd, *J* = 9.2, 8.2 Hz, 1 H), 5.43 (br q, *J* = 6.7 Hz, 1 H), 7.14 (d, *J* = 8.0 Hz, 2 H), 7.17–7.33 (m, 5 H), 7.78 (d, *J* = 8.0 Hz, 2 H); IR ($CHCl_3$) 3000, 1655 (C=C), 1630, 1475, 1440, 1225, 1175, 1115, 1005, 670 cm^{-1}. Anal. Calcd for $C_{26}H_{35}NO_4S$ (crude salt): C, 68.24; H, 7.71; N, 3.06. Found: C, 66.81; H, 7.57; N, 2.97.

[4*S*,(*Z*)]-3-(2-Butenyl)-4,5-dihydro-4-(1-methylethyl)-2-(2-phenylethyl)oxazolium 4-Methylbenzenesulfonate (3c). A mixture of oxazoline **2a** (1.65 g, 7.59 mmol) and tosylate ester **1c** (2.28 g, 10.1 mmol) was stirred for 48 h at 25 °C. Trituration with anhydrous Et_2O (3 × 25 ml) at 0 °C and evacuation at 1 torr gave **3c** as a yellow oil (3.07 g, 6.92 mmol, 91%): ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.61 (d, *J* = 7 Hz, 3 H), 0.87 (d, *J* = 7 Hz, 3 H), 1.70 (d, *J* = 7 Hz, 3 H), 1.80–2.20 (m, 1 H), 2.31 (s, 3 H), 2.77–3.48 (m, 4 H), 4.02–4.83 (m, 4 H), 5.04–5.43 (m, 2 H), 5.49–5.97 (m, 1 H), 7.12 (d, *J* = 8 Hz, 2 H), 7.07–7.47 (m, 5 H), 7.78 (d, *J* = 8 Hz, 2 H); IR ($CHCl_3$) 3090, 3040, 2995, 1655 (C=C), 1630, 1475, 1445, 1395, 1375, 1230, 1165, 1120, 1030, 1005, 810, 670 cm^{-1}.

[4*S*,(*E*)]-3-(2-Butenyl)-4,5-dihydro-4-(1-methylethyl)-2-(2-phenylethyl)oxazolium 4-Methylbenzenesulfonate (3d). A mixture of oxazoline **2a** (4.47 g, 19.8 mmol) and tosylate ester **1d** (4.94 g, 21.8 mmol) was stirred for 24 h at 25 °C. Trituration with anhydrous Et_2O (3 × 30 ml) at 0 °C and evacuation at 1 torr gave **3d** as a yellow oil (7.41 g, 16.7 mmol, 84%): ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.62 (d, *J* = 7 Hz, 3 H), 0.83 (d, *J* = 7 Hz, 3 H), 1.53 (d, *J* = 6 Hz, 3 H), 2.25 (qqd, *J* = 7, 7, 3 Hz, 1 H), 2.33 (s, 3 H), 2.76–3.60 (m, 4 H), 4.16–4.49 (m, 2 H), 4.51 (dd, *J* = 8, 6 Hz, 1 H), 4.77 (ddd, *J* = 10, 6, 3 Hz, 1 H), 5.09–5.55 (m, 1 H), 5.29 (dd, *J* = 10, 8 Hz, 1 H), 5.55–6.02 (m, 1 H), 7.17 (d, *J* = 8 Hz, 2 H), 7.05–7.47 (m, 5 H), 7.81 (d, *J* = 9 Hz, 2 H); IR ($CHCl_3$) 3090, 3040, 3000, 1640, 1475, 1445, 1230, 1165, 1120, 1030, 1005, 815, 670 cm^{-1}.

[4*S*,(*Z*)]-3-(2-Butenyl)-4,5-dihydro-2-ethyl-4-(1-methylethyl)oxazolium 4-Methylbenzenesulfonate (3e). A mixture of oxazoline **2b** (1.61 g, 11.4 mmol) and tosylate ester **1c** (3.03 g, 13.4 mmol) was stirred for 48 h at 25 °C. Trituration with anhydrous Et_2O (3 × 25 ml) and evacuation at 1 torr gave **3e** as a yellow oil (4.10 g, 11.2 mmol, 98%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.8 Hz, 3 H), 0.97 (d, *J* = 7.0 Hz, 3 H), 1.31 (t, *J* = 7.4 Hz, 3 H), 1.76 (d, *J* = 6.9 Hz, 3 H), 2.20 (ddd, *J* = 7.0, 6.9, 3.1 Hz, 1 H), 2.33 (s, 3 H), 2.70 (dq, *J* = 16.7, 7.4 Hz, 1 H), 3.13 (dt, *J* = 16.7, 7.4 Hz, 1 H), 4.34 (dd, *J* = 16.4, 5.8 Hz, 1 H) 4.59

(11) Hall, L. D.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1980**, *102*, 5703.
(12) Additional positive NOE's were observed for the geminal C(4)-CH_3 and the syn C(5)-CH_3 groups in both **11** and **12**.
(13) Kurth, M. J.; Brown, E. G.; Decker, O. H. W. *J. Org. Chem.* **1985**, *50*, 4984.

(d, J = 9.1, 5.7 Hz, 1 H), 4.75 (dd, J = 16.4, 7.8 Hz, 1 H), 4.87 (ddd, J = 7.8, 5.8, 3.1 Hz, 1 H), 5.33 (J = 10.0, 9.9 Hz, 1 H), 5.48–5.56 (m, 1 H), 5.82–5.90 (m, 1 H), 7.14 (d, J = 7.14 Hz, 2 H), 7.77 (d, J = 7.9 Hz, 2 H); IR ($CHCl_3$) 3040, 2960, 1660 (C=C), 1645, 1485, 1460, 1395, 1375, 1225, 1175, 1120, 1035, 1010, 940, 815, 670 cm^{-1}.

[4*S*,(*E*)]-3-(2-Butenyl)-4,5-dihydro-2-ethyl-4-(1-methylethyl)oxazolium 4-Methylbenzenesulfonate (3f). A mixture of oxazoline **2b** (1.13 g, 8.03 mmol) and tosylate ester **1d** (2.00 g, 8.84 mmol) was stirred for 42 h at 25 °C. Trituration at 0 °C with anhydrous Et_2O (3 × 30 ml) and evacuation at 1 torr gave **3f** as a yellow oil (2.61 g, 7.10 mmol, 88%): ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (d, J = 6.8 Hz, 3 H), 0.95 (d, J = 6.9 Hz, 3 H), 1.30 (t, J = 7.5 Hz, 3 H), 1.74 (d, J = 6.4 Hz, 3 H), 2.25 (qqd, J = 6.9, 6.8, 3.2 Hz, 1 H), 2.33 (s, 3 H), 2.73 (dq, J = 16.8, 7.5 Hz, 1 H), 3.12 (dq, J = 16.8, 7.5 Hz, 1 H), 4.34 (dd, J = 15.7, 5.9 Hz, 1 H), 4.46 (dd, J = 15.7, 8.0 Hz, 1 H), 4.58 (dd, J = 9.3, 5.8 Hz, 1 H), 4.83 (ddd, J = 10.3, 5.8, 3.2 Hz, 1 H), 5.30 (dd, J = 10.3, 9.3 Hz, 1 H), 5.60 (ddd, J = 15.5, 8.0, 5.9 Hz, 1 H), 5.92 (dq, J = 15.5, 6.4 Hz, 1 H), 7.13 (d, J = 7.9 Hz, 2 H), 7.77 (d, J = 7.9 Hz, 2 H); IR ($CHCl_3$) 3040, 3000, 1645, 1585, 1395, 1375, 1230, 1165, 1120, 1033, 1010, 965, 815, 770, 675 cm^{-1}.

