Enantioselective Synthesis of Primary Amines via Grignard Additions to Stereogenic *N*-(α-Phenyl-β-(benzyloxy)ethyl)nitrones[1]

Zen-Yu Chang[2] and Robert M. Coates*

Department of Chemistry, University of Illinois, 1209 W. California Street, Urbana, Illinois 61801

Received November 21, 1989

Addition of a wide range of Grignard to *C*-aryl- and *C*-alkyl-*N*-(α-phenyl-β-(benzyloxy)ethyl)nitrones (**4–7**) occurred with high diastereoselectivity (90:10 to 97:3 ratios) and good yields (56–97%). Notable exceptions are allyl- and (*o*-methoxyphenyl)magnesium bromides (low selectivity but satisfactory yields) and isopropyl- and *tert*-butylmagnesium chlorides (high selectivity but 33–34% yields) with *C*-phenylnitrone **4**. The relative stereochemistry of hydroxylamine adducts **8a,b** (from reaction of **4** with CH_3MgBr) and **19a,b** (from *C*-pentylnitrone **7** with MeMgBr) was proven by various correlations and/or by degradation to enantiomerically enriched amines. The other stereochemical assignments are based upon ^1H NMR spectral and polarity correlations and/or by analogy to the two proven cases. The configuration of the major product can be rationalized by assuming that the Grignard reagents attack the nitrone face opposite to the pseudoequatorial *N*-(α-phenyl) group in a six-membered magnesium chelate (**27** → **28**). ^1H NMR spectral evidence indicates that a 1:1 complex of nitrone **4** and magnesium bromide exists in a chelated structure (**29B**) in CD_2Cl_2. Enantioselective syntheses of (*S*)-α-phenylethylamine (94% ee) and (*S*)-2-heptylamine (82% ee) were accomplished in five steps (33–39% overall yields) from optically pure (*S*)-nitrones **4** and **7**.

The importance of absolute stereochemistry in determining the chemical and biological properties of chiral amines[3] provdes a major incentive for developing enantioselective methods for amine synthesis. Known approaches to optically active amines include resolution both classical and chromatographic,[4] asymmetric reduction of imines[5] and oximes,[6] enantioselective organometallic additions to imines and their derivatives,[7,8] asymmetric hydroboration,[9] and stereoselective alkylation of metalated amidines.[10] We have found that high and complementary facial selectivity can be achieved in organometallic additions to nitrones bearing stereogenic *N*-(β-methoxyethyl)

Scheme I

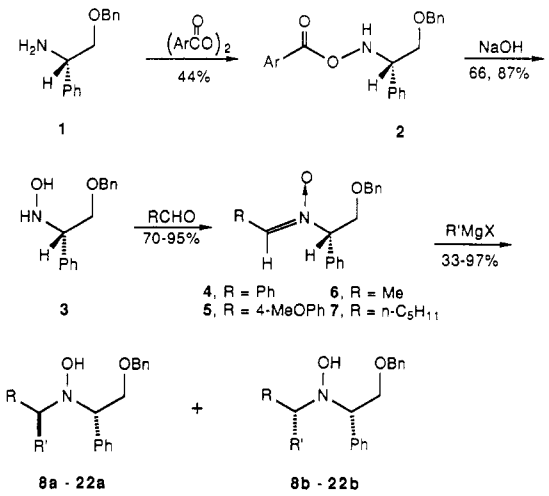
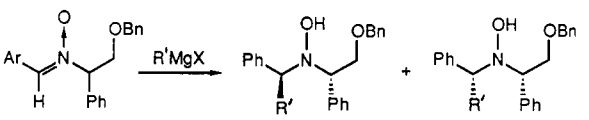


Table I. Yields and Diastereoselectivity of Grignard Additions to *C*-Arylnitrones 4 and 5



entry	R'MgX[a]	product[b]	yield, %	a:b ratio
1	MeMgBr	**8a,b**	90	90:10
2	MeMgBr (THF)		56	85:15
3	MeMgBr (CH_2Cl_2)		80	95:5
4	EtMgBr	**9a,b**	74	91:9
5	*i*-PrMgCl	**10a,b**	33	94:6
6	*t*-BuMgCl (25 °C)	**11a,b**	34	95:5
7	$PhCH_2MgCl$	**12a,b**	97	89:11
8	vinyl-MgBr (25 °C)	**13a,b**	83	90:10
9	allyl-MgBr	**14a,b**	87	78:22
10	1-naphthyl-MgBr	**15a,b**	78	90:10
11	2-methoxy-C_6H_4-MgBr	**16a,b**	82	75:25
12	4-methoxy-C_6H_4-MgBr	**17a,b**	82	97:3
13	PhMgBr		85	2:98

[a] At 0 °C in ether unless indicated otherwise. Nitrone **4** was used in all entries except 13. [b] Stereochemistry of **9a,b–17a,b** assigned by analogy and ^1H NMR spectral characteristics.

(1) (a) Portions of this work were presented at the joint American Chemical Society–Canadian Institue of Chemistry conference in Toronto, Ontario, June 7, 1988. (b) Taken in part from the Ph.D. thesis of Z.-Y. Chang, University of Illinois, 1988.

(2) University of Illinois Fellow 1984–1986.

(3) Ariens, E. J., Soudijn, W., Timmermans, P. B. M. W. M., Eds. *Stereochemistry and Biological Activity of Drugs*; Blackwell Scientific: Oxford, 1983.

(4) (a) Jacques, J.; Collet, A.; Wilen, S. H. *Enantiomers, Racemates, and Resolutions*; J. Wiley: New York, 1981. (b) Wilen, S. H. *Tables of Resolving Agents and Optical Resolutions*; University of Notre Dame Press: Notre Dame, 1972.

(5) (a) Morrison, J. D.; Mosher, H. S. *Asymmetric Organic Reactions*; Prentice Hall: Englewood Cliffs, NJ, 1971. (b) Izumi, Y.; Tai, A. *Stereo-Differentiating Reactions*; Kodansha, Ltd.: Tokyo, 1977. (c) Krzyanowska, B.; Stec, W. J. *Synthesis* **1982**, 270–273. (d) Hutchins, R. O.; Abdel-Magid, A.; Stercho, Y. P.; Wambsgans, A. *J. Org. Chem.* **1987**, *52*, 702–704.

(6) (a) Itsuno, S.; Nakano, M.; Miyazaki, K.; Masuda, H.; Ito, K.; Hirao, A.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2039. (b) Itsuno, S.; Sakurai, Y.; Ito, K.; Hirao, A.; Nakahama, S. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 395. (c) Sakito, Y.; Yoneyoshi, Y.; Suzukamo, G. *Tetrahedron Lett.* **1988**, *29*, 223.

(7) For reviews of this approach to the synthesis of amino acids, see: (a) Morrison, J. D.; Mosher, H. S. *Asymmetric Organic Reactions*; American Chemical Society: Washington, DC, 1980; p 327. (b) Seebach, D.; Imwinkelreid, R.; Weber, T. In *Modern Synthetic Methods 1986*, Scheffold, R., Ed.; Springler-Verlag: Aarau, 1986; pp 125–259. For reviews on organometallic additions to imines and their derivatives, see: (c) Volkmann, R. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1990; Vol. 1, Schreiber, S. L., Ed. (d) Kleinman, E.; Volkmann, R. A. *Ibid.* Vol. 2, Heathcock, C. H., Ed.

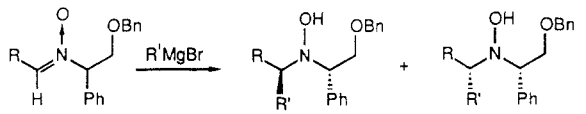
(8) (a) Fuganti, C.; Grasselli, P.; Pedrocchi-Fantoni, G. *J. Org. Chem.* **1983**, *48*, 909–910. (b) Claremon, D. A.; Lumma, P. K.; Phillips, B. T. *J. Am. Chem. Soc.* **1986**, *108*, 8265. (c) Takahashi, H.; Tomita, K.; Otomasu, H. *J. Chem. Soc., Chem. Commun.* **1979**, 668. (d) Takahashi, H.; Tomita, K.; Noguchi, H. *Chem. Pharm. Bull.* **1981**, *29*, 3387. (e) Takahashi, H.; Inagaki, H. *Ibid.* **1982**, *30*, 922–926. (f) Takahashi, H.; Suzuki, Y. *Chem. Pharm. Bull.* **1983**, *31*, 4295–4299. (g) Enders, D.; Schubert, H.; Nübling, C. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1109–1110. (h) Denmark, S. E.; Weber, T.; Piotrowski, D. W. *J. Am. Chem. Soc.* **1987**, *109*, 2224–2225. (i) Ermert, P.; Meyer, J.; Stucki, C.; Schneebeli, J.; Obrecht, J.-P. *Tetrahedron Lett.* **1988**, *29*, 1265–1268.

(9) Brown, H. C.; Kim, K.-W.; Cole, T. E.; Singaram, B. *J. Am. Chem. Soc.* **1986**, *108*, 6761–6764.

(10) Meyers, A. I. *Aldrichimica Acta* **1985**, *18*, 59–68.

