in 1.0 mL of anhydrous tetrahydrofuran was added a solution of 0.41 M formic–acetic anhydride (2.42 mL, 0.993 mmol) and activated zinc dust (0.233 g, 3.556 mmol). The reaction was monitered by TLC over a period of 3 h. The zinc was removed by filtration and washed with tetrahydrofuran, and the filtrate was evaporated. This was dissolved in chloroform, applied to a preparative TLC plate, and chromatographed, eluting with 17% methanol–83% chloroform to afford 0.085 g of the acetate ester as an oil as observed by the infrared absorption at 1740 cm^{-1} and by proton NMR. This ester was dissolved in anhydrous methanol and stirred with a catalytic amount of potassium bicarbonate under nitrogen with TLC monitoring for a period of 48 h. The methanol was evaporated, the residue was dissolved in chloroform, washed with water and brine, and then dried, and the solvents were removed by evaporation. The remaining residue was purified on two analytical (20 cm × 20 cm) silica gel plates, eluting with 17% methanol–83% chloroform to give 0.049 g (49%) of **24** as an oil: $[\alpha]^{25}_D = -25°$ (c = 0.020, CH_3OH); IR (TF) 3260 (br), 3070, 2940, 2880, 1665 (br), 1545, 1455, 910, 735, 695 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.45–1.85 (m, 12 H, CH_2), 1.97 (s, 3 H, CH_3CO), 3.20–3.90 (m, 8 H, CH_2N and NCHCO), 3.92–4.10 (2 br s, 2 H, CH_2O), 4.60–4.74 (m, 1 H, NCHCO), 4.80 (br s, 2 H, benzylic H), 4.82 (br s, 2 H, benzylic H), 4.86 and 4.87 (2 br s, 2 H, benzylic H), 4.89–5.00 (m, 1 H, NCHCO), 6.67 (br s, 1 H, NH), 7.20–7.50 (m, 15 H, aromatic H), 7.67 (br s, 1 H, NH), 7.95 (br s, 2 H, NH), 8.12 (br s, 1 H, CHO), 8.18 (br s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 75 MHz, all signals reported as observed at 20 °C) δ 21.40, 21.43, 22.28, 22.8–22.94 (m), 23.00, 23.55, 23.59, 22.39, 29.42, 29.48, 29.67, 29.94, 30.01, 43.02 (m), 43.58 (m), 45.04 (m), 51.07, 51.21, 51.26, 52.28, 53.57, 54.20, 61.62, 61.64, 61.67, 76.86, 77.20, 77.67, 128.40, 128.46, 128.81, 129.14, 129.41, 129.50, 133.91, 134.0–134.2 (m), 163.26, 163.28, 163.32, 163.68, 163.70, 168.40, 168.60, 170.79, 170.83, 171.55, 172.98; MS (positive ion FAB, chloroform–glycerol matrix) m/z 846 (M + H).

Foroxymithine: (3*S*,6*S*)-3-[3-[*N*-[*N*-(*N*²-Acetyl-*N*⁵-formyl-*N*⁵-hydroxy-L-ornithinyl)-L-seryl]-*N*-hydroxyamino]propyl]-6-[3-(*N*-formyl-*N*-hydroxyamino)propyl]-2,5-piperazinedione (1). To a solution of **24** (0.0175 g, 0.0207 mmol) in 0.5 mL of methanol and 0.5 mL of deionized distilled water was added 10% palladiumon carbon (0.005 g). This mixture was exposed to hydrogen for 2.5 h, filtered, and lyophilized to afford 0.0117 g (98%) of foroxymithine (**1**) as a glass. This synthetic material proved to be one spot (1% ferric chloride spray indication) by silica gel TLC (R_f 0.32) using a 2:1 mixture of ethanol–28% ammonium hydroxide as a solvent system in excellent agreement with the literature[1] R_f value of 0.33: $[\alpha]^{25}_D = -38°$ (c = 0.034, deionized distilled water) [lit.[1] $[\alpha]^{25}_D = -44°$ (c = 1.00, water)]; IR (KBr) 3420 (br), 3260 (br), 2940, 2880, 1660 (br), 1540, 1460, 875 cm^{-1}; ^1H NMR (D_2O, 300 MHz) δ 1.35–1.80 (m, 12 H, CH_2), 1.83 (s, 3 H, CH_3CON), 3.00–3.12 (m, 1 H, diastereotopic CH_2N), 3.30–3.45 (m, 3 H, CH_2N), 3.46–3.55 (m, 2 H, NCHCO), 3.60–3.75 (m, 2 H, CH_2N), 3.95–4.05 (m, 2 H, CH_2O, 4.20–4.30 (m, 1 H, NCHCO), 4.88 (t, 1 H, J = 5.1 and 5.4 Hz, NCHCO), 7.76, 7.83, 8.11 (3 s, 2 H, CHO): ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.28, 21.57, 22.54, 27.94, 28.14, 30.02, 30.39, 37.27, 45.94, 46.09, 48.00, 49.90, 52.31, 53.24, 53.98, 54.04, 60.42, 159.54, 163.76, 164.21, 164.23, 169.82, 169.87, 169.92, 170.06, 173.65, 174.19; MS (positive ion FAB, glycerol matrix) m/z 598 (M + Na), 576 (M + H), 561 (M − CH_3CO + CHO), 517 (M − 2CHO).

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Supplementary Material Available: ^1H NMR, ^{13}C NMR, and DEPT spectra of new compounds (55 pages). Ordering information is given on any current masthead page.

Syntheses and Rearrangements of Spirocyclic Oxaziridines Derived from Unsymmetrical Ketones

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Oxaziridines provide useful alternatives to the Beckmann rearrangement and Schmidt reaction for ring enlargement of cyclic ketones. The procedure involves the condensation of the ketone in question with optically active α-methylbenzylamine, oxidation of the resultant imine, and photolysis to afford ring-expanded lactams. The α-phenylethyl substituent can be removed after photolysis to yield the N-unsubstituted lactam. When a distal ketone substituent is present, the oxaziridines can be synthesized stereoselectively. Thus, optically active ketones can be converted to either ring-expanded lactam by choice of either enantiomer of optically active α-methylbenzylamine. Ketones bearing adjacent substitution are generally not amenable to such regiocontrol because the resident substituent is the key stereocontrol element for the oxaziridine synthesis, although a notable exception is 2-methoxycyclohexanone. Stereogenic centers present in such compounds undergo epimerization during the couse of the reaction sequence; in addition, substrates containing substantial amounts of enamine give rise to novel doubly oxygenated products upon oxidation. Finally, the conformational behavior of the side chains in both oxaziridines and their product lactams permits some key stereochemical assignments to be made, on the basis of chemical shift trends in the NMR spectra of these materials.

The conversions of cyclic ketones to heterocycles using ring-expansion reactions have been featured in the preparations of such disparate materials as nylon (cyclohexanone → caprolactam[1]) and the plant growth promoter brassenolide (Baeyer–Villiger reaction on a 6-keto steroid[2]). The more sophisticated applications of such reactions require careful planning with respect to a number of chemical issues, chief among these being regioselectivity. In the formal insertion of a nitrogen substituent into a carbocyclic ring, the regiochemistry is controllable only in cases in which the ketone undergoing reaction is locally dissymmetric. For example, the standard Beckmann and Schmidt sequences afford primarily products which result from the migration of the most highly substituted group.[3]

† Eli Lilly Grantee, 1989–1991.
‡ Department of Chemistry.

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0022-3263/91/1956-0499$02.50/0

It is more desirable to have on hand complementary reaction sequences that could covert a single starting material to either potential ring-expansion product. In cases where the point of differentiation is further removed from the reacting ketone, such as 3-methylcyclohexanone,[4] the Beckmann and Schmidt reactions afford an essentially equimolar mixture of products.

The problem results from an inability to predictably control the stereochemistry of a substituted oxime, the cornerstone of the Beckmann reaction. In our laboratory, we have investigated the synthesis of chiral lactams based on the stereospecific rearrangement reactions of spirocyclic oxaziridine stereoisomers derived from *symmetrical* ketones.[5] By use of chiral nitrogen substituents (typically α-methylbenzyl), it is possible to control the absolute stereochemistry of the oxaziridine nitrogen atom. In addition, this stereocenter is "frozen" by virtue of its presence in the strained oxaziridine ring[6,7] and can undergo a stereospecific rearrangement reaction in which the group syn to the chiral N-substituent undergoes preferential migration to nitrogen upon photolysis.[5,8]

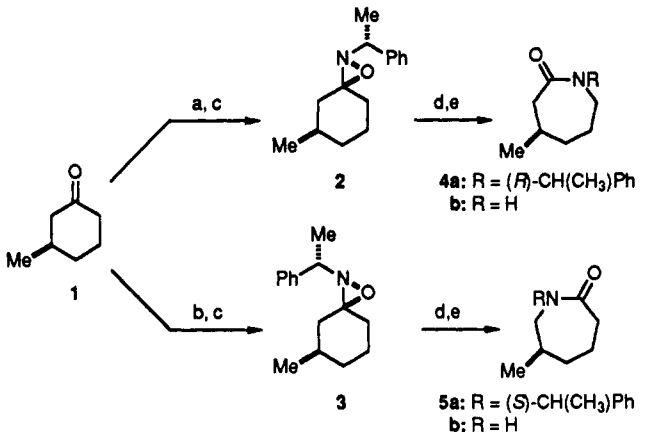
When the ketone is substituted at an adjacent carbon, the derived oxaziridines have been known for some time to afford product lactams which are regiochemically complementary to those obtained from Schmidt or Beckmann reactions.[9,10] We were nevertheless interested in examining the chemistry of N-chiral oxaziridines in this context as well. Specifically, the use of chiral imines as oxaziridine precursors permits the intersection of the ring-expansion chemistry with other types of stereoselective synthesis. These intermediates, which are in equilibration with their tautomeric enamines, have been found quite effective tools for carbon–carbon bond formation in the "deracemization" chemistry recently exploited by d'Angelo, Pfau, and coworkers.[11]

In this paper, we survey the synthesis and utilization of spirocyclic oxaziridines prepared from unsymmetrical ketones. In two cyclohexanones substituted at the β-position, it is possible to exert control over nitrogen stereochemistry and therefore effect rearrangement to *either* regioisomeric ring-expansion product. The chemistry of α-substituted ketones is considerably more complex and depends on the nature of the substitution. For these examples, a spectrum of behaviors with respect to stereochemical control, regiochemistry of the rearrangement, and even the chemoselectivity of the oxidation progress will be described.