Procedure for the Preparation of Oxazolines by Aza-Claisen Rearrangement. To the crude oxazolinium salt under nitrogen were added a few crystals of 1,10-phenanthroline and enough dry THF to form a 0.15 M solution. The solution was cooled to −78 °C and BuLi (1.5 M in hexanes) was added over 30 min to a rust-colored endpoint. An equal volume of dry decalin was added. The flask was swirled to wet its inner surfaces, then additional BuLi added to the reappearance of the end point. The solution was then warmed to room temperature and the low-boiling solvents were removed by rotary evaporation at 5 torr. The resulting decalin mixture was heated for 4 h at 180 °C under N_2. After being cooled to room temperature, the mixture was extracted twice with cold 10% HCl. The aqueous layer was washed with petroleum ether, then neutralized with cold 40% NaOH, and extracted twice with Et_2O. Combined Et_2O extracts were washed with brine, dried over Na_2SO_4/K_2CO_3, filtered, and evaporated to give mixtures of C(α),C(β)-epimeric oxazolines **5*u*,*l*** to **10*u*,*l*** as yellow oils which were purified by MPLC chromatography. Product ratios were determined by 360-MHz ^1H NMR analysis of the dimethyl sulfate salts **13*u*,*l*** to **18*u*,*l***.

[4*S*,1′*R*,2′*S*]-2-[2,3-Dimethyl-1-(phenylmethyl)-3-butenyl]-4,5-dihydro-4-(1-methylethyl)oxazole (5*u*). Following the general aza-Claisen rearrangement procedures, oxazolinium salt **3a** (7.80 g, 17.0 mmol) was neutralized and the resulting N-allyloxazolidine ketene N,O-acetal rearranged without isolation. Workup and MPLC gave a colorless oil which 360-MHz ^1H NMR analysis of its dimethyl sulfate adducts **13*u***, **14*u***, **13*l***, and **14*l*** showed to be a 91.6:2.8:5.3:0.3 mixture of diastereomers **5*u***, **6*u***, **5*l***, and **6*l*** (4.07 g, 14.3 mmol, 84%): for the major diastereomer (**5*u***) ^1H NMR (360 MHz, $CDCl_3$) δ 0.64 (d, J = 6.8 Hz, 3 H), 0.69 (d, J = 6.7 Hz, 3 H), 1.05 (d, J = 6.9 Hz, 3 H), 1.42 (qqd, J = 6.8, 6.7, 6.7 Hz, 1 H), 1.73 (s, 3 H), 2.48 (ddd, J = 11.4, 6.9, 3.7 Hz, 1 H), 2.61 (dd, J = 11.4, 13.2 Hz, 1 H), 2.73 (dqd, J = 6.9, 6.9, 1.2 Hz, 1 H), 2.85 (dd, J = 13.2, 3.7 Hz, 1 H), 3.71–3.83 (m, 2 H), 4.05–4.14 (m, 1 H), 4.84 (d, J = 1.2 Hz, 1 H), 4.87 (br s, 1 H), 7.09–7.25 (m, 5 H); IR (CCl_4) 3090, 3040, 1665, 1605, 1495, 1450, 1370, 1230, 1175, 990, 890, 700 cm^{-1}.

[4*S*,1′*R*,2′*R*]-2-[2,3-Dimethyl-1-(phenylmethyl)-3-butenyl]-4,5-dihydro-4-(1-methylethyl)oxazole (5*l*). Following the general aza-Claisen rearrangement procedure, oxazolinium salt **3b** (7.72 g, 16.9 mmol) was neutralized and the resulting N-allyloxazolidine ketene N,O-acetal rearranged without isolation. Workup and MPLC gave a colorless oil which 360-MHz ^1H NMR analysis of its dimethyl sulfate adducts **13*l***, **14*l***, **13*u***, and **14*u*** showed to be an 87.0:2.1:10.5:0.4 mixture of diastereomers **5*l***, **6*l***, **5*u***, and **6*u*** (4.16 g, 14.6 mmol, 86%): for the major diastereomer **5*l*** ^1H NMR (360 MHz, $CDCl_3$) δ 0.59 (d, J = 6.8 Hz, 3 H), 0.70 (d, J = 6.8 Hz, 3 H), 1.18 (d, J = 6.9 Hz, 3 H), 1.47 (qqd, J = 6.8, 6.8, 6.8 Hz, 1 H), 1.74 (s, 3 H), 2.48–2.62 (m, 1 H), 2.72 (dd, J = 12.6, 11.4 Hz, 1 H), 2.77–2.90 (m, 1 H), 2.95 (dd, J = 12.6, 3.1 Hz, 1 H), 3.67–3.80 (m, 2 H), 3.93–4.04 (m, 1 H), 4.73 (d, J = 1.2 Hz, 1 H), 4.75 (s, 1 H), 7.10–7.26 (m, 5 H); for the mixture of diastereomers IR (CCl_4) 3090, 3040, 1665, 1605, 1495, 1455, 1370, 1230, 1175, 990, 890, 700 cm^{-1}. Anal. Calcd for $C_{19}H_{27}NO$: C, 79.95; H, 9.54; N, 4.91. Found: C, 79.77; H, 9.63; N, 4.77.

[4*S*,1′*R*,2′*R*]-4,5-Dihydro-4-(1-methylethyl)-2-[2-methyl-1-(phenylmethyl)-3-butenyl]oxazole (7*l*). Following the general aza-Claisen rearrangement procedure, oxazolinium salt **3c** (3.04 g, 6.85 mmol) was neutralized and the resulting N-allyloxazolidine ketene N,O-acetal rearranged without isolation. Workup and MPLC gave a colorless oil which 360-MHz ^1H NMR analysis of its dimethyl sulfate adducts **15*l***, **16*l***, **15*u***, and **16*u*** showed to be an 82.6:2.1:13.6:1.7 mixture of diastereomers **7*l***, **8*l***, **7*u***, and **8*u*** (1.35 g, 5.01 mmol, 73%): for the major diastereomer **7*l*** ^1H NMR (90 MHz, $CDCl_3$) δ 0.67 (d, J = 7 Hz, 3 H), 0.70 (d, J = 7 Hz, 3 H), 1.06 (d, J = 6 Hz, 3 H), 1.15–1.65 (m, 1 H), 2.25–3.01 (m, 4 H), 3.55–4.25 (m, 3 H), 5.03 (d, J = 12 Hz, 1 H), 5.06 (d, J = 17 Hz, 1 H), 5.77 (ddd, J = 17, 12, 8 Hz, 1 H), 6.90–7.37 (m, 5 H); IR (CCl_4) 3090, 3040, 2980, 2930, 1660, 1450, 1380, 1360, 980, 915, 700 cm^{-1}.