0022-3263/90/1955-3475$02.50/0

Table II. Yields and Diastereoselectivity of Grignard Additions to *C*-Alkylnitrones 6 and 7



entry	nitrone	R'MgBr[a]	product[b]	yield, %	isomer ratio
1	6	PhMgBr	**8a,b**	58	91:9
2		EtMgBr	**18a,b**	67	92:8
3		n-C_5H_{11}MgBr	**19a,b**	58	90:10
4		n-C_5H_{11}MgBr (CH_2Cl_2)		33	82:18
5	7	MeMgBr		88	10:90
6		MeMgBr (CH_2Cl_2)		83	8:92
7		vinyl-MgBr (25°C)	**20a,b**	56	87:13
8		allyl-MgBr	**21a,b**	50	60:40
9		t-Bu MgCl (25°C)	**22a,b**	69[c]	>99:1

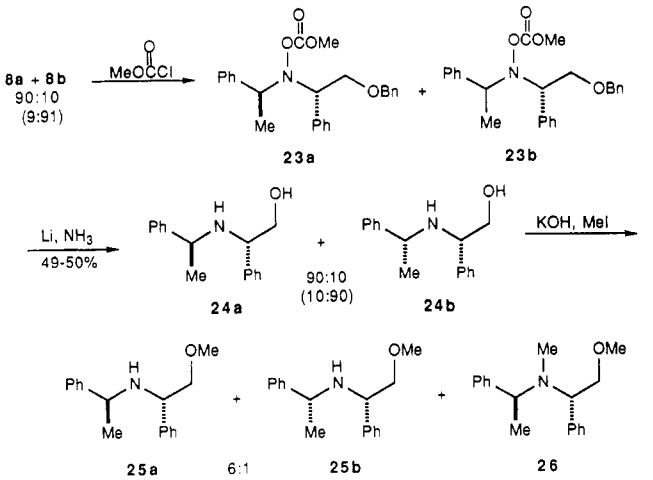
[a] At 0 °C in ether unless specified otherwise. [b] The relative configuration of the major product is assigned as 1*R**,1′*S** in all entries except 5 and 6. The stereochemistry of **18a,b** and **20a,b–22a,b** is assigned by analogy. [c] The yield was estimated by ^1H NMR analysis of the crude product.

substituents.[11] In this paper we report a new enantioselective synthesis of primary amines via Grignard additions to nitrones bearing the detachable *N*-(α-phenyl-β-(benzyloxy)ethyl) group on nitrogen.

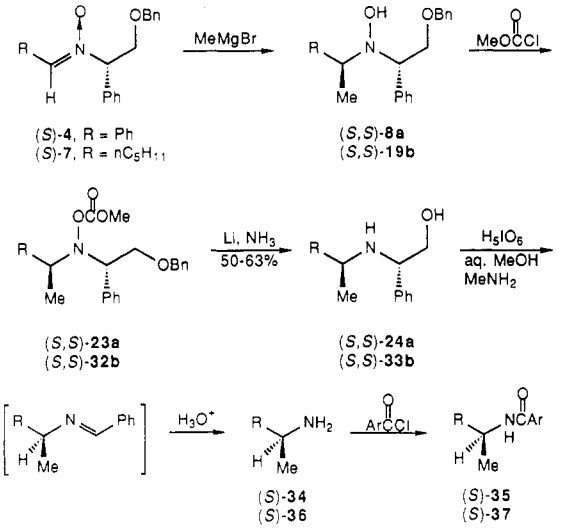
Synthesis and Grignard Stereoselectivity of *N*-(β-(Benzyloxy)ethyl)nitrones. The hydroxylamine precursor **3** was prepared in both racemic and optically active form by N-oxygenation of (*R,S*)- and (*S*)-phenylglycinol benzyl ether (**1**) with 2-chlorobenzoyl peroxide followed by hydrolysis of hydroxyamino ester **2** (Scheme I).[12] Condensation of **3** with benzaldehyde, *p*-methoxybenzaldehyde, acetaldehyde, and hexanal (CH_2Cl_2, Na_2SO_4)[13] afforded nitrones **4–7** in 70–95% yield. The enantiomeric purity of (*S*)-**4** was shown to be >98% by ^1H NMR spectral analysis in the presence of the chiral shift reagent (*R*)-2,2,2-trifluoro-1-(9-anthryl)ethanol. The yields and isomer ratios of the diastereomeric hydroxylamine adducts **8a,b–22a,b** formed upon reactions of the nitrones with a wide range of Grignard reagents are presented in Tables I and II.

High and complementary diastereoselectivity (90–95% of major isomer) was observed in most cases. The ratio was usually less favorable in THF and more favorable in CH_2Cl_2 (Table I, entries 1–3).[11] An exception to this generalization is the reaction of n-C_5H_{11}MgBr with nitrone **6** in CH_2Cl_2 which lead to a lower isomer ratio than observed in ether (Table II, entries 3 and 4). Significantly lower ratios were found for allyl and *o*-methoxyphenyl Grignard reagents (Table I, entries 9 and 11; Table II, entry 8). Although high diastereofacial discrimination was maintained with isopropyl (94:6) and *tert*-butyl (95:5) Grignard reagents, low yields of adducts **10a,b** (33%) and **11a,b** (34%) were obtained from *C*-phenylnitrone **4** owing to formation of significant amounts of several unidentified byproducts. However, both the stereoselectivity and yield (>99:1, 69%) were satisfactory in the reaction of *tert*-butyl Grignard reagent with *C*-alkylnitrone **7**.

Scheme II



Scheme III



In contrast to the low selectivity observed in the addition of 2-methoxyphenyl Grignard reagent to *C*-phenylnitrone **4**, the *p*-methoxy isomer afforded a high proportion of one isomer (97:3). Since there was some uncertainty whether the minor isomer would exhibit significantly different ^1H NMR spectral characteristics, it was prepared as the predominant isomer (98:2) by addition of phenylmagnesium bromide to *C*-(*p*-methoxyphenyl)nitrone **5**.

Stereochemical Proofs and Assignments. The relative stereochemistry of hydroxylamine adducts **8a** and **8b** was established by the correlations shown in Scheme II. Isomer mixtures rich in **8a** (90:10) and in **8b** (91:9) were converted to the carbonates **23a** and **23b** which underwent concomitant N–O bond cleavage and debenzylation upon exposure to lithium in liquid ammonia. The stereochemistry of amino alcohol **24b** was established by ^1H and ^{13}C NMR spectral comparisons with a sample prepared by hydrogenation of the imine resulting from acetophenone and phenylglycinol.[14] Methylation of the 90:10 mixture

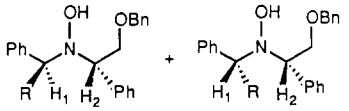
(11) Chang, Z.-Y.; Coates, R. M. *J. Org. Chem.*, preceding paper in this issue.

(12) (a) Zinner, G. *Arch. Pharm. (Weinheim, Ger.)* **1963**, *296*, 57–60. (b) Zinner, G. *Ibid.* **1963**, *296*, 420–426. (c) Biloski, A. J.; Ganem, B. *Synthesis* **1983**, 537–538. (d) For alternative procedures to oxidize amines to hydroxylamines, see: Murry, R. W.; Singh, M. *Synth. Commun.* **1989**, *19*, 3509. Danishefsky, S.; Wittman, M. D.; Halcomb, R. L. *J. Org. Chem.* **1990**, *55*, 1981.

(13) Torssell, K.; Zeuthen, O. *Acta Chem. Scand. Ser. B* **1978**, *B32*, 118–124.

(14) Eleveld, M. B.; Hogeveen, H.; Schudde, E. P. *J. Org. Chem.* **1986**, *51*, 3635.

Table III. Diagnostic ^{1}H NMR Spectral Data for Diastereomeric Hydroxylamines in $CDCl_3$



hydroxylamine no.	R	$\delta_{(H1)}$ isomer a	$\delta_{(H1)}$ isomer b	$\delta_{(H2)}$ isomer a	$\delta_{(H2)}$ isomer b
8	CH_3	3.85	3.75	4.18	3.90
9	C_2H_5	3.70	3.42	4.15	–[a]
10	*i*-Pr	3.67	3.16	–[a]	–[a]
11	*t*-Bu	3.78	3.19	3.89	3.64
12	vinyl	~4.20	–[a]	4.22	–[a]
13	allyl	3.91	3.64	4.11	3.84

[a] Data not available.

of **24a** and **24b** afforded a 6:1 mixture of the known methyl ethers **25a** and **25b**[14] as well as some *N,O*-dimethyl product **26** derived from **25a**. The conversion of optically adducts (*S,S*)-**8a** and (*S,S*)-**19b** to (*S*)-α-phenethylamine and (*S*)-2-heptylamine (Scheme III) affords independent proof for the stereochemistry of **8a** and **19b**.

The relative configuration of the other diastereomeric hydroxylamines shown in Tables I and II are assigned by ^{1}H NMR spectral comparisons, by their relative polarity on silica gel, and/or by analogy to **8a,b** and **19a,b**. The ^{1}H NMR chemical shifts for both benzylic protons in the major adducts 8–14 derived from *C*-phenylnitrone **4** appear at lower field than those in the minor adducts ($\Delta\delta$ = 0.10–0.59, Table III). The major adducts **8a–14a** all proved to be less polar than their isomers **8b–14b** in TLC analyses on silica gel. It seems reasonable to assume that the correspondence of ^{1}H NMR data and relative polarity arise from common stereochemistry and similar conformations of **8a,b–14a,b**.