Results and Discussion

Oxaziridines from Nonepimerizable Ketones.[12] We begin with 3-methylcyclohexanone because its chemistry is most straightforward and provides a ready review of the principles of spirocyclic oxaziridine stereocontrol. Throughout, a general protocol for oxaziridine synthesis was followed: a toluene solution of the starting ketone and α-methylbenzylamine (α-MBA) was refluxed using a Dean–Stark apparatus for azeotropic removal of water. The imine solution was then added dropwise to a stirred toluene suspension of (+)-monoperoxycamphoric acid ((+)-MPCA)[13] at −78 °C. Previous experience showed that superior selectivities could be obtained using this optically active oxidizing agent and that product ratios using this reagent were independent of substrate stereochemistry (i.e. no effects arising from double diastereoselectivity were observed).[5] The reactions were followed by thin-layer chromatography (TLC) and were generally complete within 10 min, at which time saturated sodium thiosulfate was added. Aqueous workup followed by silica gel chromatography of the organic residue provided the oxaziridines.

Scheme I[a]



[a] Reagents: (a) (*R*)-α-MBA; (b) (*S*)-α-MBA; (c) (+)-MPCA; (d) *hν*, 254 nm, quartz tube; (e) Na/NH_3.

Following this procedure, (*R*)-(+)-3-methylcyclohexanone (1, Scheme I) was condensed with (*R*)-α-methylbenzylamine ((*R*)-α-MBA) and the imine oxidized with (+)-MPCA. The product was isolated as an inseparable mixture of diastereomers in 84% overall yield, with the major diastereomer accounting for ≥90% of the mixture as judged by ^{13}C NMR. Similarly, condensation of 1 with (*S*)-α-MBA followed by oxidation gave a mixture of diastereomeric oxaziridines in 89% yield in a ratio of 90:4:6. The major isomers of the two reactions were determined to be **2** and **3**, respectively (see below). In each case, attack of the oxidizing agent took place from an equatorial[14] direction, leading to the cis relationship between the C-5 methyl group and the oxaziridine oxygen shown.[15] In addition, oxidation is known to predominantly afford product in which the the benzylic stereogenic center and the oxaziridine nitrogen have *unlike*[16] relative stere-

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(14) Oliveros, E.; Rivière, M.; Lattes, A. *J. Heterocycl. Chem.* **1980**, *17*, 107–112.
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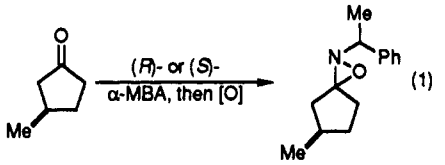
ochemistry.[17] For these compounds, the side chain largely adopts a folded conformation in which the proton bearing a 1,3-syn-diaxial relationship to the *N*-phenylethyl substituent is placed in the shielding cone of the phenyl group.[5,18] Thus, irradiation of the C-5 methyl doublet in **3** led to the collapse of the signal appearing at 0.68 ppm, while analogous irradiation of the doublet in **2** resulted in no observable collapse of the signal at 0.52 ppm, verifying that the latter signal resulted from a methylene proton.

Each oxaziridine mixture was photolytically rearranged in methylene chloride to afford the formal nitrogen-insertion products (Rayonet merry-go-round reactor, quartz tube, 254 nm, ca. 0.1 M). Photolysis of oxaziridine **2** produced lactam **4a** in 71% yield, along with an additional 9% of the corresponding regioisomer. These isomers were easily separable by chromatography. Reductive debenzylation using Na/NH_3 produced N-unsubstituted lactam **4b** in 66% yield. The optical rotation, melting point, and IR spectrum of this lactam were all in agreement with literature values.[19] Similarly, photolysis of oxaziridine **3** resulted in a 78% yield of an inseparable mixture of two lactam regioisomers in a ratio of 85:15. The major regioisomer is given in Scheme I as compound **5a**. Subsequent debenzylation of the lactam mixture yielded 65% of the unsubstituted lactam **5b**. Recrystallization from petroleum ether produced pure **5b**, mp 99–100 °C.[20]

The overall stereochemical control results from "matching" the effects of the resident stereogenic center (which is manifested as equatorial attack by the oxidizing agent) and the benzylic stereogenic center of the chiral amine (which gives rise to products have the *unlike* relative stereochemistry between the benzylic carbon and the nitrogen stereocenter). Thus, the use of racemic ketone in a similar process requires that each enantiomer react to form opposing regioisomers as has been previously described.[12]

The oxidation of the condensation products of (*R*)-3-methylcyclopentanone with optically active α-MBA did not take place with useful levels of stereoselectivity as determined by ^{13}C NMR (eq 1). This is due both to the decreased *unlike* selectivity in such systems[21] and a lack of useful face selectivity imparted by the C-3 methyl substituent. The stereochemistry of the various products was not determined, and their conversion to lactams not pursued.

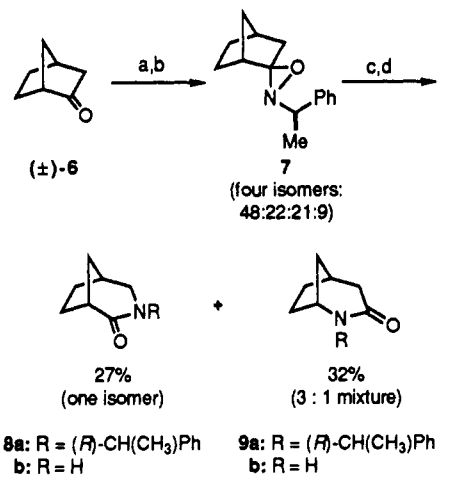


(1)

amine used	ratio of isomers	yield
R	51 : 30 : 19	87%
S	35 : 43 : 5 : 7 : 10	86%

This ring-expansion sequence was also applied to the bridged bicyclic ketone norcamphor (Scheme II). Racemic norcamphor ((±)-**6**) was condensed with (*R*)-α-MBA and oxidized with *m*-chloroperoxybenzoic acid (*m*-CPBA). A mixture of four diastereomeric oxaziridines **7** was isolated in 81% yield after chromatography (ratio ca. 48:22:21:9, as determined by ^{13}C NMR). The stereochemistry of the oxaziridines was not determined, but the major isomer is likely to be that arising from one of the enantiomers of the norcamphor undergoing an *unlike* attack of the oxidizing agent coupled with a sterically favored exo approach. The mixture of diastereomers was photolyzed in cyclohexane to give both lactam regioisomers. Regioisomer **8a** was obtained in 27% yield and was >90% diastereomerically pure (^1H and ^{13}C NMR). The other regioisomer, **9a**, was produced in 32% yield, as an approximately 3:1 mixture of diastereomers. The regiochemistries of **8a** and **9a** were confirmed by reductive dealkylation to give known lactams **8b** (**8a** → **8b**, 70% yield) and **9b** (**9a** → **9b**, 52% yield), respectively.[22]

Scheme II[a]



[a] Reagents: (a) (*R*)-α-MBA; (b) mCPBA; (c) *hν*, 254 nm, quartz tube; (d) Na/NH_3.

Oxaziridine Synthesis from Epimerizable Ketones. Five α-substituted ketones were subjected to standard protocols for imine formation and oxidation. The results of these experiments are summarized in Scheme III and Table I.

Racemic 2-methylcyclohexanone (**10**) was condensed with (*R*)-α-MBA, followed by oxidation with *m*-CPBA. The resulting product was a mixture of seven diastereomers, from which one pure diastereomer (**12**) and another isomer in approximately 90% diastereomeric purity (the major isomer, **11**) could be isolated by careful chromatography. Similarly, condensation of racemic 2-methoxycyclohexanone **13** with (*R*)-α-MBA and oxidation with (+)-MPCA resulted in the formation of a mixture of four diastereomers in a 95% yield, from which the two predominant isomers could be isolated by preparative medium-pressure liquid chromatography (MPLC). In this way, diastereomer **15** was isolated as a colorless solid in 24% yield and ≥95% diastereomeric purity by NMR analysis. Additionally a sample enriched in oxaziridine **14** was collected. The structures of these oxaziridines were determined as described in the following secton.