[4*S*,1′*R*,2′*S*]-4,5-Dihydro-4-(1-methylethyl)-2-[2-methyl-1-(phenylmethyl)-3-butenyl]oxazole (7*u*). Following the general aza-Claisen rearrangement procedure, oxazolinium salt **3d** (7.40 g, 16.7 mmol) was neutralized and the resulting N-allyloxazolidine ketene N,O-acetal rearranged without isolation. Workup and MPLC gave a colorless oil which 360-MHz ^1H NMR analysis of its dimethyl sulfate adducts **15*u***, **16*u***, **15*l***, and **16*l*** showed to be a 79.4:2.0:17.2:1.4 mixture of diastereomers **7*u***, **8*u***, **7*l***, and **8*l*** (3.42 g, 12.6 mmol, 75%): for the major diastereomer **7*u*** ^1H NMR (90 MHz, $CDCl_3$) δ 0.68 (d, J = 7 Hz, 3 H), 0.76 (d, J = 7 Hz, 3 H), 1.11 (d, J = 7 Hz, 3 H), 1.30–1.70 (m, 1 H), 2.22–3.07 (m, 4 H), 3.58–4.23 (m, 3 H), 4.87–5.22 (m, 2 H), 5.87 (ddd, J = 17, 9, 7 Hz, 1 H), 7.02–7.41 (m, 5 H); IR (CCl_4) 3090, 3040, 2980, 2930, 1450, 1380, 1360, 980, 915, 700 cm^{-1}.

[4*S*,1′*R*,2′*R*]-2-(1,2-Dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole (9*l*). Following the general aza-Claisen rearrangement procedure, oxazolinium salt **3e** (4.01 g, 10.9 mmol) was neutralized and the resulting N-allyloxazolidine ketene N,O-acetal rearranged without isolation. Workup and MPLC gave a colorless oil which 360-MHz ^1H NMR analysis of its dimethyl sulfate adducts **17*l***, **18*l***, **17*u***, and **18*u*** showed to be an 82.4:2.0:13.7:1.9 mixture of diastereomers **9*l***, **10*l***, **9*u***, and **10*u*** (1.76 g, 9.04 mmol, 83%): for the major diastereomer **9*l*** ^1H NMR (90 MHz, $CDCl_3$) δ 0.86 (d, J = 7 Hz, 3 H), 0.94 (d, J = 7 Hz, 3 H), 1.02 (d, J = 7 Hz, 3 H), 1.11 (d, J = 7 Hz, 3 H), 1.45–1.94 (m, 1 H), 2.20–2.64 (m, 2 H), 3.68–4.40, (m, 3 H), 4.98 (d, J = 11 Hz, 1 H), 5.00 (d, J = 19 Hz, 1 H), 5.48–6.02 (m, 1 H); IR (CCl_4) 3095, 2990, 2910, 1665, 1450, 1375, 1235, 1185, 1075, 1015, 985, 915 cm^{-1}. Anal. Calcd for $C_{12}H_{21}NO$: C, 73.80; H, 10.84; N, 7.17. Found: C, 73.66; H, 10.95; N, 7.21.

[4*S*,1′*R*,2′*S*]-2-(1,2-Dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole (9*u*). Following the general aza-Claisen rearrangement procedure, oxazolinium salt **3f** (3.28 g, 8.94 mmol) was neutralized and the resulting N-allyloxazolidine ketene N,O-acetal rearranged without isolation. Workup and MPLC gave a colorless oil which 360-MHz ^1H NMR analysis of its dimethyl sulfate adducts **17*u***, **18*u***, **17*l***, and **18*l*** showed to be an 81.2:1.5:15.7:1.6 mixture of diastereomers **9*u***, **10*u***, **9*l***, and **10*l*** (1.45 g, 7.44 mmol, 83%): for the major diastereomer **9*u*** ^1H NMR (90 MHz, $CDCl_3$) δ 0.87 (d, J = 7 Hz, 3 H), 0.94 (d, J = 7 Hz, 3 H), 1.01 (d, J = 7 Hz, 3 H), 1.13 (d, J = 7 Hz, 3 H), 1.45–2.00 (m, 1 H)8 2.17–2.70 (m, 2 H), 3.76–4.35 (m, 3 H), 4.97 (d, J = 11 Hz, 1 H), 4.99 (d, J = 19 Hz, 1 H), 5.45–6.02 (m, 1 H); IR (CCl_4) 3095, 2990, 2910, 1665, 1460, 1375, 1235, 1185, 1075, 1015, 985, 915 cm^{-1}. Anal. Calcd for $C_{12}H_{21}NO$: C, 73.80; H, 10.84; N, 7.17. Found: C, 73.64; H, 10.91; N, 7.41.

[4*S*,1′*S*,2′*R*]-2-[2,3-Dimethyl-1-(phenylmethyl)-3-butenyl]-4,5-dihydro-4-(1-methylethyl)oxazole (6*u*). A sample of an 85:15 mixture of (4*S*,2′*R*)- and (4*S*,2′*S*)-2-(2,3-dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole, synthesized by an aza-Claisen rearrangement (0.279 g, 1.43 mmol), was dissolved in dry THF under a nitrogen atmosphere and cooled to −78 °C. To this was added n-butyllithium (1.1 mL of a 1.45 M solution in hexanes, 1.57 mmol) over 5 min. After 30 min of stirring, benzyl bromide (0.269 g, 1.57 mmol) was added; the solution was stirred at −78 °C for 1 h, then allowed to warm and stir at 25 °C for 2 h. A little solid NH_4Cl was added to quench the reaction, then it was concentrated by rotary evaporation. The residue was partitioned between H_2O and Et_2O. The Et_2O layer was washed with brine, dried over K_2CO_3, filtered, and concentrated by rotary

evaporation. MPLC chromatography (*n*-hexane:ethyl acetate/silica) gave as one peak a yellow oil (0.325 g, 1.14 mmol, 80%) which 360-MHz ^{1}H NMR analysis of its dimethyl sulfate adducts **14*u***, **13*l***, **14*l***, and **13*u*** showed to be an approximately 40:45:5:10 mixture of **6*u***, **5*l***, **5*u***, and **6*l***: for diastereomer **6*u*** ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.79 (d, J = 6.9 Hz, 3 H), 0.90 (d, J = 6.8 Hz, 3 H), 1.06 (d, J = 7.0 Hz, 3 H), 1.47 (qqd, J = 6.9, 6.8, 6.8 Hz, 1 H), 1.73 (s, 3 H), 2.48–2.62 (m, 1 H), 2.72 (dd, J = 12.6, 11.4 Hz, 1 H), 2.77–2.90 (m, 1 H), 2.95 (dd, J = 12.6, 3.1 Hz, 1 H), 3.67–3.80 (m, 2 H), 3.93–4.04 (m, 1 H), 4.83 (s, 1 H), 4.87 (s, 1 H), 7.10–7.26 (m, 5 H); IR (CCl_4) essentialy superimposable on that of **5*l***.