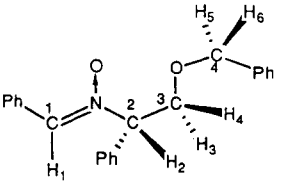
The stereochemistry assigned to the other diastereomeric pairs of hydroxylamines are based solely on the assumption that the configuration of the major product is the one predicted by the chelation model. While this assumption seems reasonable for the reactions proceeding with high selectivity (≥90:10), the lower isomer ratios obtained with allyl (78:22 and 60:40) and *o*-methoxyphenyl (75:25) Grignard reagents render these assignments tentative. Furthermore, other sites of coordination and transition states could influence the stereochemistry in these cases.

Chelated Transition-State Model. The stereochemistry of the major isomers formed in the addition of Grignard reagents to nitrones 4–7 can be rationalized by assuming prior formation of a half-chair magnesium chelate **27**. Both steric approach control (attack anti to the phenyl group) and stereoelectronic considerations predict that stereoisomeric adduct **28** should be favored.

27 28

The ^{1}H and ^{13}C NMR spectral properties of a $MgBr_2$ complex of nitrone **4** were investigated in order to find evidence for or against magnesium chelation. Mixing of equimolar amounts of $MgBr_2$ etherate and nitrone **4** in ether resulted in precipitation of a hygroscopic 1:1 complex (**29**). The similarity of the ^{1}H NMR spectrum of the complex in THF-d_8 to that of **4** indicates complete or

Table IV. Selected ^{1}H NMR Spectra Data for Nitrone 4 and Its Magnesium Bromide Complex (29)

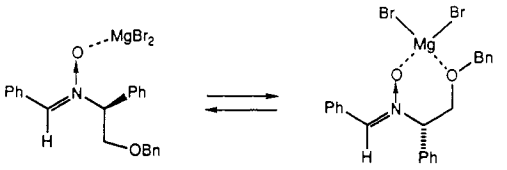


4

	nitrone[a] δ_0[b] (m)	nitrone[a] *J*, Hz	$MgBr_2$ complex[a] δ_+ (m)	$MgBr_2$ complex[a] *J*, Hz	$\Delta\delta$
H_1	7.58 (s)		7.61 (s)		0.03
H_2	5.15 (dd)	9.4, 3.6	5.87 (br d)	7.4	0.72
H_3	4.54 (t)	9.7	4.82 (dd)	12.6, 8.9	0.28
H_4	3.78 (dd)	10.2, 3.6	3.96 (dd)	12.6, 2.4	0.18
H_5	4.56 (d)[b]	12.0	5.08 (d)[b]	13.1	0.52
H_6	4.63 (d)[b]	12.0	5.25 (d)[b]	13.1	0.62

[a] In CD_2Cl_2 at 300 MHz. [b] These assignments could be reversed.

nearly complete dissociation to the free nitrone in this solvent. Small downfield shifts of H_1 and H_2 observed in the presence of additional $MgBr_2$ suggest that some coordination of the Lewis acid to the nitrone was occurring.



29A 29B

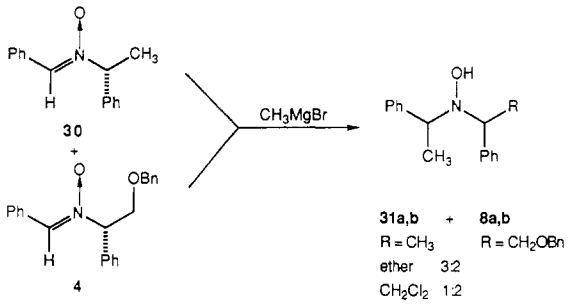
Although the low solubility of complex **29** in ether was insufficient to allow NMR measurements in this solvent, spectra recorded in CD_2Cl_2 exhibited significant downfield shifts ($\Delta\delta$ 0.18–0.72) for all five aliphatic hydrogens (H_2–H_6) on the (benzyloxy)ethane group (Table IV). Furthermore, small changes in the coupling constants presumably indicate some alteration in the conformation of the complex. The large difference in the vicinal coupling constants, $J_{2,3}$ (8.9 Hz) and $J_{2,4}$ (2.4 Hz), point to ≈180° and ≈30° dihedral relationships between the H_2/H_3 and H_2/H_4 pairs of hydrogens. These ^{1}H NMR spectral changes indicate coordination of magnesium ion with the nitrone and the coupling constants observed, albeit only slightly changed from those in the free nitrone, are consistent with a 6-membered chelate structure (**29B**) in which the phenyl group adopts an equatorial orientation.

The apparent absence of magnesium coordination in THF is consistent with the reduced diastereoselectivity usually observed in this solvent.[11] Similarly the improved selectivities in CH_2Cl_2 may be attributed to heightened coordination and chelation in this less basic medium. The lower isomer ratio observed with 2-methoxyphenyl Grignard reagent (75:25) may be a consequence of competing coordination of the metal with the *o*-methoxy group. The allylic rearrangement associated with the addition of allyl Grignard reagents to carbonyl compounds is usually explained by means of a cyclic transition state involving prior metal coordination with oxygen.[15] The lower stereoselectivities observed in addition of allyl Grignard reagent to nitrones **4** and **7** may be explained by competing reaction via a cyclic transition state which would presumably

(15) (a) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1–44. (b) Benkeser, R. A. *Synthesis* **1971**, 347. (c) DeWolfe, R. H.; Young, W. G. *Chem. Rev.* **1956**, *56*, 753–901.

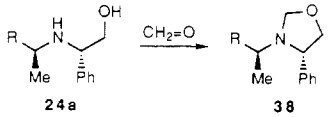
require breakdown of the 6-membered chelate structure.

A competition experiment was carried out to determine whether reaction via the proposed chelated transition state might occur with an accelerated rate. A 1:1 mixture of nitrone **4** and nonchelating nitrone **30** was allowed to react with a limited amount of methylmagnesium bromide in ether and in CH_2Cl_2. While addition to the nonchelating nitrone occurred somewhat faster in ether (**31a,b/8a,b** = 60:40 ratio), the reverse was observed in CH_2Cl_2 (33:67 ratio). In any case, the formation of comparable amounts of adducts from both **4** and **30** demonstrates that the high diastereoselectivity of Grignard additions to **4** is not the result of enhanced reactivity.



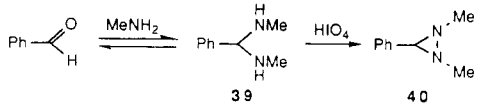
Asymmetric Synthesis of Amines. A four-step reaction sequence was developed in order to convert the hydroxylamine adducts to optically active amines (Scheme III). Addition of methylmagnesium bromide to optically active nitrones (*S*)-**4** and (*S*)-**7** afforded *S,S* adducts **8a** (91:9) and **19b** (91:9) as major products. The minor isomers (**8b** and **19a**) were not separated and were carried through all subsequent reactions. Lithium–ammonia reduction of the corresponding carbonates (**23a** and **32b**) afforded (*S,S*)-amino alcohols **24a** and **33b** in 50 and 63% yield, respectively. Oxidative cleavage of **24a** and **33b** with periodic acid in aqueous methanol containing 10 equiv of methylamine followed by hydrolysis with aqueous HCl liberated (*S*)-α-phenethylamine **34** (70%, 94% ee) and (*S*)-2-heptylamine **36** (68%, 82% ee). The enantiomeric purity of the amines was determined by HPLC analysis of their 3,5-dinitrobenzamides on a D-naphthylalanine column.[16] Evidently some enrichment of the major diastereomer occurred during the chromatographic purification of **23a** and/or **24a**.

The periodic acid cleavages of amino alcohols **24a** and **33b** were conducted in the presence of 10 equiv of methylamine in order to scavenge formaldehyde liberated in the oxidative cleavage. In the absence of methylamine, formaldehyde reacted competitively with **24a** to give oxazolidine **38** as a major product (oxazolidine/imine ratio ≅ 2:1) which was stable to the reaction conditions.



The oxidative cleavage of **33b** in the presence of methylamine gave rise to a somewhat volatile byproduct identified as 1,2-dimethyl-3-phenyldiaziridine (**40**) in 48% yield. The initial structure assignment based upon ^1H NMR and mass spectral data as well as elemental analysis was confirmed by comparison of ^1H NMR spectral data with the literature values for this known compound.[17]

Diaziridine **40** was also prepared by reaction of methylamine, periodic acid, and benzaldeyde in aqueous methanol. The formation of the diaziridine presumably occurs by oxidative cyclization of an aminal intermediate (**39**).



Conclusion

The high stereoselectivity associated with the addition of Grignard reagents to nitrones bearing *N*-(α-phenyl-β-alkoxyethyl) can be utilized for enantioselective synthesis of amines. The configuration of the predominant diastereomer formed in the initial Grignard addition can be predicted by consideration of magnesium-chelated intermediates and transition states. Overall yields of 33–39% of enantiomerically enriched amines (*S*)-**34** and (*S*)-**36** were achieved in five-steps from nitrones (*S*)-**4** and (*S*)-**7**, albeit with destruction of the stereogenic auxiliary group.