A surprising difference in chemoselectivity was obtained using 2-phenylcyclohexanone **16** as substrate. Application of the standard procedure afforded two fractions which

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(20) This melting point is higher than that previously reported in the literature[19] for **4b**, and we were unable to reproducibly determine the optical rotation in water due to solubility problems. However, the IR spectrum is similar to that reported and other analytical data collected (^1H and ^{13}C NMR, elemental analysis) were completely in accord with **5b**. In addition, the value obtained for the optical rotation of lactam **5b** in ethanol did closely match the literature[19] value.
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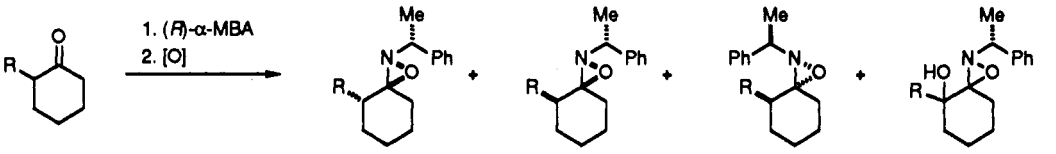
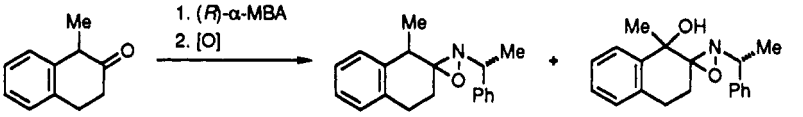
Scheme III



R					
-Me	10	11	12	-	-
-OMe	13	14	-	15	-
-Ph	16	17	18	19	20
-CO_2Et	21	-	-	-	22



23 24 25

Table I. Synthesis of Oxaziridines from Epimerizable Ketones

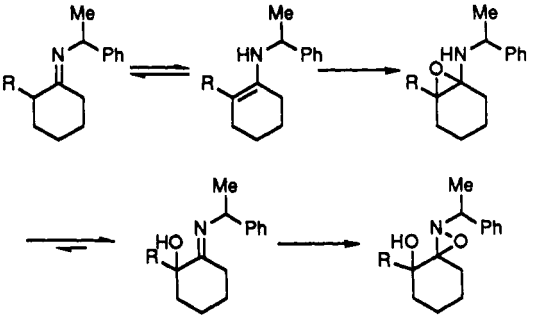
			monooxygenated products		bisoxygenated products	
entry	ketone[a]	[O][b]	yield (%)[c]	products (ratios[d])	yield (%)[c]	products (ratios[d])
1	10	*m*-CPBA	81	11 (46) 12 (38) others[f] (8:4:3:2:1)	*e*	
2	(*R*)-(−)-10	*m*-CPBA	81	11 (48) 12 (37) others[f] (6:4:2:2:1)	*e*	
3	13	(+)-MPCA	95	14 (51) 15 (38) others[f] (7:4)	*e*	
4	16	(+)-MPCA	56	17 (53) 18 (16) 19 (25) other[f] (9)	24	20[g,h]
5	(*S*)-(−)-16	(+)-MPCA	54	17 (60) 18 (14) 19 (25) other[f] (1)	23	20[g,h]
6	(*S*)-(−)-16[i]	(+)-MPCA	54	17 (54) 18 (19) 19 (17) other[f] (10)	24	20[g,h]
7	16	MMPP	74	17–19 and others[h]	6	20[g,h]
8	21	(+)-MPCA	*e*		75	22[g] (46:31:23)
9	23	(+)-MPCA	9	24[g,h]	86	25[g] (48:32:30)
10	23	MMPP	25	24[g,h]	53	25[g,h]

[a] Ketones were racemic and reacted with (*S*)-α-MBA unless otherwise noted. [b] Oxidizing agent used for the preparation of the oxaziridine. Abbreviations: *m*-CPBA, *m*-chloroperoxybenzoic acid; (+)-MPCA, monoperoxycamphoric acid; MMPP, magnesium monoperoxyphthalate. [c] Yields refer to chromatographically purified products. [d] Ratios estimated by measuring the heights of the benzylic and/or the oxaziridine carbon signals in the ^{13}C NMR spectrum of the crude reaction mixture. The ratios in entries 4–6 were determined by HPLC. [e] Not observed in this experiment. [f] "Other" isomers refer to oxaziridines observed in the crude NMR spectra of the reaction but not isolated or otherwise elucidated. [g] Stereochemical structure(s) not determined. [h] Ratio not determined. [i] The imine in this experiment was prepared from (*S*)-α-MBA.

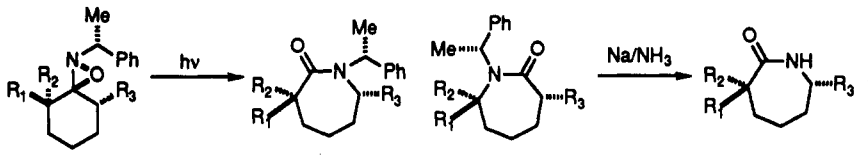
could readily be separated by flash chromatography. The less polar fraction comprised the expected oxaziridines, obtained in 56% yield as a mixture of four diastereomers. Careful column chromatography allowed the isolation of the major diastereomer **17**. When the oxaziridine was prepared using (±)-α-MBA, **17** could be crystallized as a racemate, which afforded material suitable for X-ray analysis. Two more oxaziridine isomers were isolated by HPLC and assigned as **18** and **19**. Additionally, a 2:1:1 mixture of more polar 4-hydroxyoxaziridines **20** was obtained in 24% yield.

Our feeling that this product probably arose by initial oxidation of the enamine tautomer[23] (Scheme IV) led us

Scheme IV



Scheme V



R_1	R_2	R_3				
H	CH_3	H	11	26	-	(*S*)-33
CH_3	H	H	12	27	-	(*R*)-33
H	OCH_3	H	14	28	29	34
H	H	OCH_3	15	30	-	35
H	C_6H_5	H	17	31	32	36

to attempt the oxidation on the condensation product of α-MBA and 2-carbethoxycyclohexanone **21**. In this case, the exclusive products in experiments involving >2 equiv of oxidant were α-hydroxyoxaziridines **22**. When ≤1 equiv of (+)-MPCA or *m*-CPBA was used, mixtures of unreacted starting material and **22** were obtained with no sign of 2-carbethoxy-2-hydroxycyclohexanone, which would arise from hydrolysis of the presumed intermediary 2-hydroxy imine. Similar treatment of 1-methyl-2-tetralone **23**[24] afforded only 9% of the simple oxaziridines **24** and a mixture of hydroxy oxaziridines **25** in 86% combined yield.

Thus, imines with a greater amount of enamine content are more likely to give doubly oxygenated products than simple alkyl or alkoxy imines. The lack of products resulting from only α-oxidation of the imine even when only 1 equiv of oxidant is used suggests that oxaziridine formation in the α-hydroxy imines is faster than the corresponding reaction of simple imines. Such a rate enhancement may be due to coordination and delivery of the oxidant by the adjacent hydroxyl group, but we have as yet no stereochemical or direct kinetic evidence for this effect.

The effect of oxidizing agent on the product mixtures resuting from these oxaziridines was briefly examined. When magnesium monoperoxyphthalate (MMPP) (in alcoholic solvents) was substituted for *m*-CPBA or (+)-MPCA, the relative proportions of simple oxaziridine formation increased (cf. entries 4 vs 7 and 9 vs 10). These results are consistent with the idea that MMPP, bearing a substantial negative charge, is a more nucleophilic oxidant than either *m*-CPBA or (+)-MPCA. Thus, MMPP is more likely to react with the electrophilic imine tautomer relative to the nucleophilic enamine moiety; however, solvent effects cannot be dismissed.

We were interested in finding the extent to which the enamine tautomer was intercepting the reactions of those substrates that did not afford doubly oxygenated oxaziridines. To this end, optically enriched 2-methylcyclohexanone (*R*)-(−)-**10**[25] and (*S*)-(−)-2-phenylcyclohexanone (−)-**16**[26] were prepared. In both cases, the application of the general procedure using (*R*)-(+)-α-MBA and these optically active ketones gave product mixtures that were indistinguishable from those obtained starting with racemic ketone within experimental error (cf. entries 2 vs 1 and 5 and 6 vs 4). These experiments unambiguously show that the stereogenic center adjacent to the imine center is undergoing equilibration at some point in the reaction sequence. The ^{13}C NMR spectra of the crude imines formed by condensation with (*R*)-(−)- or (*S*)-(+)-α-MBA with (*S*)-(−)-2-phenylcyclohexanone (−)-**16** were complex but nearly identical, suggesting that substantial stereochemical scrambling had already taken place at that point in the sequence.

These results demonstrate that these oxidations are considerably more complex when there is opportunity for direct steric interaction between the cyclohexyl substituent and the reacting imine center. The stereoselectivity of such reactions is often considerably diminished, with a number of very minor oxaziridine products accompanying one or two major isomers in the reaction mixtures. For 2-alkyloxaziridines, epimerization is also occurring at the C-2 carbon of the starting ketone (probably during the course of imine formation, although our results do not address whether this epimerization occurs at a rate competitive with oxaziridine formation). It is apparent, however, that the product formed in highest yield accords with the principles described in the previous section, i.e. formation of the new nitrogen stereocenter such that it bears an *unlike* relationship to the benzylic stereogenic center, and attack opposite to the ketone C-2 substituent.[27] In addition, there is an intrinsic preference to form the anti oxaziridine stereoisomer with respect to the plane of the oxaziridine ring, in order to avoid unfavorable 1,3-steric interactions between the C-4 and nitrogen substituents. The other isomers formed in appreciable amounts in these reactions are those for which one of the latter two conditions are not met; however, we have yet to isolate and identify an oxaziridine in >10% yield that does not result

(23) (a) Oxidation of an enamine: Davis, F. A.; Sheppard, A. C. *Tetrahedron Lett.* **1988**, *29*, 4365–4369. (b) Double oxidation of silyl enol ethers using *m*-CPBA: Horiguchi, Y.; Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1989**, *30*, 3323–3326. Horiguchi, Y.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1989**, *111*, 6257–6265.

(24) Oxaziridines derived from 1-tetralone derivatives: Johnson, G. P.; Marples, B. A. *Tetrahedron Lett.* **1984**, *25*, 3359–3362. Johnson, G. P.; Marples, B. A. *Tetrahedron Lett.* **1985**, *26*, 4115–4118.