[4*S*,1′*S*,2′*S*]-2-[2,3-Dimethyl-1-(phenylmethyl)-3-butenyl]-4,5-dihydro-4-(1-methylethyl)oxazole (6*l*). A sample of a 90:10 mixture of (4*S*,2′*S*)- and (4*S*,2′*R*)-2-(2,3-dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole, synthesized by an aza-Claisen rearrangement[5] (0.306 g, 1.57 mmol), was benzylated in the manner described for **6*u***, using *n*-butyllithium (1.2 mL of a 1.45 M solution in hexanes, 1.72 mmol) and benzyl bromide (1.294 g, 1.72 mmol) in THF (10 mL). Workup and MPLC chromatography (*n*-hexane:ethyl acetate/silica) gave as one peak a yellow oil (0.326 g, 1.14 mmol, 73%) which 360-MHz ^{1}H NMR analysis of its dimethyl sulfate adducts **14*l***, **13*u***, **14*u***, and **13*l*** showed to be an approximately 45:45:5:5 mixture of **6*l***, **5*u***, **6*u***, and **5*l***: for diastereomer **6*l*** ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.74 (d, J = 6.8 Hz, 3 H), 0.83 (d, J = 6.8 Hz, 3 H), 1.16 (d, J = 6.9 Hz, 3 H), 1.58 (dqq, J = 7, 6.8, 6.8 Hz, 1 H), 1.75 (s, 3 H), 2.55 (ddd, J = 7, 7, 7 Hz, 1 H), 2.70–2.95 (m, 3 H), 3.64 (ddd, J = 10, 7.9, 7 Hz, 1 H), 3.78 (dd, J = 8.0, 7.9 Hz, 1 H), 4.04 (dd, J = 10.0, 3.0 Hz, 1 H), 4.74 (br s, 1 H), 4.76 (br s, 1 H), 7.10–7.25 (m, 5 H); IR (CCl_4) essentially superimposable on that of **5*u***. Anal. Calcd for $C_{19}H_{27}NO$: C, 79.95; H, 9.54; N, 4.91. Found: C, 79.99; H, 9.50; N, 4.87.

[4*S*,1′*S*,2′*S*]-4,5-Dihydro-4-(1-methylethyl)-2-[2-methyl-1-(phenylmethyl)-3-butenyl]oxazole (8*l*). The four diastereomeric oxazolines (0.283 g, 1.04 mmol) obtained from rearrangement of **4d** were heated in *n*-hexane in a sealed tube at 200 °C for 30 min. Evaporative concentration gave, according to 360-MHz ^{1}H NMR analysis of dimethyl sulfate adducts **16*l***, **15*u***, **16*u***, and **15*l***, and approximately 40:40:10:10 mixture of **8*l***, **7*u***, **8*u***, and **7*l*** (0.267 g, 94.5 mmol, 95%) as a slightly yellow oil whose ^{1}H NMR (90 MHz, $CDCl_3$) and IR (CCl_4) spectra were essentially superimposable on those of the preepimerization mixture. Anal. Calcd for $C_{18}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.23; H, 9.10; N, 5.04.

[4*S*,1′*S*,2′*R*]-4,5-Dihydro-4-(1-methylethyl)-2-[2-methyl-1-(phenylmethyl)-3-butenyl]oxazole (8*u*). The four diastereomeric oxazolines (0.233 g, 1.858 mmol) obtained from rearrangement of **4c** were heated in *n*-hexane in a sealed tube at 200 °C for 30 min. Evaporative concentration gave, according to 360-MHz ^{1}H NMR analysis of dimethyl sulfate adducts **16*u***, **15*l***, **16*l***, and **15*u***, an approximately 40:40:10:10 mixture of **8*u***, **7*l***, **8*l***, and **7*u*** (0.202 g, 0.744 mmol, 87%) as a slightly yellow oil whose ^{1}H NMR (90 MHz, $CDCl_3$) and IR (CCl_4) spectra were essentially superimposable on those of the preepimerization mixture. Anal. Calcd for $C_{18}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.27; H, 9.09; N, 5.04.

[4*S*,1′*S*,2′*S*]-2-(1,2-Dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole (10*l*). The four diastereomeric oxazolines (0.227 g, 1.16 mmol) obtained from rearrangement of **4f** were refluxed for 48 h in mixed xylenes under a Dean–Stark trap.[4] Filtration through a short column of silica gel gave, according to 360-MHz ^{1}H NMR analysis of dimethyl sulfate adducts **18*l***, **16*u***, **18*u***, and **17*l***, an approximately 40:40:10:10 mixture of **10*l***, **9*u***, **10*u***, and **9*l*** (0.196 g, 1.00 mmol, 87%) as a colorless oil whose ^{1}H NMR (90 MHz, $CDCl_3$) and IR (CCl_4) spectra were essentially superimposable on those of the preepimerization mixture.

[4*S*,1′*S*,2′*R*]-2-(1,2-Dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole (10*u*). The four diastereomeric oxazolines (0.22 g, 1.13 mmol) obtained from rearrangement of **4e** were refluxed for 48 h in mixed xylenes under a Dean–Stark trap.[4] Filtration through a short column of silica gel gave, according to 360-MHz ^{1}H NMR analysis of dimethyl sulfate adducts **18*u***, **17*l***, **18*l***, and **17*u***, an approximately 40:40:10:10 mixture of **10*u***, **9*l***, **10*l***, and **9*u*** (0.187 g, 0.96 mmol, 85%) as a colorless oil whose ^{1}H NMR (90 MHz, $CDCl_3$) and IR (CCl_4) spectra were essentially superimposable on those of the preepimerization mixture.

[3*R*,4*S*]-4,5-Dihydro-3-(phenylmethyl)-4,5,5-trimethyl-2-(3*H*)-furanone (11). A sample of the 91.6:2.8:5.3:0.3 mixture of oxazolines **5*u***, **6*u***, **5*l***, and **6*l*** (0.339 g, 1.19 mmol) obtained from **4a** was stirred 90 min in 10% aqueous HCl (10 mL) at 100 °C. The solution was cooled and extracted with Et_2O (2×). The combined ethereal extracts were washed with water and brine, then dried over Na_2SO_4. Filtration and evaporative concentration gave a yellow oil. This oil was chromatographed (90:10 *n*-hexane/EtOAc on silica gel, R_f 0.24) to give a faintly yellow oil (0.206 g, 1.00 mmol, 88%) which ^{1}H NMR analysis showed to be an approximately 9:1 mixture of **11** and **12**. The following analyses were performed for **11**: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.96 (d, J = 7.3 Hz, 3 H), 1.36 (s, 3 H), 1.42 (s, 3 H), 2.26 (dq, J = 7.3, 7.3 Hz, 1 H), 2.71 (dd, J = 14.7, 10.5 Hz, 1 H), 3.27 (dd, J = 14.7, 5.3 Hz, 1 H), 3.32 (ddd, J = 10.5, 7.3, 5.3 Hz, 1 H), 7.20–7.34 (m, 5 H); ^{1}H NMR (360 MHz, $CDCl_3$, NOED) irradiation of the ring proton at 2.26 enhanced the methyl signals at 0.96 and 1.42, and, significantly the ring proton at 3.32 ppm; IR (neat, NaCl) 3080, 3040, 3000, 2845, 1760, 1600, 1495, 1445, 1375, 1265, 1135, 1040, 1020, 950, 925, 740, 695 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.80; H, 8.39.