Experimental Section[18]

(−)-(*S*)-2-Amino-2-phenylethanol was prepared according to the procedure of Meyers.[19] A suspension of 9.91 g (65.5 mmol) of (*S*)-phenylglycine in 50 mL of methanol was stirred and cooled at 0 °C as 12 mL of thionyl chloride was added dropwise over 15 min. The white suspension was warmed to room temperature. After 3 h the solid had dissolved and the solution was stirred for another 7 h. Concentration on a rotatory evaporator gave a white solid which was washed with 80 mL of ether and dried under reduced pressure to afford 13.1 g (99%) of phenylglycine methyl ester hydrochloride.

A solution of 11.8 g (0.31 mol) of sodium borohydride in 180 mL of 50% of aqueous ethanol was stirred and cooled at 0 °C as a solution of 13.11 g (0.065 mol) of the hydrochloride salt in 80 mL of 50% of aqueous ethanol was added dropwise. The resulting suspension was stirred at room temperature for 9 h, refluxed for 5.5 h, and stirred at room temperature for another 8 h. Two clear layers had formed in the flask. The top layer was decanted and evaporated to give an aqueous solution. The viscous bottom layer was extracted with ethanol (3 × 25 mL), and the ethanol extracts were combined and evaporated to give a wet oil. The aqueous solution from the top layer was combined with the wet oil and extracted with ethyl acetate (5 × 18 mL). The organic extracts were combined, washed with 10 mL of saturated sodium chloride, dried (Na_2SO_4), and concentrated to give 8.00 g of a white solid. Recrystallization from ethyl acetate–hexane afforded 7.07 g of white crystals: $[\alpha]^{25}_D$ −33.4° (*c* 0.76, 1 N HCl); mp 75.5–78 °C. Further recrystallization gave 0.36 g of a white crystalline solid: $[\alpha]^{25}_D$ −31.9° (*c* 0.78, 1 N HCl); mp 75–78 °C. The total yield was 7.43 g (83%). A larger scale run (70.4 g of the hydrochloride salt) carried out in the same way afforded 38 g (60%) of white crystals.

2-(Phenylmethoxy)-1-phenylethanamine (1) was prepared according to Meyers' procedure[20] using 3.86 g (28.1 mmol) of phenylglycinol **24**, 1.17 g (29.2 mmol) of potassium hydride, and 4.81 g (28.1 mmol) of benzyl bromide. Kugelrohr distillation at 165 °C (1.2 mm) gave 4.70 g (73%) of a slightly yellow liquid: IR (neat) 3380, 3086, 3063, 3029, 2855, 1954, 1877, 1603, 1495, 741, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.81 (s, 2 H, NH_2), 3.44 (t, 1 H, *J* = 8.8 Hz, OCH_AH_B), 3.66 (dd, 1 H, *J* = 3.8, 9.3 Hz, OCH_AH_B), 4.23 (dd, 1 H, *J* = 3.8, 9.0 Hz, NCH), 4.54 (s, 2 H, CH_2Ph), 7.3 (m, 10 H, 2 C_6H_5).

(±)- and (+)-(*S*)-2-(phenylmethoxy)-*N*-[(2-chlorobenzoyl)oxy]-1-phenylethanamine [(±)-2 and (*S*)-2] were prepared according to the procedure described previously.[11]

(16) Pirkle, W. H.; Pochapsky, T. C.; Mahler, G. S.; Corey, D. E.; Reno, D. S. *J. Org. Chem.* **1986**, *51*, 4991.

(17) Akiyama, T.; Kitamura, T.; Isida, T.; Kawanisi, M. *Chem. Lett.* **1974**, 185–186.

(18) For a description of the General Aspects see ref 11.

(19) (a) Meyers, A. I.; Williams, D. R.; Erickson, G. W.; White, S.; Druelinger, M. *J. Am. Chem. Soc.* **1981**, *103*, 3081–3087. (b) Seki, H.; Koga, K.; Matsuo, H.; Ohki, S.; Matsuo, I.; Yamada, S. *Chem. Pharm. Bull.* **1965**, *13*, 995.

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

Bis(2-chlorobenzoyl) peroxide prepared according to Blomquist's procedure[21] was used. Purification by flash chromatography (10% ethyl acetate in hexane) yielded 2.58 g (44%) of racemic hydroxylamino ester **2** as an oil. Purification of optically active (*S*)-**2** by flash chromatography (10% ethyl acetate in hexane) followed by recrystallization from petroleum ether yielded a crystalline solid: mp 59.5–60.5 °C; $[\alpha]^{25}_D$ +63.8° (*c* 1.01, $CHCl_3$); IR (neat) 3241, 3063, 3030, 2863, 1732, 1591, 1495, 746, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.73 (m, 2 H, $CHCH_2$), 4.53 (apparent t, 1 H, NCH), 4.59 (s, 2 H, $PhCH_2$), 7.18–7.60 (m, 14 H), 8.35 (br s, 1 H, NH). Anal. Calcd for $C_{22}H_{20}NO_3Cl$: C, 69.20; H, 5.28; N, 3.67. Found: C, 68.91; H, 5.08; N, 3.62.

(±)- and (+)-(*S*)-*N*-hydroxy-2-(phenylmethoxy)-1-phenylethanamine [(±)-3 and (*S*)-3] were prepared according to the procedure described previously.[11] Purification by flash chromatography (30% ethyl acetate in hexane) yielded 1.09 g (66%) of racemic hydroxylamine **3** as an oil. Optically active (*S*)-**3** was also obtained as an oil: yield, 1.72 g (87%); $[\alpha]^{25}_D$ +55.2° (*c* 0.71, $CHCl_3$); IR (neat) 3250, 3063, 3030, 2860, 1954, 1877, 1813, 1605, 1495, 1452, 738, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.6 (5-line m, 2 H, $CHCH_2$), 4.22 (dd, 1 H, *J* = 5.4, 7.6 Hz, $CHCH_2$), 4.50 (s, 2 H, CH_2Ph), 7.3 (m, 10 H, 2 C_6H_5). Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 74.19; H, 6.89; N, 5.87.

The following nitrones were prepared according to the general procedure described previously.[11]

(±)- and (−)-(*S*)-*N*-Benzylidene-2-(phenylmethoxy)-1-phenylethanamine *N*-Oxide [(±)-4 and (*S*)-4]. Recrystallization from hexane afforded 1.19 g (80%) of racemic nitrone **4** as a white crystalline solid. Purification of the mother liquor by flash chromatography (30% ethyl acetate in hexane) gave another 0.22 g (15%) of a white solid. The combined yield was 1.41 g (95%): mp 88–89.5 °C; IR (CCl_4) 3069, 3032, 2867, 1578, 1563, 1495, 1454, 772, 762, 698 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.82 (dd, 1 H, *J* = 3.9, 10.1 Hz, $NCHCH_AH_B$), 4.55 and 4.69 (AB q, 2 H, *J* = 12.1 Hz, CH_2Ph), 4.58 (t, 1 H, *J* = 10.9 Hz, $NCHCH_AH_B$), 5.14 (dd, 1 H, *J* = 3.8, 9.4 Hz, $NCHCH_2$), 7.25–7.6 and 8.2–8.3 (2 m, 14 H and 2 H, 3 C_6H_5 and $=CHCH_3$). Anal. Calcd for $C_{22}H_{21}NO_2$: C, 79.73; H, 6.39; N, 4.23. Found: C, 79.71; H, 6.33; N, 4.30.

Optically active (*S*)-**4** was prepared from (*S*)-**3** in the same way. Purification by flash chromatography (30% ethyl acetate in hexane) and recrystallization afforded 1.06 g (93%) of a white crystalline solid: mp 77.5–79.5 °C; $[\alpha]^{25}_D$ −30.5° (*c* 1.08, $CHCl_3$).

(−)-(*S*)-*N*-(4-Methoxybenzylidene)-2-(phenylmethoxy)-1-phenylethanamine *N*-oxide (5) was prepared from hydroxylamine (*S*)-**3** and *p*-anisaldehyde. Purification by flash chromatography afforded a white crystalline solid: yield, 0.17 g (70%); mp 116–117 °C; $[\alpha]^{25}_D$ −36.3° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3023, 2868, 1605, 1507, 1454, 1306, 1256, 1213, 1173, 1140, 1032, 930, 843 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.80–3.86 (dd, 1 H, *J* = 3.6, ~9.1 Hz, $CHCH_AH_BO$), 3.84 (s, 3 H, OCH_3), 4.54 (d, 1 H, *J* = 12.1 Hz, CH_AH_BPh), 4.57 (t, 1 H, *J* ~ 9.1 Hz, CH_AH_BO), 4.64 (d, 1 H, *J* = 12.1 Hz, CH_AH_BPh), 5.10 (dd, 1 H, *J* = 3.6, 9.1 Hz, $NCHCH_2$), 6.92 (d, 2 H, *J* = 8.9 Hz, *m*-H of C_6H_4), 7.26–7.37 (m, 7 H), 7.49–7.55 (m, 3 H), 8.26 (d, 2 H, *J* = 8.9 Hz, *o*-H of C_6H_4). Anal. Calcd for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88. Found: C, 76.46; H, 6.47; N, 3.89.