(25) Meyers, A. I.; Poindexter, G. S.; Brich, Z. *J. Org. Chem.* **1978**, *43*, 892–898.

(26) (a) Oxidation of optically active 2-phenylcyclohexanol: Berti, G.; Macchia, B.; Macchia, F.; Monti, L. *J. Chem. Soc. C* **1971**, 3371–3375. (b) Enzymatic resolution of 2-phenylcyclohexanol: Whitesell, J. K.; Lawrence, R. M. *Chimia* **1986**, *40*, 318–321.

(27) It is unclear whether the attack anti to the C-2 ketone substituent results from equatorial attack on the chair form, followed by a conformational equilibration that places the C-4 substituent in an axial position and the N(oxaz) in an equatorial position, or if the imine suffers axial attack in a conformation with the C-2 substituent already in a pseudoaxial position.

(28) E.g., see: Vedejs, E.; Dent, W. H., III *J. Am. Chem. Soc.* **1989**, *111*, 6861–6862.

(29) Oliveros, E.; Rivière, M.; Malrieu, J. P.; Teichteil, C. *J. Am. Chem. Soc.* **1979**, *101*, 318–322.

Table II. Photolyses and Debenzylation Reactions

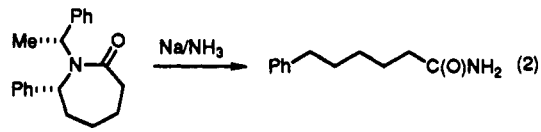
		photolysis		debenzylation	
entry	oxaziridine[a]	product[a]	% yield[b]	product[a,c]	% yield[b]
1	11[d]	26	57	(S)-33[e]	78
2	12[d]	27	62	(R)-33[e]	77
3	14[d]	28	32	34	77[e]
		29	18		
4	15	30	60	35	89[f]
5	17	31	59	36[g]	91[f]
		32	5	37	65

[a] See Scheme V and text for structures. Homogeneous oxaziridines were used except where noted. [b] Yields refer to chromatographically purified products except where noted. [c] The products obtained by sodium/ammonia treatment of the purified lactam in the same row of this table. [d] Mixture of stereoisomers. [e] (S)-33 was obtained in 84% ee, whereas (R)-33 was formed in 74% ee (determined by optical rotation and analysis of the derived diastereomeric ureides, see ref 35). [f] Crude yield. [g] Obtained in racemic form (determined by optical rotation and analysis of the derived diastereomeric ureides, see ref 35).

from *unlike* attack controlled by the benzylic stereocenter. For imines bearing an adjacent alkyl or aryl substituent, there is apparently a strong preference against formation of syn oxaziridines, leading to the substantial formation of a minor product in which attack of the oxidizing agent has occurred cis to the nearby methyl substituent. Conversely, the imine from 2-methoxycyclohexanone reacts to afford trans attack relative to the methoxy group (≥90% of the products formed) but gives an approximately equimolar mixture of syn and anti oxaziridine stereoisomers. This is probably due to both the greater ability of an alkoxy group to direct attack of the oxidant in a trans direction[30] and the smaller size of a methoxy (vs methyl) substituent.

Photolysis of Oxaziridines and Conversions to N-Unsubstituted Lactams. The purified oxaziridine stereoisomers were converted to the ring-expanded lactams under photolytic conditions as previously described (Scheme V and Table II).[5]

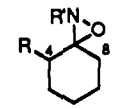
Generally, the oxaziridines underwent rearrangement to afford the product resulting from migration of the substituent syn to the oxaziridine N-substituent. Thus, oxaziridines **11** and **12** mainly afforded epimeric lactams **26** and **27**, respectively (a small amount (ca. 5–10%) of epimerization, presumably at C-3, was detected by NMR in these photolyses). Although not optically pure, the major lactams derived from the two experiments were clearly epimeric at C-3 as shown by debenzylation under Birch conditions to give optically active (*S*)- or (*R*)-**33**, respectively. For the major oxaziridine derived from 2-phenylcyclohexanone (**17**), a small amount of the regioisomeric lactam (5%) resulting from migration of the anti substituent was isolated in addition to a 59% yield of the expected **31**. Lactam **32** was isolated in >90% diastereomeric purity, indicating that very little epimerization had occurred at the migrating stereogenic center. In contrast to the 3-methyl lactams above, debenzylation of **31** under similar conditions led to *racemic* **36**. The regiochemistry of **32** was confirmed by its conversion to open-chain amide **37** upon treatment with sodium in liquid ammonia (eq 2).



32 **37**

(30) Oliveros, E.; Rivière, M.; Lattes, A. *Org. Magn. Reson.* **1976**, *8*, 601–606.

Table III. Selected Chemical Shift and Vicinal Coupling Data for Oxaziridines



	^{13}C NMR chemical shifts (δ)		J_{vic} for C-4 and C-5 protons
oxaziridine[a]	C_4	C_8	
40[b]	36.5	27.6	
41[c]	36.4	28.0	
42[c]	38.4	26.7	
11	38.3	26.0	6.2, 4.3[d]
12	37.5	26.4	8.5, 3.6[d]
14[e]	81.6		br s
15	65.4		3.9
17	49.3		6.8, 4.9
18	49.0		10.0, 3.7
19	42.4		br s

[a] See Scheme IV and text for structures of oxaziridines. [b] Reference 31. [c] Reference 14. [d] Obtained by the irradiation of the C-4 methyl doublet. [e] Other isomers isolated accompanying **14** had chemical shifts of δ 81.7 and 81.8.

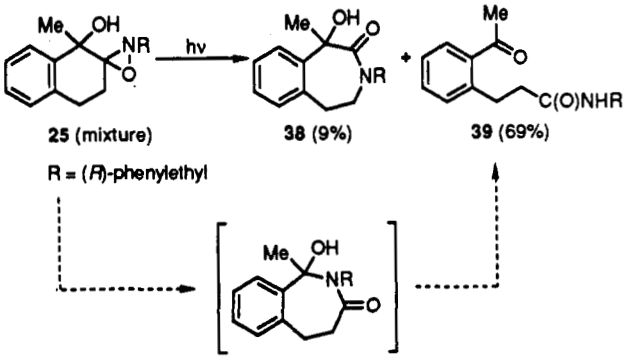
The syn and anti oxaziridines derived from 2-methoxycyclohexanone differed with respect to the regioselectivity of the ring expansion processes. Syn oxaziridine **15**, which was photolyzed as a single diastereomer, gave exclusively **30**, resulting from migration of the substituent syn to the *N*-phenylethyl group (60% isolated yield). However, **14**—consisting of three oxaziridines—gave a complex product mixture of four lactams, two of which resulted from migration of the α-carbon syn to the *N*-phenylethyl group (32% for both products) and two from migration of the normally disfavored anti α-carbon (15%). All of the isomers present in the oxaziridine mixture represented by **14** are assigned as having the anti relationship between the *N*-phenylethyl group and the methoxy substituent because of the similarity of the chemical shifts of the C-4 methine in the ^{13}C NMR spectrum (see Table III). This implies a ratio of syn/anti migratory ability in **14** of about 70:30, a value consonant with literature experience.[14]

The substantial amount of "anti-Lattes" product formed in this experiment may be rationalized by considering the methoxy group to stabilize a putative radical[8,9,29] intermediate during the rearrangement, thus reinforcing the stereoelectronic preference for **15** but opposing the same for **14**. It is worth noting, however, that if orbital overlap from the nonbonded electrons on nitrogen is indeed the regiochemistry-controlling factor as suggested,[29] a nonbonded orbital placed on oxygen could exert a similar effect. Thus, this effect would reinforce that of the nitrogen lone pair for the rearrangement of **15** but the two effects would favor different products in the case of **14**, which could also account for the observed results.

It is also interesting that several oxaziridines gave some product resulting from migration of a carbon atom bearing a stereogenic center (e.g. formation of **30** and **32**). The lactams obtained in these examples were formed as predominantly or exclusively one isomer, a result consistent with earlier work.[10] If radical intermediates are involved in the migration reaction, then, this result requires either that (1) the migration is too fast to allow epimerization at the migrating center, or (2) the following ring-closure step is stereoselective. Alternatively, the lack of observed epimerization in these examples is consistent with a concerted migration in the excited state of the oxaziridine.

When the mixture of doubly oxygenated oxaziridines **25** was submitted to photolysis, only 9% of the product re-

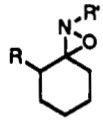
Scheme VI



sulting from simple migration of the unsubstituted carbon adjacent to the spiro junction was obtained (Scheme VI). The major product was the open chain amide **39**, obtained in 69% yield. This product could arise via the breakdown of the intermediate shown, the result of migration of the quaternary stereogenic center in **25**. Amide **39** was also formed when **25** was refluxed overnight in methylene chloride (TLC).

Structure Elucidation and Conformational Analysis

Oxaziridines. Previous work on oxaziridines **40–42** has shown that it is possible to differentiate the two groups adjacent to the spiro carbon of cyclohexanone-derived oxaziridines by ^1H and ^{13}C NMR.[14,30,31] Thus, the signal of the methylene carbon syn to the nitrogen substituent is generally found ca. 7–10 ppm upfield from the anti carbon. Thus, examination of these signals in the NMR spectra for the various oxaziridines isolated in this study and comparison with literature values allowed us to assign structures as syn or anti with respect to the plane of the oxaziridine ring with confidence (Table III).