[3*R*,4*R*]-4,5-Dihydro-3-(phenylmethyl)-4,5,5-trimethyl-2-(3*H*)-furanone (12). A sample of the 87.0:2.1:10.5:0.4 mixture of oxazolines **5*l***, **6*l***, **5*u***, and **6*u*** (0.324 g, 1.14 mmol) obtained from **4b** was stirred 90 min in 10% aqueous HCl (10 mL) at 100 °C. The solution was cooled and extracted with Et_2O (2×). The combined ethereal extracts were washed with water and brine, then dried over Na_2SO_4. Filtration and evaporative concentration gave a yellow oil. This oil was chromatographed (90:10 *n*-hexane/EtOAC on silica gel, R_f 0.24) to give a faintly yellow oil (0.204 g, 0.99 mmol, 83%) which ^{1}H NMR analysis showed to be an approximately 9:1 mixture of **12** and **11**. The following analyses were performed for **12**: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.81 (d, J = 6.8 Hz, 3 H), 1.20 (s, 3 H), 1.32 (s, 3 H), 1.94 (dq, J = 12.1, 6.8 Hz, 1 H), 2.60 (ddd, J = 12.1, 6.7 , 5.3 Hz, 1 H), 2.91 (dd, J = 14.1, 6.7 Hz, 1 H), 3.15 (dd, J = 14.1, 5.3 Hz, 1 H), 7.20–7.34 (m, 5 H); ^{1}H NMR (360 MHz, $CDCl_3$, NOED), irradiation of the ring proton at 1.94 ppm enhanced the methyl signals at 0.81 and 1.32, but not of the ring proton at 2.60 ppm; IR (neat, NaCl) 3080, 3040, 1760, 1600, 1495, 1445, 1375, 1265, 1225, 1130, 1065, 1035, 955, 915, 745, 700 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.69; H, 8.39.

Preparation of *N*-Methyloxazolinium Salts on an Analytical Scale. The oxazoline (5–20 mg) and dimethyl sulfate (1.2 equiv) were centrifuged to the bottom of a dry 5-mL flask. The solution was blanketed with nitrogen and stirred 1.5 h at room temperature, yielding the salts as highly viscous, clear, colorless oils or as white crystalline solids. Excess dimethyl sulfate does not usually interefere with NMR analysis and was not removed in most cases. It can, however, be removed by heating the solid salts to melting or the liquid salts to 50 °C at 1 torr for 1 h. Portions can be removed by spatula or pipette for spectroscopic analysis.

CAUTION: Unreacted dimethyl sulfate present in these preparations is a potent carcinogen. Handle with gloves in an efficient hood. The salts are moderately hygroscopic and should be protected from moisture. Kept dry, they are stable indefinitely. Deuteriochloroform solutions, even containing traces of water, are stable for at least a week at 0 °C. In deuterium oxide these salts hydrolyze slowly over several hours. However, addition of lithium deuteroxide causes hydrolysis in a few minutes.

[4*S*,1′*R*,2′*S*]-2-[2,3-Dimethyl-1-(phenylmethyl)-3-butenyl]-3-methyl-4-(1-methylethyl)oxazolium Methanesulfonate (13*u*). By the described procedure, a the mixture of oxazolines obtained from **4a** gave a 91.6:2.8:5.3:0.3 mixture of oxazolinium salts **13*u***, **14*u***, **13*l***, and **14*l*** as a white crystalline solid: **13*u***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.09 (d, J = 6.8 Hz, 3 H), 0.79 (d, J = 7.0 Hz, 3 H), 1.26 (d, J = 6.9 Hz, 3 H), 1.82 (s, 3 H), 2.03 (qqd, J = 7.0, 6.8, 4.0 Hz, 1 H), 2.65 (dd, J = 14.2, 11.9 Hz, 1 H), 2.67 (dq, J = 7.7, 6.9 Hz, 1 H), 3.14 (dd, J = 14.2, 4.3 Hz, 1 H), 3.25 (ddd, J = 12.0, 7.7, 4.3 Hz, 1 H), 3.26 (s, 3 H), 3.71 (s, 3 H), 4.46 (dd, J = 8.6, 7.2 Hz, 1 H), 4.98 (br s, 2 H), 5.11 (ddd, J = 10.7, 7.2, 4.0 Hz, 1 H), 5.20 (dd, J = 10.7, 8.6 Hz, 1 H), 7.13 (d, J = 7.1 Hz, 2 H), 7.21–7.34 (m, 3 H); IR (neat, NaCl) 3060, 2990, 2900, 1650, 1455, 1380, 1240, 1200, 1060, 1000, 900, 825, 730 cm^{-1}.

[4*S*,1′*R*,2′*R*]-2-[2,3-Dimethyl-1-(phenylmethyl)-3-butenyl]-3-methyl-4-(1-methylethyl)oxazolium Methanesulfonate (13*l*). By the described procedure, the mixture of oxazolines obtained from **4b** gave a 87.0:2.1:10.5:0.4 mixture of oxazolinium salts **13*l***, **14*l***, **13*u***, and **14*u*** as a colorless oil: for **13*l***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.08 (d, *J* = 6.8 Hz, 3 H), 0.79 (d, *J* = 7.0 Hz, 3 H), 1.31 (d, *J* = 6.9 Hz, 3 H), 1.89 (s, 3 H), 2.04 (qqd, *J* = 7.0, 6.8, 3.8 Hz, 1 H), 2.76 (dd, *J* = 13.8, 12.0 Hz, 1 H), 2.90 (dq, *J* = 6.9, 6.1 Hz, 1 H), 3.17 (dd, *J* = 13.8, 4.1 Hz, 1 H), 3.24 (s, 3 H), 3.44 (ddd, *J* = 12.0, 6.1, 4.1 Hz, 1 H), 3.72 (s, 3 H), 4.30 (dd, *J* = 9.4, 7.4 Hz, 1 H), 4.83 (ddd, *J* = 10.8, 7.4, 3.8 Hz, 1 H), 4.92 (br s, 1 H), 5.04 (br s, 1 H), 5.06 (dd, *J* = 10.8, 9.4 Hz, 1 H), 7.17 (d, *J* = 7.1 Hz, 2 H), 7.19–7.33 (m, 3 H); IR (neat, NaCl) 3090, 3040, 2960, 1650, 1450, 1380, 1230, 1060, 990, 820, 735 cm^{-1}.