***N*-Ethylidene-2-(phenylmethoxy)-1-phenylethanamine *N*-Oxide (6).** Purification by flash chromatography (70% ethyl acetate in hexane) afforded 0.33 g (91%) of the nitrone as an oil: IR (neat) 3387, 3088, 3063, 3032, 2914, 2862, 1597, 1097, 741, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.99 (d, 3 H, *J* = 6.1 Hz, $CHCH_3$), 3.73 (dd, 1 H, *J* = 3.8, 10.0 Hz, $CHCH_AH_B$), 4.48 (t, 1 H, *J* = 9.7 Hz, $CHCH_AH_B$), 4.51 and 4.66 (AB q, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.95 (dd, 1 H, *J* = 3.4, 9.2 Hz, $NCHCH_2$), 6.91 (q, 1 H, *J* = 6.1 Hz, $CHCH_3$), 7.2–7.5 (m, 10 H, 2 C_6H_5). Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.59; H, 7.22; N, 5.30.

(±)- and (−)-(*S*)-*N*-Hexylidene-2-(phenylmethoxy)-1-phenylethanamine *N*-Oxide [(±)-7 and (*S*)-7]. Purification by flash chromatography (30–50% ethyl acetate in hexane) afforded 0.83 g (77%) of the racemic nitrone as an oil which, upon standing, crystallized to give a low-melting solid: mp 45–47 °C; IR (CCl_4) 3069, 3032, 2959, 2930, 2863, 1586, 1497, 1454, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.85 (t-like, 3 H, CH_2CH_3), 1.2–1.4 (m, 4 H, $(CH_2)_2CH_3$), 1.4–1.6 (m, 2 H, $CHCH_2CH_2$), 2.35–2.70 (m, 2 H, $CHCH_2CH_2$), 3.75 (dd, 1 H, *J* = 3.6, 10.2 Hz, $CHCH_AH_BO$), 4.48 (dd, 1 H, *J* = 9.2, 10.2 Hz, $CHCH_AH_BO$), 4.53 and 4.68 (AB q, 2 H, *J* = 12.1 Hz, CH_2Ph), 4.94 (dd, 1 H, *J* = 3.6, 9.2 Hz, NCH), 6.84 (t, 1 H, *J* = 6.9 Hz, $=CHCH_2$), 7.2–7.6 (m, 10 H, 2 C_6H_5). Anal. Calcd for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.49; H, 8.18; N, 4.28.

Optically active (*S*)-**7** was prepared from (*S*)-**3**. Purification by flash chromatography afforded 1.71 g (89%) of an oil: $[\alpha]^{25}_D$ −3.4° (*c* 1.21, $CHCl_3$).

(1*R,1′*R**)- and (1*R**,1′*S**)-*N*-[2′-(Phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-1-phenylethanamine (8a and 8b). A. From Nitrone 4.** A solution of 0.609 g (1.84 mmol) of nitrone **4** in 60 mL of ether was stirred at 25 °C as 0.93 mL (2.90 mmol) of 3.1 M methylmagnesium bromide in ether was added. The resulting white suspension was stirred for 30 min, and 15 mL of saturated ammonium chloride was added at 0 °C. The ether layer was separated from the aqueous layer, which was extracted with ether (2 × 20 mL). The combined ether layers were dried (K_2CO_3) and concentrated. Purification of the residue by flash chromatography (30% ethyl acetate in hexane) afforded 0.58 g (92%) of a 91:9 mixture of **8a:8b** as an oil: IR (neat) 3530, 3376, 1603, 1495, 742, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) for the less polar **8a** δ 1.35 (d, 3 H, *J* = 6.6 Hz, $CHCH_3$), 3.78 (dd, 1 H, *J* = 6.0, 9.6 Hz, CH_AH_BCH), 3.85 (q, 1 H, *J* = 6.6 Hz, $CHCH_3$), 4.08 (dd, 1 H, *J* = 6.1, 9.6 Hz, CH_AH_BCH), 4.18 (t, 1 H, *J* = 6.0 Hz, CHPh), 4.49 (AB q, 2 H, *J* = 12.5 Hz, CH_2Ph), 4.60 (s, 1 H, OH), 7.15–7.50 (m, 15 H, 3 C_6H_5). Anal. Calcd for $C_{23}H_{25}NO_2$: C, 79.51; H, 7.25; N, 4.03. Found: C, 79.47; H, 7.31; N, 3.99.

The following organometallic reactions of nitrones were performed according to the same procedure. The nitrone, solvent, temperature, purification method, yield, isomer ratio, and physical state are given in abbreviated form.

B. From nitrone 6: ether, 0 °C; flash chromatography (23% ethyl acetate in hexane); 0.28 g (58%) of a 9:91 mixture of **8a:8b** as an oil; IR (neat) 3533, 3360, 1603, 1493, 739, 699 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) for the more polar **8b** δ 1.44 (d, 3 H, *J* = 6.7 Hz, $CHCH_3$), 3.68 (dd, 1 H, *J* = 5.0, 9.6 Hz, $CHCH_AH_B$), 3.75 (q, 1 H, *J* = 6.7 Hz, $CHCH_3$), 3.90 (dd, 1 H, *J* = 5.0, 6.9 Hz, PhCH), 4.04 (dd, 1 H, *J* = 9.6, 6.9 Hz, $CHCH_AH_B$), 4.45 (s, 2 H, CH_2Ph), 4.98 (s, 1 H, OH), 7.15–7.5 (m, 15 H, 3 C_6H_5). The ratios of **8a:8b** were determined by integrating the two doublets at δ 1.35 (**8a**) and 1.44 (**8b**).

(1*S*,1′*S*)- and (1*R*,1′*S*)-*N*-[2′-(phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-1-phenyl-1-propanamine (9a and 9b): ethylmagnesium bromide in ether, 0 °C for 20 min; flash chromatography (10% ethyl acetate in hexane); 56 mg (74%) of a 91:9 mixture of **9a:9b** as an oil; IR (neat) 3540, 3420, 3029, 2959, 2870, 1952, 1883, 1808, 1601, 1493, 1364, 1100, 1028, 752, 698 cm^{-1}. Hydroxylamine **9a**: ^1H NMR ($CDCl_3$, 300 MHz) δ 0.64 (t, 3 H, *J* = 7.4 Hz, CH_3), 1.76 and 2.05 (2 m, 2 H, CH_2H_3), 3.70 (dd, 1 H, *J* = 4.1, 9.7 Hz, $CHCH_2CH_3$), 3.80 (dd, 1 H, *J* = 5.5, 9.5 Hz, $CHCH_AH_BO$), 4.08 (dd, 1 H, *J* = 6.0, 9.5 Hz, $CHCH_AH_BO$), 4.15 (t, 1 H, *J* = 5.8 Hz, $CHCH_2$), 4.47 and 4.52 (AB q, 1 H, *J* = 12.4 Hz, CH_2Ph), 4.55 (br s, 1 H, OH), 7.0–7.45 (m, 15 H, 3 C_6H_5). Hydroxylamine **9b**: ^1H NMR ($CDCl_3$, 300 MHz) δ 3.42 (dd, 1 H, *J* = 5.3, 9.0 Hz, $CHCH_AH_BO$), 3.96 (dd, 1 H, *J* = 6.5, 9.6 Hz, $CHCH_AH_BO$). Anal. Calcd for $C_{24}H_{27}NO_2$: C, 79.74; H, 7.53; N, 3.89. Found: C, 79.64; H, 7.59; N, 3.95.

(1*S*,1′*S*)- and (1*R*,1′*S*)-*N*-[2′-(phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-2-methyl-1-phenyl-1-propanamine (10a and 10b): isopropylmagnesium chloride in ether, 0 °C for 30 min; flash chromatography (5% ethyl acetate in hexane); 67 mg (30%) of **10a** as an oil and 3 mg (1.3%) of **10b** as an oil. Hydroxylamine **10a**: IR (neat) 3530, 3391, 3063, 3029, 2965, 2874, 1952, 1885, 1813, 1603, 1493, 1364, 1028, 741, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.75 and 0.91 (2 d, 6 H, *J* = 6.8 and 6.7 Hz, 2 CH_3), 2.40 (6-line, 1 H, *J* = 6.7 Hz, $CHCH_3$), 3.67 (d, 1 H, *J* = 7.0 Hz, NCHCH), 3.73 and 4.02 (2 m, 1 H and 2 H, $CHCH_2O$), 4.29 (s, 1 H, OH), 4.46 (s, 2 H, CH_2Ph), 7.2–7.45 (m, 15 H, $3C_6H_5$). Anal. Calcd for $C_{25}H_{29}NO_2$: C, 79.96; H, 7.78; N, 3.73. Found: C, 79.69; H, 8.00; N, 4.08. Hydroxylamine **10b**: ^1H NMR ($CDCl_3$,

(21) Blomquist, A. T.; Buselli, A. J. *J. Am. Chem. Soc.* **1951**, *73*, 3883–3888.

(22) Helferich, B.; Portz, W. *Chem. Ber.* **1953**, *86*, 1034.

300 MHz) δ 0.60 and 1.01 (2 d, 6 H, J = 6.7 and 6.5 Hz, 2 CH_3), 2.42 (6-line, 1 H, CHCH$_3$), 3.16 (d, 1 H, J = 8.4 Hz, NCHCH), 3.70 (3-line, 2 H), 3.9 (m, 1 H), 4.39 and 4.43 (AB q, 2 H, J = 12.3 Hz, CH_2Ph).