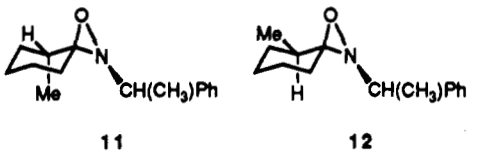


40, R = H, R' = CH_3
41, R = H, R' = CH_2Ph
42, R = CH_3, R' = CH_2Ph

The close chemical shifts of the α-carbons in **11** and **12** suggested that both isomers had the same relative stereochemical relationship between C-4 and N-2, which we assigned as anti based on analogy with **40–42**. If we also assume an *unlike* relationship between C-α and N-2, the lack of a methylene resonance at high field suggested that the two oxaziridines were in a conformation which placed the nitrogen of the oxaziridine nitrogen in an equatorial position. Vicinal coupling constants were consistent with an equatorial C-4 H for **11** and an axial C-4 H for **12** and their conversions to epimeric lactams **31** and **32** showed them to be epimeric at C-4. An X-ray crystallographic study carried out on **12** (supplementary material) revealed the alternate chairlike conformation in the solid state, with both the nitrogen atom and the C-4 methyl group occupying pseudoaxial positions. In all, these data also strongly support the stereostructure of **11** as shown (involving attack of the oxidant trans to the resident methyl substituent) and the populated solution state conformations of **11** and **12** as depicted in Figure 1.

That oxaziridines **14** and **15** differ in the syn/anti relationship of C-4 and N(oxaz) was strongly suggested by the ca. 7 ppm chemical shift difference in their C-4 resonances in the ^{13}C NMR spectra (Table III) and was confirmed by a 2D NOESY NMR study. Thus, an NOE was

(31) Jordan, G. J.; Crist, D. R. *Org. Magn. Reson.* **1977**, *9*, 322–324.



11 **12**

Figure 1. Proposed solution conformations of **11** and **12**.

observed between the C-4 proton and the C(benzylic) proton of **15**, while no such interaction was present in oxaziridine **14**, allowing **14** and **15** to be assigned as anti and syn, respectively. In addition, the C-4 proton appeared about 0.8 ppm downfield in **15** relative to **14**. Here, the line widths and vicinal coupling constants of the C-4 proton in the ^1H NMR of the two oxaziridines strongly supported solution-state conformations in which the methoxy groups were axial in the oxaziridines, and the attack of oxidant trans to the methoxy group in the intermediate imines would imply an equatorial N(oxaz) atom. This last point is again supported by the circumstantial evidence of the absence of a high-field signal due to the syn-1,3-diaxial proton. The structure of **14** was proved by an X-ray structure (supplementary material); in this case, the conformation predicted by examination of the NMR data is also present in the solid state.

The structure of (±)-**17** was also solved by an X-ray study which showed the molecule to adopt a solid-state conformation in which the phenyl group was axial and the N-2 group equatorial (supplementary material). In addition, the ^1H NMR spectrum clearly established the C-4 proton to be equatorial in the predominant solution-state conformer, signifying a similar conformation. The structures of **18** and **19** were assigned as shown using the same chemical shift and coupling constant arguments given above and collected in Table III.

These data suggest that the oxaziridines exist predominantly in a stable chairlike conformations. Previous workers have suggested that, for spirocyclic oxaziridines derived from cyclohexanone itself, the conformation in which the nitrogen atom occupies a pseudoequatorial position is favored.[14] However, the conformations of the major oxaziridines derived from 3- and 4-alkylcyclohexanones are primarily controlled by the alkyl substituent. In these compounds, e.g. **2** and **3** in this paper, the nitrogen atom is forced into an axial orientation. In contrast, it appears that the favored solution-state conformation for oxaziridines in which an alkyl or aryl substituent is adjacent to the spirocyclic linkage is that which places the oxaziridine nitrogen equatorial and the alkyl or aryl group axial.

Lactams. Mainly, the lactam structures were evident by inspection of the ^1H NMR spectra of the compounds as summarized in the Experimental Section and supplementary material.[32] There is also a ^1H NMR trend, reminiscent of that observed in the N-axial oxaziridines, which is summarized in Figure 2.[33]

The lactams are presumed to mainly exist in the chairlike conformations, with the C-3 substituent occupying an equatorial position, and with the chiral side chain adopting a rotamer in which the benzylic hydrogen is very nearly in the plane of the amide linkage. Both of these

(32) The ball-and-stick depictions in Figure 2 were constructed using the previously reported X-ray crystallographic structure of [*R*-(*R**,*R**)]-hexahydro-5-(1,1-dimethylethyl)-1-(1-phenylethyl)-2*H*-azepin-2-one[8] as a model for caprolactam ring system and the conformation of the phenylethyl side chain. The *R**,*S** diastereomer was constructed by simply switching the positions of the phenyl and methyl groups on the side chain.

(33) The structural elucidations of both oxaziridines and lactams are described in more detail in the M.S. Thesis of M.H. (ref 12b).

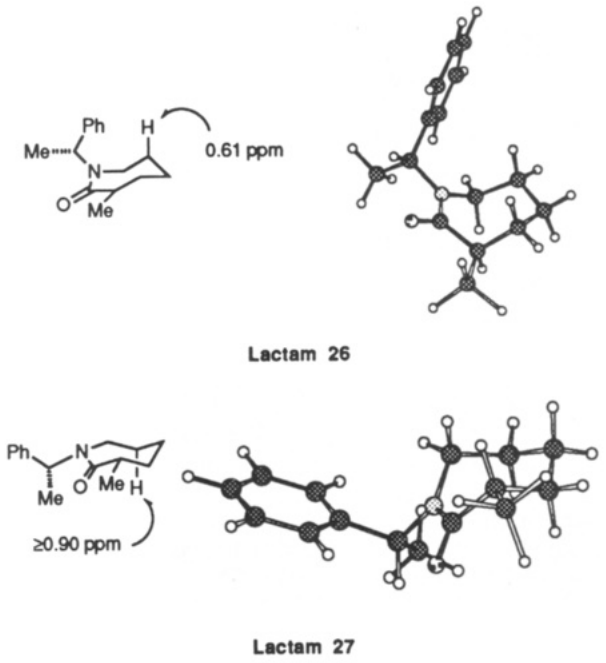


Figure 2. Proposed solution conformations of **26** and **27**.

features were previously observed in an X-ray structure of a related *N*-phenylethyl lactam.[8] The lactam ring conformation is partially supported for **26** and **27** by the ^{1}H NMR coupling constant for the C-7 H: $J_{vic}(H_{ax}-H_{eq})$ = 9 Hz, with no coupling observed between the C-7 H and the C-6 equatorial proton due to a dihedral angle of approximately 90°. For diastereomer **27** (Figure 2), the proposed rotamer places the phenylethyl substituent in the extended conformation shown. However, in diastereomer **26**, placement of the C-α H in the plane of the amide induces the side chain to fold over the caprolactam ring as shown, leading to shielding of a C-3 axial proton.

Summary

The oxaziridine syntheses described in this paper depend on a combination of three chiral agents: the substrate ketone, α-methylbenzylamine, and (in most cases) optically active oxidizing agent. These combine to afford structures with up to four stereogenic atoms in an essentially one-pot operation. The chiral oxidant was shown in related work to have little effect on the diastereoselectivity of the oxaziridine preparations and appears to be unimportant here as well as indicated by comparison of the results obtained using both antipodes of α-MBA. With respect to the former two considerations, when they do not directly interact, as in the phenylethyl imine derived from 3-methylcyclohexanone, one obtains high diastereoselectivity resulting from simultaneous direction of oxidation stereochemistry from each stereogenic center. In this way, it is possible to control nitrogen stereochemistry for these examples and convert the products reliably to regiochemically predictable lactams. However, the synthesis of oxaziridines from ketones having an adjacent chiral center is considerably complicated by the formation of up to four reacting imines, due to *E*/*Z* isomerism about the C=N bond and mixtures of stereoisomers resulting from epimerization at the enolizable center. These reactions yield a number of products, the plurality of which can be predicted by general considerations obtained from the study of the simpler cases. These analyses afford some insight into the relative importance of the various stereochemical elements in the direction of oxidant attack. In addition, new products apparently resulting from oxidation at the α-carbon prior to oxaziridine formation were also observed. The photochemistry of the oxaziridines was also examined and shown in most cases to depend only on the stereochemistry of the nitrogen atom.

Experimental Section[34]

General Procedure for Synthesis of Oxaziridines. A toluene solution of ketone (1.0 equiv) and α-methylbenzylamine (1.2 equiv) was refluxed using a Dean–Stark apparatus for 3–4 h. The crude solution of imine was added dropwise to a solution of (+)-monoperoxycamphoric acid ((+)-MPCA, 2.0 equiv) or *m*-CPBA in a minimum amount of toluene at −78 °C. After 10 min, saturated $Na_2S_2O_3$ was added, and the mixture allowed to warm to room temperature. The layers were separated, and the organic layer was washed with saturated $NaHCO_3$ and brine and dried over Na_2SO_4. Column chromatography on silica gel provided the product oxaziridine. Spectral and physical data for typical oxaziridines synthesized follow.

[2*S*-(2*R(*S**),3*S**(*R**))]-5-Methyl-2-(1-phenylethyl)-1-oxa-2-azaspiro[2.5]octane (2).** Column chromatography with 1:9 ethyl acetate (EtOAc)/hexane (C_6H_{14}) afforded a light yellow oil: IR (neat) 2956, 1487, 1388, 752, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.52 (qt, J = 12.8, 3.8 Hz, 1 H, C-7 axial H), 0.81 (m, 1 H), 0.87 (d, J = 6.2 Hz, 3 H, C-5 methyl), 1.42 (complex, 5 H), 1.56 (d, J = 6.4 Hz, 3 H, CH(C*H*$_3$)Ph), 1.78 (td, J = 12.9, 4.6 Hz, 1 H), 1.90 (m, 1 H), 3.61 (q, J = 6.4 Hz, 1 H, NC*H*(CH$_3$)Ph), 7.31 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 21.8, 23.3, 23.7, 26.9, 31.2, 33.3, 44.8, 62.4, 85.4, 126.8, 127.4, 128.5, 141.5; MS *m*/*e* 231 (M$^+$) 105 (100). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.89; H, 9.15; N, 6.05. Found: C, 77.69; H, 9.17; N, 6.00.