[4*S*,1′*S*,2′*R*]-2-[2,3-Dimethyl-2-(phenylmethyl)-3-butenyl]-3-methyl-4-(1-methylethyl)oxazolium Methanesulfonate (14*u*). By the described procedure, the mixture of oxazolines obtained from C(α)-benzylation of (4*S*,2′*R*)- and (4*S*,2′*S*)-2-(2,3-dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole (85:15) gave a 40:45:5:10 mixture of oxazolinium salts **14*u***, **13*l***, **14*l***, and **13*u*** as a colorless oil: for **14*u***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.87 (d, *J* = 6.8 Hz, 3 H), 0.99 (d, *J* = 7.0 Hz, 3 H), 1.10 (d, *J* = 7.0 Hz, 3 H), 1.68 (br s, 3 H), 2.30 (qqd, *J* = 7, 7, 4 Hz, 1 H), 2.49 (dq, *J* = 8, 7 Hz, 1 H), 2.95 (dd, *J* = 13, 8 Hz, 1 H), 3.08 (s, 3 H), 3.32 (dd, *J* = 14, 7 Hz, 1 H), 3.42–3.51 (m, 1 H), 3.74 (s, 3 H), 4.62 (dd, *J* = 9, 8 Hz, 1 H), 4.75–4.85 (m, 1 H), 4.90 (s, 1 H), 4.97 (s, 1 H), 5.24 (dd, *J* = 11, 10 Hz, 1 H), 7.16–7.46 (m, 5 H); IR (neat, NaCl) superimposable on that of **13*l***.

[4*S*,1′*S*,2′*S*]-2-[2,3-Dimethyl-2-(phenylmethyl)-3-butenyl]-3-methyl-4-(1-methylethyl)oxazolium Methanesulfonate (14*l*). By the described procedure, the mixture of oxazolines obtained from the C(α)-benzylation of (4*S*,2′*S*)- and (4*S*,2′*R*)-2-(2,3-dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole (90:10) gave a 45:45:5:5 mixture of oxazolinium salts **14*l***, **13*u***, **14*u***, and **13*l*** as a colorless oil: for **14*l***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.74 (d, *J* = 6.9 Hz, 3 H), 0.94 (d, *J* = 7.0 Hz, 3 H), 1.31 (d, *J* = 6.9 Hz, 3 H), 1.72 (br s, 3 H), 2.24 (qqd, *J* = 7, 7, 4 Hz, 1 H), 2.60 (qd, *J* = 10, 7 Hz, 1 H), 2.87 (s, 3 H), 2.87 (dd, *J* = 13, 10 Hz, 1 H), 3.33 (dd, *J* = 13, 5 Hz, 1 H), 3.43 (ddd, *J* = 10, 10, 5 Hz, 1 H), 3.74 (s, 3 H), 4.50 (ddq, *J* = 8, 5, 4 Hz, 1 H), 4.52 (dd, *J* = 7, 5 Hz, 1 H), 4.79 (br s, 1 H), 4.81 (br s, 1 H), 5.16 (dd, *J* = 8, 7 Hz, 1 H), 7.29–7.34 (m, 3 H), 7.41–7.46 (m, 2 H); IR (neat, NaCl) 3040, 2990, 1650, 1455, 1380, 1250, 1220, 1055, 1000, 905, 825, 730, 705 cm^{-1}.

[4*S*,1′*R*,2′*R*]-4,5-Dihydro-3-methyl-4-(1-methylethyl)-2-[2-methyl-1-(phenylmethyl)-3-butenyl]oxazolium Methanesulfonate (15*l*). By the described procedure, the mixture of oxazolines obtained from **4c** gave an 82.6:2.1:13.6:1.7 mixture of oxazolinium salts **15*l***, **16*l***, **15*u***, and **16*u*** as a white crystalline solid: for **15*l***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.07 (d, *J* = 6.9 Hz, 3 H), 0.78 (d, *J* = 7.0 Hz, 3 H), 1.27 (d, *J* = 6.8 Hz, 3 H), 2.03 (qqd, *J* = 7.0, 6.9, 4.0 Hz, 1 H), 2.69 (dd, *J* = 14.1, 12.1 Hz, 1 H), 2.77 (ddq, *J* = 8.6, 7.6, 6.8 Hz, 1 H), 3.23 (dd, *J* = 14.1, 4.4 Hz, 1 H), 3.28 (s, 3 H), 3.39 (ddd, *J* = 12.1, 7.6, 4.4 Hz, 1 H), 3.72 (s, 3 H), 4.43 (dd, *J* = 9.2, 7.3 Hz, 1 H), 4.99 (ddd, *J* = 10.9, 7.3, 4.0 Hz, 1 H), 5.14 (dd, *J* = 10.9, 9.2 Hz, 1 H), 5.22 (d, *J* = 10.2 Hz, 1 H), 5.26 (d, *J* = 17.1 Hz, 1 H), 5.92 (ddd, *J* = 14.1, 10.2, 8.6 Hz, 1 H), 7.17–7.33 (m, 5 H); IR ($CHCl_3$) 3090, 3040, 2990, 1645, 1445, 1380, 1230, 1190, 1050, 995, 920 cm^{-1}.

[4*S*,1′*R*,2′*S*]-4,5-Dihydro-3-methyl-4-(1-methylethyl)-2-[2-methyl-1-(phenylmethyl)-3-butenyl]oxazolium Methanesulfonate (15*u*). By the described procedure, the mixture of oxazolines obtained from **4d** gave a 79.4:2.0:17.0:1.4 mixture of oxazolinium salts **15*u***, **16*u***, **15*l***, and **16*l*** as a colorless oil: for **15*u***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.06 (d, *J* = 6.9 Hz, 3 H), 0.79 (d, *J* = 7.0 Hz, 3 H), 1.32 (d, *J* = 6.8 Hz, 3 H), 2.03 (ddq, *J* = 7.0, 6.9, 3.9 Hz, 1 H), 2.76 (dd, *J* = 14.0, 13.6 Hz, 1 H), 2.87 (dqd, *J* = 8.1, 6.8, 6.2 Hz, 1 H), 3.22 (dd, *J* = 13.6, 4.5 Hz, 1 H), 3.27 (s, 3 H), 3.46 (ddd, *J* = 14.0, 6.2, 4.5 Hz, 1 H), 3.73 (s, 3 H), 4.42 (dd, *J* = 9.3, 7.3 Hz, 1 H), 4.84 (ddd, *J* = 10.8, 7.3, 3.9 Hz, 1 H), 5.08 (dd, *J* = 10.8, 9.3 Hz, 1 H), 5.21 (d, *J* = 17.1 Hz, 1 H), 5.25 (d, *J* = 10.2 Hz, 1 H), 5.93 (ddd, *J* = 14.1, 10.2, 8.1 Hz, 1 H), 7.18–7.34 (m, 5 H); IR (neat, NaCl) 3090, 3040, 2990, 1645, 1445, 1375, 1220, 1050, 985, 920, 817, 725, 705 cm^{-1}.

[4*S*,1′*S*,2′*S*]-4,5-Dihydro-3-methyl-4-(1-methylethyl)-2-(2-methyl-1-(phenylmethyl)-3-butenyl)oxazolium Methanesulfonate (16*l*). By the described procedure, the mixture of oxazolines obtained by rearrangement of **4d** and subsequent acid-catalyzed isomerization gave a 40:40:10:10 mixture of oxazolium salts **16*l***, **15*u***, **16*u***, and **15*l*** as a colorless oil: for **16*l***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.88 (d, *J* = 6.8 Hz, 3 H), 0.99 (d, *J* = 7.0 Hz, 3 H), 1.11 (d, *J* = 6.9 Hz, 3 H), 2.29 (qqd, *J* = 7, 7, 4 Hz, 1 H), 2.58 (qdd, *J* = 7, 6, 4 Hz, 1 H), between 3.15 and 3.50 (2 H obscured), 3.25 (s, 3 H), 3.73 (s, 3 H), 4.61 (dd, *J* = 9.2, 7.3 Hz, 1 H), 4.77 (ddd, *J* = 10, 7, 4 Hz, 1 H), between 5.05 and 5.30 (3 H, obscured), 5.76 (ddd, *J* = 17.1, 10.2, 6.4 Hz, 1 H); IR (neat, NaCl) superimposable on that of **16*u***.