(1*S*,1′*S*)- and (1*R*,1′*S*)-*N*-[2′-(phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-2,2-dimethyl-1-phenyl-1-propanamine (11a and 11b): *tert*-butylmagnesium chloride in ether, 25 °C for 1.5 h; flash chromatography (2.5% ethyl acetate in hexane); 74 mg (32%) of **11a** as an oil and 4 mg (2%) of **11b** as an oil. Hydroxylamine **11a**: IR (neat) 3540, 3061, 2953, 2865, 1952, 1881, 1811, 1603, 1493, 1478, 1453, 1393, 1362, 1101, 739, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.01 (s, 9 H, 3 CH_3), 3.56 (dd, 1 H, J = 4.6, 10.2 Hz, CHCH$_A$H$_B$O), 3.71 (dd, 1 H, J = 5.7, 10.2 Hz, CHCH_AH$_B$O), 3.78 (s, 1 H, NCHC), 3.89 (t, 1 H, J = 5.1 Hz, CHCH$_2$O), 4.25 (s, 1 H, OH), 4.32 and 4.36 (AB q, 1 H, J = 12.1 Hz, CH_2Ph), 7.2–7.43 (m, 15 H, 3 C_6H_5). Anal. Calcd for $C_{26}H_{31}NO_2$: C, 80.17; H, 8.02; N, 3.60. Found: C, 80.25; H, 7.74; N, 3.49. Hydroxylamine **11b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.94 (s, 9 H, 3 CH_3), 3.19 (s, 1 H, NCHC), 3.64 (t, 1 H, J = 4.9 Hz, CHCH$_2$O), 3.73 (dd, 1 H, J = 5.3, 9.5 Hz, CHCH$_A$H$_B$O), 3.84 (dd, 1 H, J = 4.9, 9.5 Hz, CHCH_AH$_B$O), 4.35 and 4.43 (AB q, 2 H, J = 12.2 Hz, CH_2Ph), 4.66 (s, 1 H, OH), 7.1–7.4 (m, 15 H, 3 C_6H_5).

(1*S*,1′*S*)- and (1*R*,1′*S*)-*N*-[2′-(phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-1,2-diphenylethanamine (12a and 12b): benzylmagnesium chloride in ether, 0 °C for 20 min; flash chromatography (20% ethyl acetate in hexane); 99 mg (97%) of a 89:11 mixture of **12a**:**12b** as an oil; IR (neat) 3527, 3397, 3061, 3027, 2928, 2866, 1952, 1881, 1800, 1602, 1495, 1453, 1362, 1307, 1204, 1100, 1029, 763, 744, 697 cm^{-1}. Anal. Calcd for $C_{29}H_{29}NO_2$: C, 82.24; H, 6.90; N, 3.31. Found: C, 82.25; H, 6.82; N, 3.34. Major product (**12a**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.97 (dd, 1 H, J = 9.8, 13.1 Hz, CHCH$_A$H$_B$Ph), 3.47 (dd, 1 H, J = 4.5, 13.1 Hz, CHCH_AH$_B$Ph), 3.78 (dd, 1 H, J = 5.6, 9.9 Hz, CHCH$_A$H$_B$O), 4.04 (dd, 1 H, J = 6.0, 9.9 Hz, CHCH_AH$_B$O), 4.10 (dd, 1 H, J = 4.6, 9.8 Hz, CHCH$_2$Ph), 4.22 (t, 1 H, J = 5.7 Hz, CHCH$_2$O), 4.44 and 4.47 (AB q, 2 H, OCH_2Ph), 6.8 (m, 2 H), 7.05–7.5 (m, Ar-H). Minor product (**12b**): ^{1}H NMR ($CDCl_3$) δ 3.63 (dd, 1 H, J = 5.1, 9.6 Hz), 3.83 (dd, 1 H, J = 5.2, 11.6 Hz), 3.94 (dd, 1 H, J = 6.4, 9.6 Hz).

(1*S*,1′*S*)- and (1*R*,1′*S*)-*N*-[2′-(phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-1-phenyl-2-propen-1-amine (13a and 13b): vinylmagnesium bromide in ether, 25 °C for 30 min; flash chromatography (10% ethyl acetate in hexane); 90 mg (83%) of a 90:10 mixture of **13a**:**13b** as an oil; IR (neat) 3530, 3414, 3063, 3030, 2978, 2865, 1954, 1879, 1813, 1638, 1586, 1493, 1453, 1362, 1098, 739, 700 cm^{-1}. Major product (**13a**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.80 (dd, 1 H, J = 5.9, 9.8 Hz, CHCH$_A$H$_B$O), 4.07 (dd, 1 H, J = 6.1, 9.8 Hz, CHCH_AH$_B$O), 4.19–4.27 (5-line, 2 H, CHNCH), 4.48 and 4.52 (AB q, 2 H, J = 12.2 Hz, CH_2Ph), 4.63 s, 1 H, OH), 5.01 dd, 1 H, J = 1.6, 17.2 Hz, CH=CH$_t$H$_c$), 5.27 (dd, 1 H, J = 1.6, 10.3 Hz, CH=CH$_t$H$_c$), 6.12–6.24 (7-line, 1 H, CH=CH$_2$), 7.2–7.5 (m, 15 H, 3 C_6H_5). Minor product (**13b**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.70 (dd, 1 H, J = 4.2, 8.7 Hz, CHCH$_A$H$_B$O), 4.03 (dd, 1 H, buried in the peaks of the major product). The ^{1}H NMR spectrum of the sample showed that it was about 98% pure. HRMS calcd for $C_{24}H_{25}NO_2$ 359.188 516 4, found: 359.187 514 4. The ratio of the two diastereomers was determined by comparison of the peaks at δ 3.80 (**13a**) and 3.70 (**13b**).

(1*S*,1′*S*)- and (1*R*,1′*S*)-*N*-[2′-(phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-1-phenyl-3-buten-1-amine (14a and 14b): allylmagnesium bromide in ether, 0 °C for 30 min; flash chromatography (9% ethyl acetate in hexane); 97 mg (87%) of a 78:22 mixture of **14a**:**14b** as an oil; IR (neat) 3528, 3393, 3063, 3029, 2922, 2863, 1952, 1883, 1813, 1755, 1640, 1603, 1584, 1493, 1453, 845, 746, 700 cm^{-1}. Anal. Calcd for $C_{25}H_{27}NO_2$: C, 80.40; H, 7.29; N, 3.75. Found: C, 80.22; H, 7.44; N, 3.81. Major product (**14a**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.42–2.62 and 2.72–2.90 (2 m, 2 H, CHCH_2CH), 3.77 (dd, 1 H, J = 5.6, 9.6 Hz, CHCH$_A$H$_B$O), 3.91 (dd, 1 H, J = 4.8, 9.2 Hz, NCHCH$_2$CH), 4.06 (dd, 1 H, J = 5.9, 9.6 Hz, CHCH_AH$_B$O), 4.11 (t, 1 H, J = 5.7 Hz, NCHCH$_2$O), 4.45 and 4.48 (AB q, 2 H, J = 12.4 Hz, CH_2Ph), 4.68 (s, 1 H, OH), 4.87 (3-line, 2 H, CH=CH_2), 5.5 (m, 1 H, CH=CH$_2$), 7.18–7.50 (m, 15 H, 3 C_6H_5). Minor product (**14b**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.46–2.63 and 2.75–2.92 (2 m, 2 H, CHCH_2CH), 3.64 (dd, 1 H, J = 5.5, 8.1 Hz, NCHCH$_2$CH), 3.68 (dd, 1 H, J = 5.3, 9.7 Hz, CHCH$_A$H$_B$O), 3.84 (t, 1 H, J = 5.9 Hz, NCHCH$_2$O), 3.98 (dd, 1 H, J = 6.4, 9.7 Hz, CHCH_AH$_B$O), 4.43 (s, 2 H, CH_2Ph), 4.88 (4-line, 2 H, CH=CH_2), 5.58 (m, 1 H, CH=CH$_2$), 7.2–7.5 (m, 15 H, 3 C_6H_5).

(1*S*,α*R*)- and (1*S*,α*S*)-*N*-hydroxy-*N*-[(1-naphthyl)-phenylmethyl]-2-(phenylmethoxy)-1-phenylethanamine (15a and 15b): 1-naphthylmagnesium bromide in ether, 0 °C for 1 h; flash chromatography (5% ethyl acetate in hexane); 68 mg (78%) of a >90:10 mixture of **15a**:**15b** as a solid: IR (CCl_4) 3580, 3063, 3032, 2955, 2865, 1946, 1644, 1495, 1454, 1100, 1030 cm^{-1}. Anal. Calcd for $C_{32}H_{29}NO_2$: C, 83.63; H, 6.36; N, 3.05. Found: C, 83.75; H, 6.33; N, 2.83. Major product (**15a**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.82 (dd, 1 H, J = 4.6, 9.1 Hz, CHCH$_A$H$_B$O), 4.25–4.35 (6-line, 2 H, CHCH$_A$H$_B$O), 4.56 (s, 2 H, CH_2Ph), 5.67 (s, 1 H, CHC$_{10}$H$_7$), 7.0–7.5 (m Ar-H), 7.8 (4-line, 2 H), 8.01 (d, 2 H, J = 7.4 Hz). Minor product (**15b**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.52 (s, 2 H, CH_2Ph), 5.0 (s, 1 H, CHC$_{10}$H$_7$). The ratio of the two isomers was determined by measuring the peak heights of the two singlets at δ 4.56 (**15a**) and 4.52 (**15b**).