[2*R*-(2*R(*S**),3*S**(*R**))]-5-Methyl-2-(1-phenylethyl)-1-oxa-2-azaspiro[2.5]octane (3).** Column chromatography with 1:9 EtOAc/C_6H_{14} afforded a light yellow oil: IR (neat) 2942, 1490, 1393, 1275, 1068, 755 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.67 (m, 1 H, C-5 axial H), 0.77 (d, J = 6.3 Hz, 3 H, C-5 methyl), 0.83 (m, 1 H), 1.17 (m, 1 H), 1.41 (m, 2 H), 1.51 (m, 1 H), 1.56 (d, J = 6.5 Hz, 3 H, NCH(C*H*$_3$)Ph), 1.69 (m, 2 H), 1.88 (br d, J = 13.8 Hz, 1 H), 3.62 (q, J = 6.5 Hz, 1 H, NC*H*(CH$_3$)Ph), 7.31 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 21.6, 23.3, 23.5, 30.9, 33.2, 35.6, 36.0, 62.4, 85.2, 126.5, 127.3, 128.3, 141.4; MS *m*/*e* 231 (M$^+$) 105 (100). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.89; H, 9.15; N, 6.05. Found: C, 77.69; H, 9.38; N, 5.98.

[2*S*-(2*R(*S**),3*S**(*R**))]-4-Methyl-2-(1-phenylethyl)-1-oxa-2-azaspiro[2.5]octane (11) and [2*S*-(2*R**(S*),3*S**-(*S**))]-4-Methyl-2-(1-phenylethyl)-1-oxa-2-azaspiro[2.5]octane (12).** Chromatography with 9:1 C_6H_{14}/EtOAc afforded the title compound as a colorless oil (mixture of isomers). Further chromatography with 99:1 C_6H_{14}/EtOAc allowed for the partial separation of the two major diastereomers. Diastereomer **12** was isolated as a colorless solid. Recrystallization from C_6H_{14} produced colorless crystals: mp 70–73 °C; $[\alpha]_D$ +13.1° (*c* 0.665, $CHCl_3$); IR ($CHCl_3$) 2975, 1489, 1370, 1081, 880, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (d, J = 7.0 Hz, 3 H, C-4 methyl), 1.25 (m, 2 H), 1.36 (m, 1 H), 1.53 (m, 4 H), 1.57 (d, J = 6.5 Hz, 3 H, C*H*$_3$CH(Ph)N), 1.68 (m, 1 H, C-4 methine), 1.94 (m, 1 H), 3.73 (q, J = 6.4 Hz, CH$_3$C*H*(Ph)N), 7.42 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 13.7, 22.8, 23.5, 24.8, 26.4, 31.9, 37.5, 61.3, 86.9, 126.7, 127.3, 128.4, 141.7; MS *m*/*e* 231 (M$^+$) 105 (100). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.87; H, 9.15; N, 6.05. Found: C, 77.56; H, 9.40; N, 6.19. Diastereomer **11** was isolated as a light yellow oil: $[\alpha]_D$ +75.9° (*c* 0.885, $CHCl_3$); IR (neat) 2970, 1490, 1362, 1083, 850, 695 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.79 (d, J = 6.9 Hz, 3 H C-4 methyl), 1.35 (br m, 4 H), 1.56 (m, 2 H, one CH_2 and C-4 methine), 1.57 (d, J = 6.4 Hz, 3 H, C*H*$_3$CH(Ph)N), 1.75 (m, 1 H), 1.82 (m, 2 H), 3.74 (q, J = 6.4 Hz, 3 H, CH$_3$C$_H$(Ph)N), 7.35 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 14.4, 22.0, 23.3, 24.8, 26.0, 31.2, 38.3, 61.4, 87.4, 127.1, 127.5, 128.5, 141.5; MS *m*/*e* 231 (M$^+$) 105 (100). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.87; H, 9.15; N, 6.05. Found: C, 77.65; H, 95.8; N, 6.00.

[2*S*-(2*R(*S**),3*S**(*S**))]-4-Methoxy-2-(1-phenylethyl)-1-oxa-2-azaspiro[2.5]octane (15) and [2*S*-(2*R**(*S**),3*R**-(*R**))]-4-Methoxy-2-(1-phenylethyl)-1-oxa-2-azaspiro[2.5]-octane (14).** Chromatography with 9:1 C_6H_{14}/EtOAc afforded

(34) See ref 5 for general experimental details.

a colorless oil. Separation of the two diastereomers was achieved by MPLC (silica, 49:1 C_6H_{14}/EtOAc). Diastereomer **15** was isolated as a colorless solid that was recrystallized from C_6H_{14}: mp 48–49 °C; $[\alpha]_D$ +0.95° (*c* 0.525, $CHCl_3$); IR ($CHCl_3$) 2940, 1490, 1449, 1100, 1087, 950, 855, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (br d, *J* = 13.2 Hz), 1.52 (complex, 4 H), 1.56 (d, *J* = 6.4 Hz, 3 H, CH_3CH(Ph)N), 1.68 (m, 1 H), 2.12 (m, 2 H), 3.05 (s, 3 H, OCH_3), 3.56 (d, *J* = 3.9 Hz, 3 H, C-4 H), 3.88 (q, *J* = 6.5 Hz, 1 H, CH_3CH(Ph)N), 7.30 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 19.2, 23.2, 27.6, 31.6, 55.4, 60.1, 75.4, 86.0, 126.8, 127.3, 128.2, 141.5; MS *m/e* 247 (M^+), 105 (100). Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.48; H, 8.56; N, 5.80. Diastereomer **14** was isolated as a colorless oil: $[\alpha]_D$ +7.29° (*c* 0.915, $CHCl_3$); IR (neat) 2980, 1490, 1448, 1133, 860, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.55 (complex, 4 H), 1.60 (d, *J* = 6.5 Hz, 3 H, CH_3CH(Ph)N), 1.81 (m, 3 H), 1.97 (m, 1 H), 2.84 (br s, 1 H, C-4 H), 2.96 (s, 3 H, OCH_3), 3.78 (q, *J* = 6.4 Hz, 1 H, CH_3CH(Ph)N), 7.30 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 19.5 22.2, 23.6, 24.1, 29.5, 56.8, 61.3, 81.6, 85.3, 127.5, 127.8, 128.4, 139.8; MS *m/e* 247 (M^+), 105 (100); HRMS calcd for $C_{15}H_{21}NO_2$ 247.15711, found 247.1570.

[2*S*-(2*R(*S**),3*R**(*R**))]-4-Phenyl-2-(1-phenylethyl)-1-oxa-2-azaspiro[2.5]octane (17) and [2*S*-(2*R**(*S**),3*R**(*S**))]-4-Phenyl-2-(1-phenylethyl)-1-oxa-2-azaspiro[2.5]octane (18) and Isomers (19 and Other) and 4-Hydroxy-4-phenyl-2-(1-phenylethyl)-1-oxa-2-azaspiro[2.5]octane (20).** 2-Phenylcyclohexanone (0.150 g, 0.86 mmol) was reacted with (*R*)-α-MBA (0.156 g, 1.29 mmol) followed by (+)-MPCA (0.372 g, 1.72 mmol). Chromatography with 9:1 C_6H_{14}/EtOAc afforded the title compounds as a high R_f mixture of isomers (singly oxygenated oxaziridines, 0.142 g, 56% yield) and a low R_f mixture of doubly oxygenated oxaziridines (0.063 g, 24%). The major isomer (isomer **17**) was isolated by HPLC on a 250 × 7 mm CN column with 2% 2-propanol (iPrOH)/C_6H_{14} (retention time 7.3 min) or by crystallization from ethanol (EtOH) to produce colorless crystals: mp 85–87 °C (only racemic compound could be crystallized); $[\alpha]_D$ −15.2° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 3010, 1490, 1448, 1383, 1083, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (m, 1 H), 1.48 (br m, 2 H), 1.51 (d, *J* = 6.4 Hz, 3 H, CH_3CH(Ph)N), 1.92 (m, 2 H), 1.98 (br t, *J* = 6.5 Hz, 2 H), 2.81 (dd, *J* = 6.8, 4.9 Hz, 1 H, C-4 methine), 3.77 (q, *J* = 6.3 Hz, 1 H, CH_3C_H(Ph)N), 7.10 (m, 5 H, aromatics), 7.38 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 22.9, 23.2, 25.0, 27.1, 30.0, 49.3, 61.8, 86.7, 126.0, 127.5, 127.8, 128.6 128.7, 139.3, 141.0; MS *m/e* 294 (M^+ + 1), 105 (100); HRMS calcd for $C_{20}H_{23}NO$ 293.17784, found 293.1779. Anal. Calcd for $C_{20}H_{23}NO$: C, 81.87; H, 7.90; N, 4.77. Found: C, 81.64; H, 8.18; N, 4.68. Isomer **18** was isolated by flash chromatography with 99:1 C_6H_{14}/EtOAc as a light yellow-green oil: $[\alpha]_D$ −75.4° (*c* 0.61, $CHCl_3$); HPLC retention time (250 × 7 mm CN column, 2% iPrOH/H) 6.00 min; IR (neat) 2975, 1490, 1385, 1310, 1085, 863, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.37 (m, 1 H), 1.40 (d, *J* = 6.4 Hz, 3 H, CH_3CH(Ph)N), 1.65 (br m, 5 H), 2.04 (m, 2 H), 2.87 (dd, *J* = 10.0, 3.7 Hz, 1 H, C-4 H), 3.71 (q, *J* = 6.4 Hz, CH_3CH(Ph)N), 9.32 (m, 10 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 23.6, 24.1, 25.0, 27.9, 30.4, 49.0, 61.3, 86.1, 126.1, 126.9, 127.4, 127.5, 128.8, 140.0, 141.9; MS *m/e* 293 (M^+), 105 (100). Isomer **19** was isolated by HPLC as above to afford a light yellow-green oil, retention time 5.5 min: $[\alpha]_D$ −87.9° (*c* 0.585, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.19 (m, 1 H), 1.46 (complex (obscured), 2 H), 1.49 (d, *J* = 6.4 Hz, 3 H, C4H_3CH(Ph)N), 1.71 (complex, 2 H), 2.08 (tt, *J* = 13.2, 4.5 Hz, 1 H), 2.29 (m, 1 H), 3.38 (br s, 1 H, C-4 H), 3.68 (q, *J* = 6.4 Hz, 1 H, CH_3CH(Ph)N), 7.00 (m, 10 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 20.3, 23.9, 24.2, 32.1, 33.9, 42.4, 60.1, 87.5, 125.8, 127.1, 127.4, 127.5, 127.8, 128.0, 128.3, 138.8, 141.9; MS *m/e* 293 (M^+), 105 (100). For **20**: IR ($CHCl_3$) 3505, 2995, 2970, 2930, 2850, 1490, 1446, 1370, 1070, 1044, 949, 910, 867, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (major diastereomer) δ 0.86 (m, 1 H), 1.33 (m, 3 H), 1.69 (d, *J* = 6 Hz, 3 H, NCH(CH_3)Ph), 1.78 (m, 2 H), 2.13 (m, 1 H), 2.57 (dq, *J* = 13.9, 2.1 Hz, 1 H), 3.05 (s, 1 H, OH), 3.92 (q, *J* = 6.3 Hz, 1 H, NC*H*(CH_3)Ph), 6.82–7.70 (complex, 10 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) (major isomer) δ 21.6, 22.3, 24.8, 25.8, 35.7, 61.4, 73.3, 87.8, 126.8, 127.2, 128.2, 128.6, 129.5, 140.8; MS *m/e* 310 (M^+ + 1), 105 (100).