[4*S*,1′*S*,2′*R*]-4,5-Dihydro-3-methyl-4-(1-methylethyl)-2-[(2-methyl-1-(phenylmethyl)-3-butenyl)oxazolium Methanesulfonate (16*u*). By the described procedure, the mixture of oxazolines obtained by rearrangement of **4c** and subsequent acid-catalyzed isomerization gave a 40:40:10:10 mixture of oxazolinium salts **16*u***, **15*l***, **16*l***, and **15*u*** as a colorless oil: for **16*u***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.8 Hz, 3 H), 0.97 (d, *J* = 7.0 Hz, 3 H), 1.19 (d, *J* = 6.9 Hz, 3 H), 2.28 (ddq, *J* = 7.0, 6.8, 3.5 Hz, 1 H), 2.59 (ddd, *J* = 8.7, 7.2, 6.9 Hz, 1 H), 3.09 (dd, *J* = 14.5, 7.9 Hz, 1 H), 3.13 (dd, *J* = 14.5, 7.1 Hz, 1 H), 3.19 (s, 3 H), 3.36 (ddd, *J* = 7.9, 7.2, 7.1 Hz, 1 H), 3.74 (s, 3 H), 4.56 (dd, *J* = 8.5, 7.9 Hz, 1 H), 4.63 (ddd, *J* = 9.8, 7.9, 3.5 Hz, 1 H), 5.10 (dd, *J* = 17.9 Hz, 1 H), 5.11 (d, *J* = 11.0 Hz, 1 H), 5.13 (dd, *J* = 10.1, 8.6 Hz, 1 H), 5.75 (ddd, *J* = 17.9, 11.0, 8.7 Hz, 1 H), 7.23–7.39 (m, 5 H); IR (neat, NaCl) 3090, 2990, 1645, 1445, 1380, 1220, 1055, 990, 915, 730, 705 cm^{-1}.

[4*S*,1′*R*,2′*R*]-2-(1,2-Dimethyl-3-butenyl)-4,5-dihydro-3-methyl-4-(1-methylethyl)oxazolium Methanesulfonate (17*l*). By the described procedure, the mixture of oxazolines obtained from **4e** gave a 82.4:2.0:13.7:1.9 mixture of oxazolinium salts **17*l***, **18*l***, **17*u***, and **18*u*** as a colorless oil: for **17*l***, 1), 5.17 (360 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.8 Hz, 3 H), 1.00 (d, *J* = 7.0 5.69 3 H), 1.19 (d, *J* = 6.8 Hz, 3 H), 1.24 (d, *J* = 7.1 Hz, 3 H), 2.34 (ddd, *J* = 7.0, 6.8, 4 Hz, 1 H), 2.63 (ddq, *J* = 7, 7, 7 Hz, 1 H), 2.95 (dq, *J* = 7, 7 Hz, 1 H), 3.51 (s, 3 H), 3.72 (s, 3 H), 4.64 (dd, *J* = 10, 6 Hz, 1 H), 5.03 (ddd, *J* = 9, 6, 4 Hz, 1 H), 5.15 (d, *J* = 10 Hz, 1 H), 5.17 (d, *J* = 17 Hz, 1 H), 5.20 (dd, *J* = 10, 9 Hz, 1 H), 5.69 (ddd, *J* = 17, 10, 9 Hz, 1 H); IR ($CHCl_3$) 3090, 3000, 1655, 1480, 1455, 1235, 1185, 1060, 1005, 925 cm^{-1}.

[4*S*,1′*R*,2′*S*]-2-(1,2-Dimethyl-3-butenyl)-4,5-dihydro-3-methyl-4-(1-methylethyl)oxazolium Methanesulfonate (17*u*). By the described procedure, the mixture of oxazolines obtained by rearrangement of **4f** and subsequent acid-catalyzed isomerization gave a 40:40:10:10 mixture of oxazolinium salts **17*u***, **18*l***, **18*u***, and **17*l*** as a colorless oil: for **17*u***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.9 Hz, 3 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 1.07 (d, *J* = 6.9 Hz, 3 H), 1.35 (d, *J* = 6.8 Hz, 3 H), 2.30 (qqd, *J* = 7, 7, 4 Hz, 1 H), 2.46 (dqd, *J* = 8, 7, 7 Hz, 1 H), 2.98 (dq, *J* = 7, 7 Hz, 1 H), 3.41 (s, 3 H), 3.73 (s, 3 H), 4.52 (dd, *J* = 9, 8 Hz, 1 H), 4.80–4.86 (m, 1 H), 5.04 (dd, *J* = 10 Hz, 1 H), 5.10 (d, *J* = 17 Hz, 1 H), 5.12 (d, *J* = 10 Hz, 1 H), 5.66 (ddd, *J* = 17, 10, 8 Hz, 1 H); IR ($CHCl_3$) superimposable on that of the enriched mixture of **18*l***.

[4*S*,1′*S*,2′*S*]-2-(1,2-Dimethyl-3-butenyl)-4,5-dihydro-3-methyl-4-(1-methylethyl)oxazolium Methanesulfonate (18*l*). By the described procedure, the mixture of oxazolines obtained from **4f** gave an 81.2:1.5:15.7:1.6 mixture of oxazolinium salts **18*l***, **18*u***, **17*l***, and **17*u*** as a colorless oil: for **18*l***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.88 (d, *J* = 6.8 Hz, 3 H), 1.01 (d, *J* = 7.0 Hz, 3 H), 1.17 (d, *J* = 6.8 Hz, 3 H), 1.29 (d, *J* = 7.0 Hz, 3 H), 2.37 (qqd, *J* = 6.9, 6.9, 3.5 Hz, 1 H), 2.66 (qdd, *J* = 8, 7, 7 Hz, 1 H), 3.11 (qd, *J* = 7, 7 Hz, 1 H), 3.52 (s, 3 H), 3.72 (s, 3 H) 4.67 (dd, *J* = 10, 6 Hz, 1 H), 4.91 (ddd, *J* = 19, 6, 3.5 Hz, 1 H), 5.09 (dd, *J* = 10, 9 Hz, 1 H), 5.12 (d, *J* = 17 Hz, 1 H), 5.16 (d, *J* = 10 Hz, 1 H), 5.79 (ddd, *J* = 17, 10, 8 Hz, 1 H); IR 3000, 1650, 1480, 1455, 1395, 1375, 1220, 1060, 1010, 930 cm^{-1}.