(1*S*,α*R*)- and (1*S*,α*S*)-*N*-[(2-methoxyphenyl)phenylmethyl]-*N*-hydroxy-1-phenylethanamine (16a and 16b): 2-methoxyphenylmagnesium bromide (generated from *o*-bromoanisole and magnesium metal turnings) in ether, 0 °C for 10 min; flash chromatography (5% ethyl acetate in hexane); 80 mg (82%) of a 75:25 mixture of **16a**:**16b** as an oil; IR (CCl_4) 3580, 3033, 2938, 2837, 1946, 1878, 1807, 1601, 1588, 1491, 1454, 1246, 1100, 1030 cm^{-1}. Anal. Calcd for $C_{29}H_{29}NO_3$: C, 79.24; H, 6.65; N, 3.19. Found: C, 79.43; H, 6.76; N, 3.06. Major product (**16a**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.65 (s, 3 H, CH_3), 3.82 (dd, 1 H, J = 8.9, 12.8 Hz, CHCH$_A$H$_B$O), 4.23 (dd, 1 H, J = 7.0, 12.8 Hz, CHCH_AH$_B$O), 4.23 (t, 1 H, J = 7.1 Hz, CHCH$_2$O), 4.45 (s, 1 H, OH), 4.54 (s, 2 H, CH_2Ph), 5.36 (s, 1 H, CHC$_6$H$_4$), 6.80 (d, 1 H, J = 8.1 Hz), 6.96 (t, 1 H, J = 7.3 Hz), 7.1–7.4 (m, 14 H), 7.45 (d, 2 H, J = 7.3 Hz), 7.77 (d, 1 H, J = 1.0, 7.4 Hz). Minor product (**16b**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.63 (s, 3 H, CH_3), 3.8 (m, 1 H, CHCH$_A$H$_B$O), 4.2 (m, 2 H, CHCH$_A$H$_B$O), 4.52 (s, 2 H, CH_2Ph), 5.37 (s, 1 H, CH), 6.73 (d, 1 H, J = 8.2 Hz), 6.96 (m, 1 H), 7.1–7.5 (m, Ar-H), 7.78 (dd, 1 H, J = 1.1, 7.4 Hz).

(1*S*,α*R*)- and (1*S*,α*S*)-*N*-Hydroxy-*N*-[(4-methoxyphenyl)phenylmethyl]-2-(phenylmethoxy)-1-phenylethanamine (17a and 17b). A. From nitrone 5: ether, 25 °C; flash chromatography (4–10% ethyl acetate in hexane); 58 mg (83%) of a 2:98 mixture of **17a**:**17b** as an oil: IR (nCCl_4) 3578, 3065, 3031, 2934, 2863, 1948, 1885, 1809, 1610, 1511, 1495, 1453, 1302, 1246, 1173, 1101, 1040, 914 cm^{-1}; ^{1}H NMR for the major isomer **17b** ($CDCl_3$, 300 MHz) δ 3.73 (s, 3 H, OCH_3), 3.79 (dd, 1 H, J = 4.7, 9.1 Hz, CHCH$_A$H$_B$O), 4.17 (6 lines, 2 H, CHCH$_A$H$_B$O), 4.51 (s, 3 H, CH_2Ph and OH), 4.79 (s, 1 H, CH), 6.78 (d, 2 H, J = 8.7 Hz, H-C3 of C$_6$H$_4$) 7.2–7.4 (m, 17 H, 3 C_6H_5 and H-C2 of C$_6$H$_4$).

B. From nitrone 4: ether, 0 °C; flash chromatography (5% ethyl acetate in hexane); 88 mg (82%) of a 97:3 mixture of **17a**:**17b** as an oil.

(4-Methoxyphenyl)magnesium bromide was generated from *p*-bromoanisole and magnesium metal turnings in ether. The product mixture exhibited the same IR properties as those given in part A above: ^{1}H NMR for **17a** ($CDCl_3$, 300 MHz) δ 3.75–3.79 (m, 1 H, CHCH$_A$H$_B$O), 3.77 (s, 3 H, OCH_3), 4.10–4.19 (5 lines, 2 H, CHCH$_A$H$_B$O), 4.51 (s, 2 H, CH_2Ph), 4.54 (s, 1 H, OH), 4.74 (s, 1 H, CH), 6.83 (d, 2 H, J = 8.6 Hz, H-C3 of C$_6$H$_4$), 7.1–7.4 (m, 17 H, 3 C_6H_5 and H-C2 of C$_6$H$_4$). Anal. Calcd for $C_{29}H_{29}NO_3$: C, 79.54; H, 6.65; N, 3.19. Found: C, 79.30; H, 6.68; N, 3.18. The ratio of **17a**:**17b** was determined by the two singlets at δ 4.79 (**17b**) and 4.74 (**17a**).

(1′*R,2*R**)- and (1′*R**,2*R**)-*N*-[2′-(Phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-2-butanamine (18a and 18b). From nitrone 6**: ether, 0 °C; flash chromatography (15% ethyl acetate in hexane); 24 mg (67%) of a 92:8 mixture of **18a**:**18b** as an oil; IR (neat) 3542, 3389 (br), 3063, 3030, 2967, 2934, 2874, 1952, 1879, 1810, 1603, 1495, 1453, 1366, 1103, 1028, 922, 737, 700 cm^{-1}; ^{1}H NMR for the major isomer **18a** ($CDCl_3$, 200 MHz) δ 0.84 (t, 3 H, J = 7.5 Hz, CH_2CH_3), 1.09 (d, 3 H, J = 6.3 Hz, $CHCH_3$), 1.3–1.5 and 1.55–1.7 (2 m, 2 H, CH_2CH$_3$), 2.65–2.81 (m, 1 H, CHCH$_3$), 3.66 (dd, 1 H, J = 4.9, 9.9 Hz, CHCH$_A$H$_B$O), 3.88 (dd, 1 H, J = 6.3, 9.9 Hz, CHCH_AH$_B$O), 4.19 (dd, 1 H, J = 4.9, 6.3 Hz, CHPh), 4.48 (s, 2 H, CH_2Ph), 4.6 (br s, 1 H, OH), 7.18–7.45 (m, 10 H, 2 C$_6$H$_5$); ^{1}H NMR for the minor isomer **18b** ($CDCl_3$, 200 MHz) δ 0.95 (d, 3 H, J = 6.3 Hz, $CHCH_3$). The ratio of **18a**:**18b** was determined by integrating the two doublets at δ 0.95 (**18b**) and 1.09 (**18a**).

(1′*R,2*S**)- and (1′*R**,2*R**)-*N*-[2′-(Phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-2-heptanamine (19a and 19b). A. From nitrone 7**: dichloromethane, 0 °C; flash chromatography (10% ethyl acetate in hexane); 0.242 g (83%) of a 8:92 mixture of **19a:19b** as an oil; IR (neat) 3418, 3063, 3029, 2928, 2859, 1948, 1875, 1811, 1603, 1495, 1453, 1366, 1010, 737, 700 cm^{-1}. Anal. Calcd for $C_{22}H_{31}NO_2$: C, 77.38; H, 9.15; N, 4.10. Found: C, 77.47; H, 9.14; N, 4.13. Hydroxylamine **19b**: ^1H NMR ($CDCl_3$, 200 MHz) δ 0.84 (t, 3 H, J = 6.8 Hz, CH_2CH_3), 0.95 (d, 3 H, J = 6.4 Hz, $CHCH_3$), 1.1–1.4 and 1.5–1.8 (2 m, 7 H and 1 H, $(CH_2)_4$), 2.58 (6 lines, 1 H, J = 6.4 Hz, $CHCH_3$), 3.74 (dd, 1 H, J = 5.8, 9.6 Hz, $CHCH_AH_BO$), 3.97 (dd, 1 H, J = 5.8, 9.6 Hz, $CHCH_AH_BO$), 4.10 (t, 1 H, J = 5.8 Hz, $CHCH_2O$), 4.43 and 4.52 (AB q, 2 H, J = 12.2 Hz, CH_2Ph), 4.8 (br s, 1 H, OH), 7.1–7.5 (m, 10 H, $2C_6H_5$).

B. From nitrone 6: ether, 0 °C; flash chromatography (10% ethyl acetate in hexane); 22 mg (58%) of a 90:10 mixture of **19a:19b** as an oil. Hydroxylamine **19a**: ^1H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, 3 H, J = 6.3 Hz, CH_2CH_3), 1.09 (d, 3 H, J = 6.3 Hz, $CHCH_3$), 1.1–1.5 and 1.5–1.8 (2 m, 7 H and 1 H, $(CH_2)_4$), 2.81 (6 lines, 1 H, J = 6.3 Hz, $CHCH_3$), 3.66 (dd, 1 H, J = 5.1, 9.7 Hz, $CHCH_AH_BO$), 3.87 (dd, 1 H, J = 6.4, 9.7 Hz, $CHCH_AH_BO$), 4.19 (dd, 1 H, J = 5.1, 6.4 Hz, $CHCH_2O$), 4.47 (s, 2 H, CH_2Ph), 7.1–7.5 (m, 10 H, 2 C_6H_5).