4-Carbethoxy-4-hydroxy-2-(1-phenylethyl)-1-oxa-2-azaspiro[2.5]octane (22). Obtained as a mixture of two diastereomers **22a** and a single oxaziridine **22b**. For **22a**: IR ($CHCl_3$) 3500, 1725, 1447, 1365, 1243, 1200, 1100, 1695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (major isomer) δ 1.10 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 1.55 (d, *J* = 6.4 Hz, 3 H, CH_3CH(Ph)N), 3.47, (s, 1 H, OH), 3.75 (q, *J* = 6.4 Hz, 1 H, CH_3CH(Ph)N), 3.95 (m, 2 H, OCH_2CH_3), 7.35 (m, 5 H, aromatics); (minor isomer) 1.35 (t, *J* = 7.1 Hz, 3 H, OCH_3CH_3), 1.46 (d, *J* = 6.9 Hz, 3 H, CH_3CH(Ph)N), 3.83 (q, *J* = 6.8 Hz, 1 H, CH_3CH(Ph)N), 4.29 (m, 2 H, OCH_2CH_3), 7.35 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) major isomer δ 13.5, 20.5, 22.8, 23.2, 24.4, 32.9, 60.8, 61.3, 75.6, 85.1, 126.9, 127.4, 128.2, 142.0, 171.4; minor isomer 13.8, 19.3, 21.5, 23.6, 24.9, 33.2, 60.5, 60.9, 74.8, 84.7, 126.4, 127.0, 128.0, 140.2, 171.2; MS *m/e* 305 (M^+), 105 (100); HRMS calcd for $C_{17}H_{23}NO_4$ 305.16257, found 305.1639. For **22b**: IR (CCL_4) 3500, 1715, 1445, 1173, 1135, 1010 cm1^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.35 (t, *J* = 7.1 hz, 3 H, OCH_2CH_3), 1.52 (d, *J* = 6.4 Hz, 3 H, CH_3CH(Ph)N), 1.58 (complex, 3 H), 3.47 (s, 1 H, OH), 3.70 (q, *J* = 6.4 Hz, 1 H, CH_3CH(Ph)N), 4.32 (m, 2 H, OCH_2CH_3), 7.35 (m, 5 H, aromatics); ^{13}C (74.5 MHz, $CDCl_3$) δ 14.0, 20.5, 23.2, 23.5, 24.6, 33.9, 61.3, 61.7, 76.4, 85.2, 126.7, 127.7, 128.6, 140.7, 172.0; MS *m/e* 305 (M^+), 105 (100); HRMS calcd for $C_{17}H_{23}NO_4$ 305.16257, found 305.1624.

General Procedure for Lactam Synthesis. The oxaziridine was dissolved in the indicated solvent (0.05–0.10 M) and placed in a quartz photolysis tube. The solution was degassed by bubbling nitrogen through it for 20 min and then photolyzed in a Rayonet RPR-100 chamber reactor (room temperature, 2537 Å) for 2 h. The products were purified by column chromatography.

[*R*-(*R,*R**)]-Hexahydro-4-methyl-1-(1-phenylethyl)-2*H*-azepin-2-one (4a).** Oxaziridine **2** (0.183 g, 0.791 mmol) was photolyzed in methylene chloride (CH_2Cl_2). Chromatography using 1:3 EtOAc/C_6H_{14} afforded **41** (0.130 g, 71% yield) as a yellow oil plus a small amount of the regioisomer (0.016 g, 9%): IR (neat) 2940, 1630, 1472, 1318, 1057, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.99 (d, *J* = 6.5 Hz, 3 H, C-4 methyl), 1.20 (m, 1 H), 1.37 (m, 1 H), 1.45 (d, *J* = 7.0 Hz, 3 H, NCH(CH_3)Ph), 1.63 (m, 1 H), 1.81 (m, 2 H), 2.48 (m, 2 H), 2.98 (m, 2 H), 6.01 (q, *J* = 7.0 Hz, 1 H, NC*H*(CH_3)Ph), 7.28 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 16.2, 23.0, 28.4, 29.5, 38.4, 43.6, 44.9, 50.6, 127.0, 127.1, 128.3, 140.9, 174.3; MS *m/e* 231 (M^+), 105 100); HRMS calcd for $C_{15}H_{21}NO$ 231.1623, found 231.1623.

[*S-(*R**,*S**)]-Hexahydro-6-methyl-1-(1-phenylethyl)-2*H*-azepin-2-one (5a).** Oxaziridine **3** (0.422 g, 1.82 mmol) was photolyzed in CH_2Cl_2. Chromatography with 1:3 EtOAc/C_6H_{14} afforded **5a** as a yellow oil (0.329 g, 78% yield): IR (neat) 2940, 2914, 2855, 1638, 1474, 1448, 1424, 1378, 1302, 1201, 1168, 780, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.83 (d, *J* = 6.9 Hz, 3 H, C-6 methyl), 1.18 (m, 1 H), 1.49 (d, *J* = 7.2 Hz, 3 H, CH(CH_3)Ph), 1.55 (complex (obscured), 2 H), 1.89 (m, 2 H), 2.58 (m, 2 H), 2.81 (m, 2 H), 6.05 (q, *J* = 7.1 Hz, 1 H, C*H*(CH_3)Ph), 7.30 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 16.1, 20.0, 22.9, 34.7, 36.8, 38.2, 49.9, 50.1, 126.6, 127.2, 127.8, 127.9, 140.7, 174.9; MS *m/e* 231 (M^+) 105 (100); HRMS calcd for $C_{15}H_{21}NO$ 231.1623, found 231.1621.

[*R*-(*R,*S**)]-Hexahydro-3-methyl-1-(1-phenylethyl)-2*H*-azepin-2-one (26).** Oxaziridine **11** (0.198 g, 0.86 mmol) was photolyzed in 15 mL of CH_3CN. Chromatography with 3:1 C_6H_{14}/EtOAc afforded **26** (0.122 g, 63%) as a light yellow oil: IR (neat) 2970, 1630, 1490, 1470, 1185, 1155, 780, 720, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.61 (m, 1 H), 1.22 (d, *J* = 6.8 Hz, 3 H, C-3 methyl), 1.41 (m, 2 H), 1.45 (d, *J* = 7.1 Hz, 3 H, CH_3CH(Ph)N), 1.60 (m, 1 H), 1.72 (m, 2 H), 2.62 (m, 1 H, C-3 H), 3.18 (m, 2 H, CH_2N), 6.17 (q, *J* = 7.0 Hz, 1 H, CH_3CH(Ph)N), 7.32 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 16.3, 18.5, 29.1, 32.3, 38.3, 42.8, 50.5, 126.7, 126.8, 128.1, 141.1, 176.9; MS *m/e* 231 (M^+), 105 (100). Anal. Calcd for $C_{15}H_{20}NO$: C, 77.87; H, 9.15; N, 6.05. Found: C, 77.80; H, 9.18; N, 5.98.