[4*S*,1′*S*,2′*R*]-2-(1,2-Dimethyl-3-butenyl)-4,5-dihydro-3-methyl-4-(1-methylethyl)oxazolium Methanesulfonate (18*u*). By the described procedure, the mixture of oxazolines obtained by rearrangement of **4e** and subsequent acid-catalyzed isomerization gave a 40:40:10:10 mixture of oxazolinium salts **18*u***, **17*l***, **18*l***, **17*u*** as a colorless oil: **18*u***, ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.85 (d, *J* = 6.8 Hz, 3 H), 0.97 (d, *J* = 7.1 Hz, 3 H), 1.12 (d, *J* = 6.8 Hz, 3 H), 1.40 (d, *J* = 7.0 Hz, 3 H), 2.37 (qqd, *J* = 7, 6, 4 Hz, 1 H), 2.44 (dqd, *J* = 8, 7, 7 Hz, 1 H), 2.98 (dq, *J* = 7, 7 Hz, 1 H),

3.42 (s, 3 H), 3.74 (s, 3 H), 4.52 (dd, J = 9, 9 Hz, 1 H), 4.85 (ddd, J = 9, 7, 4 Hz, 1 H), 5.05–5.20 (m, 3 H), 5.66 (ddd, J = 18, 10, 9 Hz, 1 H); IR ($CHCl_3$) superimposable on that of the enriched mixture of **17***l*.

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Registry No. **1a**, 99439-83-5; **1b**, 99439-82-4; **1c**, 76454-94-9; **1d**, 76454-93-8; **2ia**, 93684-44-7; **2b**, 88362-45-2; **3a**, 101030-94-8; **3b**, 101030-96-0; **3c**, 101030-98-2; **3d**, 101031-00-9; **3e**, 101031-02-1; **3f**, 101031-04-3; **5u**, 101031-05-4; **5l**, 101142-46-5; **6u**, 101142-49-8; **6l**, 101142-50-1; **7l**, 101031-06-5; **7u**, 101142-47-6; **8l**, 101142-51-2; **8u**, 101142-52-3; **9l**, 101031-07-6; **9u**, 101142-48-7; **10l**, 101142-53-4; **10u**, 101142-54-5; **11**, 101031-14-5; **12**, 101142-69-2; **13u**, 101031-09-8; **13l**, 101142-56-7; **14u**, 101142-58-9; **14l**, 101142-60-3; **15l**, 101031-11-2; **15u**, 101142-62-5; **16l**, 101143-46-8; **16u**, 101143-48-0; **17l**, 101031-13-4; **17u**, 101142-64-7; **18l**, 101142-66-9; **18u**, 101142-68-1; $C_6H_5CH_2Br$, 101142-68-1; (4*S*,2′*R*)-2-(2,3-dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole, 99440-13-8; (4*S*,2′*S*)-2-(2,3-dimethyl-3-butenyl)-4,5-dihydro-4-(1-methylethyl)oxazole, 99440-14-9.

Preparation of Vicinal *N*-Alkylamino Alcohols via Acylation–Rearrangement of Nitrones Followed by Hydride Reduction

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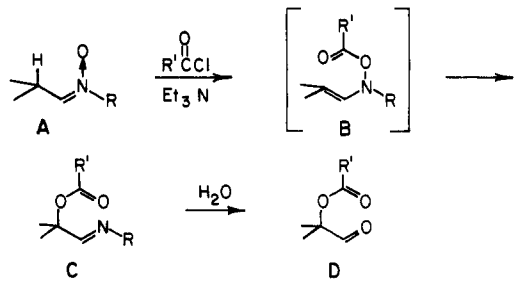
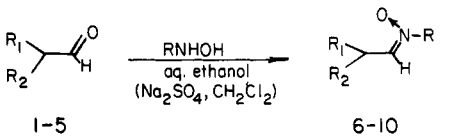
Acylation–rearrangement of *N-tert*-butyl and *N*-cyclohexyl nitrones of cyclohexanecarboxaldehyde (**1**), *n*-butyraldehyde, isobutyraldehyde, 3-cyclohexenecarboxaldehyde, and α-methylpropionaldehyde gave α-pivaloyloxy imines, which underwent reduction with lithium aluminum hydride to *N-tert*-butyl- and *N*-cyclohexylamino alcohols (Table I). Reduction of the α-pivaloyloxy imines derived from **1** with sodium borohydride gave stable *N*-alkylamino pivalates **17a,b**. Acylation–rearrangement of the *N*-methyl nitrone of **1** with pivaloyl chloride afforded a 3:1 mixture of the α-pivaloyloxy imine **11c** and an imide, *N*-pivaloyl-*N*-methylcyclohexanecarboxamide (**18**). It is proposed that the latter arises by elimination of an *O*-acyl nitrone intermediate (**22**) to a nitrilium pivalate ion pair followed by collapse to an *O*-acyl imidate and O → N rearrangement. Carboxylation of the *N-tert*-butyl, *N*-cyclohexyl, and *N*-methyl nitrones with methyl chloroformate gave imino carbonates, reduction of which with sodium borohydride afforded spiro *N*-alkyloxazolidinones **27**. 1-[(*N*-Methyl- and 1-[(*N*,*N*-dimethylamino)-methyl]cyclohexanol (**12c** and **29**) were obtained from the *N*-methyloxazolidinone by hydrolysis and lithium aluminum hydride reduction, respectively.

The reaction of nitrones A of aldehydes and ketones with acid chlorides in the presence of triethylamine at 0–25 °C affords α-acyloxy imines C, which undergo ready hydrolysis to α-acyloxy aldehydes D.[1] This novel method for α-oxygenation presumably proceeds via spontaneous [3,3]sigmatropic rearrangement of an intermediate *N*-vinyl-*O*-acylhydroxylamine (A → B → C). Since the imine double bond in the isolable intermediate C should be reduced readily by hydride reagents,[2] we considered that the acylation–rearrangement of nitrones could be adapted to provide a useful method for synthesis of the medicinally important[3] vicinal *N*-alkylamino alcohols. In fact, reduction of the α-pivaloyloxy imine from the *N-tert*-butyl nitrone of cyclohexanecarboxaldehyde with lithium aluminum hydride gave 1-[(*N-tert*-butylamino)methyl]-cyclohexanol (**12a**).[1] In this paper we report the preparation of a series of *N-tert*-butyl-, *N*-cyclohexyl-, and *N*-methylamino alcohols via acylation–rearrangement of nitrones and subsequent hydride reduction. *N*-Alkyloxazolidinones **27** were obtained by acylation–rearrangement with methyl chloroformate followed by sodium borohydride reduction.



Results and Discussion

The *N-tert*-butyl nitrones **6a–10a** were prepared as reported previously[1] by condensation of cyclohexanecarboxaldehyde (**1**), *n*-butyraldehyde (**2**), isobutyraldehyde (**3**), 3-cyclohexenecarboxaldehyde (**4**), and α-phenylpropionaldehyde (**5**) with *N-tert*-butylhydroxylamine[4] in dichloromethane containing sodium sulfate at 25 °C.[5] The



N-cyclohexyl nitrones **6b–10b** of the same five aldehydes and the *N*-methyl nitrone **6c** of cyclohexanecarboxaldehyde were formed by reaction of *N*-cyclohexyl- or *N*-methylhydroxylamine hydrochloride with the aldehyde

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