[*R*-(*R,*R**)]-Hexahydro-3-methyl-1-(1-phenylethyl)-2*H*-azepin-2-one (27).** Oxaziridine **12** (0.656 g, 2.84 mmol) was photolyzed in 30 mL of CH_3CN. Chromatography with 3:1 C_6H_{14}/EtOAc afforded **27** as a light yellow oil (0.399 g, 61%): IR (neat) 2970, 2920, 2850, 1640, 1490, 1465, 1415, 1265, 1205, 1185, 780, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (d, *J* = 6.78 Hz, 3 H, C-3 methyl), 1.40 (br m, 1 H), 1.52 (d, *J* = 7.2 Hz, 3 H, CH_3CH(Ph)N), 1.63 (m, 2 H), 1.80 (m, 2 H), 1.92 (m, 1 H), 2.67 (m, 1 H, C-3 H), 3.03 (m, 2 H, CH_2N), 6.35 (q, *J* = 7.1 Hz, 1 H, CH_3CH(Ph)N), 7.31 (m, 5 H, aromatics); ^{13}C (74.5 MHz, $CDCl_3$)

δ 16.4, 18.6, 29.2, 32.4, 38.3, 42.9, 50.6, 126.8, 127.0, 128.1, 141.2, 177.0; MS *m/e* 231 (M^+), 105 (100). Anal. Calcd for $C_{15}H_{20}NO$: C, 77.87; H, 9.15; N, 6.05. Found: C, 78.02; H, 9.32; N, 6.28.

[*R*-(*R,*S**)]-Hexahydro-3-methoxy-1-(1-phenylethyl)-2*H*-azepin-2-one (28).** Oxaziridine **14** (0.193 g, 0.78 mmol) was photolyzed in C_6H_{14}. Chromatography afforded **28** as a light yellow oil (0.067 g, 35%) along with 18% of the regioisomer: IR ($CHCl_3$) 2980, 1655, 1497, 1445, 1121, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.36 (m, 2 H), 1.49 (d, *J* = 6.7 Hz, 3 H, NCH(CH_3)Ph), 1.63–2.23 (complex, 4 H), 2.94 (m, 1 H, NCH_3), 3.29 (m, 1 H, NCH_2), 3.46 (s, 3 H, CH_3O), 4.05 (m, 1 H, CH_3OCH), 6.13 (q, *J* = 6.7 Hz, 1 H, NCH(CH_3)Ph), 7.38 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 16.0, 24.9, 28.6, 29.6, 41.6, 50.8, 57.3, 81.9, 127.1, 127.3, 128.2, 140.4, 172.8; MS *m/e* 247 (M^+), 105 (100); HRMS calcd for $C_{15}H_{21}NO_2$ 247.1572, found 247.1572.

[*R*-(*R,*R**)]-Hexahydro-7-methoxy-1-(1-phenylethyl)-2*H*-azepin-2-one (29).** Oxaziridine **15** (0.183 g, 0.74 mmol) was photolyzed in C_6H_{14}. Chromatography afforded **29** as a light yellow oil (0.110 g, 60%): IR ($CHCl_3$) 2990, 1625, 1455, 1440, 1398, 1165, 1083, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.76 (apparent dd, *J* = 14.3, 4.6 Hz, 1 H, C-6 pseudoaxial H), 1.51 (m, 2 H), 1.58 (d, *J* = 6.8 Hz, 3 H, NCH(CH_3)Ph), 2.55 (apparent dd, *J* = 13.7, 6.8 Hz, 1 H, $CH_2C(O)N$), 2.89 (t, *J* = 13.2 Hz, $CH_2C(O)N$), 3.32 (s, 3 H, CH_3O), 4.25 (d, *J* = 4.7 Hz, CH_3OCHN), 6.15 (q, *J* = 6.8 Hz, 1 H, NCH(CH_3)Ph), 7.36 (m, 5 H, aromatics); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 16.2, 22.7, 23.3, 31.7, 37.3, 50.2, 55.2, 84.5, 127.3, 127.6, 128.3, 140.6, 176.2; MS *m/e* 247 (M^+), 120 (100); HRMS calcd for $C_{15}H_{21}NO_2$ 247.15711, found 247.1558.

General Procedure for the Synthesis of N-Unsubstituted Lactams. Ammonia (NH_3) was condensed in a 2-necked flask containing lactam dissolved in a minimum amount of dry tetrahydrofuran. Small pieces of sodium were then added to the NH_3 solution until it turned deep blue. The mixture was allowed to remain blue for 1–2 min before being quenched with solid NH_4Cl. The NH_3 was allowed to evaporate, and the residue was taken up in H_2O and CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2, and the combined extracts were dried over Na_2SO_4.

(*R*)-Hexahydro-4-methyl-2*H*-azepin-2-one (4b). Lactam **4a** (0.111 g, 0.480 mmol) gave after chromatography with 2% MeOH/$CHCl_3$ the title compound as a colorless solid (0.050 g, 66% yield): mp 98–103 °C; $[\alpha]_D$ −34.0° (*c* 0.70, water) (lit. mp 105–106 °C, $[\alpha]_D$ −36.1° (*c* 25.6, water)); IR ($CHCl_3$) 3418, 1655, 1472, 1340, 1170, 1125 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.01 (d, *J* = 6.7 Hz, 3 H, C-4 methyl), 1.38 (br m, 1 H), 1.55 (m, 1 H), 1.88 (complex, 3 H), 2.39 (m, 2 H), 3.24 (m, 2 H), 7.15 (br s, 1 H, NH); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 22.8, 28.4, 29.0, 38.8, 42.6, 44.1, 177.9.

(*R*)-Hexahydro-6-methyl-2*H*-azepin-2-one (5b). Lactam **5a** (0.084 g, 0.363 mmol) gave after chromatography (2% MeOH/$CHCl_3$) **5b** as a colorless solid (0.030 g, 65% yield). Recrystallization from petroleum ether gave colorless needles: mp 99–100 °C; $[\alpha]_D$ −21.2° (*c* 0.69, EtOH) (lit.[4] mp 68–69 °C, $[\alpha]_D$ −22.2° (*c* 5.28, water)); IR ($CHCl_3$) 3408, 1650, 1471, 1385, 1312, 1115 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.91 (d, *J* = 6.8 Hz, 3 H, C-6 methyl), 1.33 (m, 1 H), 1.68 (m, 2 H), 1.86 (complex, 2 H), 2.42 (m, 2 H), 3.07 (complex, 2 H), 7.21 (br s, 1 H, NH); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 18.8, 21.6, 33.6, 36.1, 38.1, 48.1, 178.9; MS *m/e* 127 (M^+) 42 (100). Anal. Calcd for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 66.09; H, 10.28; N, 10.99.

(*R*)-Hexahydro-3-methyl-2*H*-azepin-2-one ((*R*)-33) and (*S*)-Hexahydro-3-methyl-2*H*-azepin-2-one ((*S*)-33). Lactam **26** (0.221 g, 0.96 mmol) afforded (*S*)-**33** as a colorless solid (0.102 g, 86%): mp 89–92 °C (recrystallized from C_6H_{14}); $[\alpha]_D$ +31.6° (*c* 0.50, $CHCl_3$) (84% ee as determined by HPLC analysis of diastereomeric ureides[35]); ^1H NMR (300 MHz, $CDCl_3$) δ 1.15 (d, *J* = 6.8 Hz, 3 H, C-3 methyl), 1.48 (m, 2 H), 1.65 (m, 2 H), 1.82 (m, 1 H), 2.00 (m, 1 H), 2.58 (m, 1 H, C-3 H), 3.25 (m, 2 H, CH_2CH_2NH), 6.55 (br s, 1 H, NH); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 17.6, 29.4, 29.8, 32.2, 38.1, 42.2, 180.5. (*R*)-**33**: lactam **32** (0.106 g, 0.46 mmol) afforded the title compound as a colorless solid (0.050 g, 86%); mp 89–92 °C (recrystallized from C_6H_{14}); $[\alpha]_D$ −26.2° (*c* 0.50, $CHCl_3$) (74% ee as determined by HPLC analysis of diastereomeric ureides) (lit.[36] $[\alpha]_D$ −19.9° (*c* 4.4, $CHCl_3$), mp 86–90 °C (absolute configuration unassigned)).

(*S*)-Hexahydro-3-methoxy-2*H*-azepin-2-one (34). Lactam **27** (0.038 g, 0.15 mmol) was treated with Na/NH_3. The crude residue (0.017 g, 77%) was analyzed: IR ($CHCl_3$) 3670, 3410, 3000, 2930, 1655, 1468, 1107, 696, 656 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.43–2.05 (complex, 6 H), 3.11 (m, 2 H, $CH_2C(O)NH$), 3.43 (s, 3 H, CH_3O), 3.90 (dd, *J* = 6, 3 Hz, 1 H, CH_3OCH), 6.61 (br s, 1 H, NH).

(*R*)-Hexahydro-7-methoxy-2*H*-azepin-2-one (35). According to the general procedure, lactam **30** (0.039 g, 0.16 mmol) was treated with Na/NH_3. The crude residue (0.020 g, 89%) was analyzed: IR ($CHCl_3$) 3680, 3010, 1595, 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.50–2.20 (complex, 6 H), 2.43 (dd, *J* = 15, 9 Hz, 1 H, $CH_2C(O)NH$), 2.66 (apparent t, *J* = 12 Hz, 1 H, $CH_2C(O)NH$), 3.38 (s, 3 H, CH_3O), 4.34 (apparent t, *J* = 6 Hz, 1 H, CH_3OCH), 7.00 (br s, 1 H, NH).

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Supplementary Material Available: Experimental details and spectral data for eq 2, the preparations of **7**, **8a,b**, **9a,b**, **24**, **25**, **32**, and **36–39**, experimental details of crystal data, intensity measurements, and structure solution and refinement, tables of fractional coordinates and equivalent isotropic thermal parameters, anisotropic thermal parameters, bond distances, bond angles, torsion angles, and PLUTO representations of **12**, **15**, and **17**, and proton and carbon NMR spectra for compounds **4a**, **5a**, **7**, **8a**, **9a**, **12**, **22a,b**, **25a,b**, **28**, **30**, **32**, **38**, **39** (78 pages). Ordering information is given on any current masthead page.

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