(1′*S*,3*R*)- and (1′*S*,3*S*)-*N*-[2′-(phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-1-octen-3-amine (20a and 20b): nitrone (*S*)-**7**, vinylmagnesium bromide in ether, 25 °C for 30 min; flash chromatography (5% ethyl acetate in hexane); 22 mg (56%) of a 87:13 mixture of **20a:20b** as an oil; IR (CCl_4) 3380, 3065, 3030, 2954, 2930, 2857, 1948, 1873, 1810, 1603, 1495, 1454, 1363, 923, 737, 699 cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 77.97; H, 8.76; N, 4.00. Major product (**20a**): ^1H NMR ($CDCl_3$, 300 MHz) δ 0.83 (t, 3 H, J = 6.4 Hz, CH_3), 1.05–1.4 (m, 6 H, $(CH_2)_3CH_3$), 1.4–1.6 and 1.65–1.82 (2 m, 2 H, $NCHCH_2CH_2$), 2.90 (dt, 1 H, J = 6.5, 8.1 Hz, CH_2CH_2CHN), 3.76 (dd, 1 H, J = 5.4, 9.7 Hz, $CHCH_AH_BO$), 3.95 (dd, 1 H, J = 5.7, 9.7 Hz, $CHCH_AH_BO$), 4.10 (t, 1 H, J = 5.6 Hz, $CHCH_2O$), 4.45 and 4.50 (AB q, 2 H, J = 12.2 Hz, CH_2Ph), 4.82 (dd, 1 H, J = 2.0, 17.5 Hz, $CH{=}CH_tH_c$), 5.20 (dd, 1 H, J = 2.0, 10.3 Hz, $CH{=}CH_tH_c$), 5.8–5.93 (8-line, 1 H, $CH{=}CH_2$), 7.2–7.6 (m, 10 H, 2 C_6H_5). Minor product (**20b**): ^1H NMR ($CDCl_3$, 300 MHz) δ 0.87 (t, 3 H, J = 6.6 Hz, CH_3), 1.05–1.4 (m, 6 H, $(CH_2)_3CH_3$), 1.4–1.6 and 1.65–1.82 (2 m, 2 H, $NCHCH_2CH_2$), 3.28 (dt, 1 H, J = 5.0, 8.4 Hz, CH_2CH_2CHN), 3.69 (dd, 1 H, J = 5.3 10.0 Hz, $CHCH_AH_BO$), 3.90 (dd, 1 H, J = 6.0, 10.0 Hz, $CHCH_AH_BO$), 4.19 (t, 1 H, J = 5.6 Hz, $CHCH_2O$), 5.04 (dd, 1 H, J = 1.9, 17.4 Hz, $CH{=}CH_tH_c$).

(1′*S*,4*R*)- and (1′*S*,4*S*)-*N*-[2′-(phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-1-nonen-4-amine (21a and 21b): nitrone (*S*)-**7**, allylmagnesium bromide in ether, 0 °C for 30 min; flash chromatography (5% ethyl acetate in hexane); 22 mg (50%) of a 60:40 mixture of **21a:21b** as an oil; IR (neat) 3434, 3065, 3031, 2955, 2930, 2859, 1950, 1875, 1810, 1640, 1603, 1495, 1454, 1363, 1101, 909, 736, 699 cm^{-1}. Anal. Calcd for $C_{24}H_{33}NO_2$: C, 78.43; H, 9.05; N, 3.81. Found: C, 78.46; H, 9.00; N, 3.88. Major product (**21a**): ^1H NMR ($CDCl_3$, 300 MHz) δ 0.85 (t, 3 H, J = 7.1 Hz, CH_3), 1.0–1.8 (m, 8 H, $(CH_2)_4CH_3$), 2.08–2.22 (8-line, 1 H, CH_2CHCH_2), 2.38–2.5 and 2.5–2.6 (2 m, 2 H, ${=}CHCH_2$), 3.72 (dd, 1 H, J = 5.4, 9.7 Hz, $CHCH_AH_BO$), 3.93 (dd, 1 H, J = 5.8, 9.7 Hz, $CHCH_AH_BO$), 4.21 (t, 1 H, J = 5.5 Hz, $CHCH_2O$), 4.45 and 4.50 (AB q, 2 H, J = 12.3 Hz, CH_2Ph), 4.66 (br s, 1 H, OH), 4.8–5.02 (m, 2 H, $CH{=}CH_2$), 5.6–5.75 (m, 1 H, $CH{=}CH_2$), 7.2–7.4 (m, 10 H, 2 C_6H_5). Minor product (**21b**): ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3 H, J = 6.8 Hz, CH_3), 1.0–1.8 (m, 8 H, $(CH_2)_4CH_3$), 2.38–2.5 and 2.5–2.6 (2 m, 2 H, $={}CHCH_2$), 2.65–2.98 (5-line, 1 H, CH_2CHCH_2), 3.66 (dd, 1 H, J = 5.0, 9.8 Hz, $CHCH_AH_BO$), 3.88 (dd, 1 H, J = 6.1, 9.8 Hz, $CHCH_AH_BO$), 4.8–5.02 (m, 2 H, $CH{=}CH_2$), 5.75–5.90 (m, 1 H, $CH{=}CH_2$), 7.2–7.4 (m, 10 H, 2 C_6H_5).

***N*-[2′-(Phenylmethoxy)-1′-phenylethyl]-*N*-hydroxy-2,2-dimethyl-3-octanamine (22)**: nitrone (*S*)-**7**, *tert*-butylmagnesium chloride in ether, 25 °C for 1.5 h; 44 mg of a 90:10 mixture of the addition product (**22**) and nitrone **7**. Purification by flash chromatography (2.5% ethyl acetate in hexane) gave 22 mg of **22**, which was contaminated with an unknown impurity not detected in the crude product. The purified product (**22**) exhibited the following properties: IR (neat) 3434, 3064, 3030, 2953, 2864, 1945, 1872, 1784, 1494, 1466, 1453, 1362, 1097, 911, 698 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.84 (t, 3 H, J = 7.1 Hz, CH_2CH_3), 0.94 (s, 9 H, 3 CH_3), 1.0–1.4 (m, $(CH_2)_3CH_3$), 1.43–1.65 (m, 2 H, CH_2CH_2CH), 1.6–1.8 (m, 1 H), 2.66 (t-like, 1 H, $NCHCH_2CH_2$), 3.55 (dd, 1 H, J = 4.4, 10.3 Hz, $CHCH_AH_BO$), 3.79 (dd, 1 H, J = 6.8, 10.3 Hz, $CHCH_AH_BO$), 3.94 (br s, 1 H, OH), 4.15 (dd, 1 H, J = 4.4, 6.8 Hz, $CHCH_2O$), 4.41–4.48 (AB q, 2 H, J = 12.1 Hz, CH_2Ph), 7.2–7.4 (m, 10 H, 2 C_6H_5).

(1*R,1′*R**)- and (1*R**,1′*S**)-Methyl *N*-[2′-(Phenylmethoxy)-1′-phenylethyl]-*N*-(1-phenylethyl)amino Carbonate (23a and 23b)**. A solution of 0.58 g (1.66 mmol) of a 91:9 mixture of hydroxylamines **8a:8b**, 0.36 g (4.59 mmol) of pyridine, and 42 mg (0.34 mmol) of 4-(dimethylamino)pyridine in 24 mL of anhydrous dichloromethane was stirred at 25 °C as 0.3 mL (0.37 g, 3.88 mmol) of methyl chloroformate was added. The solution was refluxed for 30 min and diluted with 20 mL of dichloromethane. The dichloromethane solution was washed with water (2 × 10 mL) and 10 mL of saturated sodium chloride, dried (K_2CO_3), and concentrated. Purification of the residue by flash chromatography (30% ethyl acetate in hexane) afforded 0.66 g (97%) of a mixture of **23a** and **23b** as an oil. The mixture exhibited the following spectral properties: IR (neat) 3061, 3030, 2982, 2953, 1777, 1603, 1495, 1453, 763, 700 cm^{-1}. Carbonate **23a**: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.43 (d, 3 H, J = 6.7 Hz, $CHCH_3$), 3.47 (s, 3 H, OCH_3), 3.76 (br t, 1 H, J = 8.0 Hz), 4.09 (br t, 2 H), 4.3–4.5 (m, 3 H), 7.1–7.5 (m, 15 H, 3 C_6H_5). Anal. Calcd for $C_{25}H_{27}NO_4$: C, 74.05; H, 6.71; N, 3.45. Found: C, 73.90; H, 6.53; N, 3.53.

The reaction of a 9:91 mixture of hydroxylamines **8a:8b** with methyl chloroformate was carried out according to the procedure described above to give, after purification by flash chromatography (30% ethyl acetate in hexane), 0.12 g (71%), of a mixture of carbonate **23a** and **23b**. Carbonate **23b**: ^1H NMR ($CDCl_3$) δ 1.25–1.5 (br m, 3 H, $CHCH_3$), 3.5–3.7 (m, 1 H), 3.75 (s, 3 H, OCH_3), 3.8–4.1 (br m, 3 H), 4.2–4.45 (br s, 2 H, CH_2Ph), 7.05–7.50 (m, 15 H, 3 C_6H_5).

(1′*R,2*R**)- and (1′*R**,2*S**)-2-[(1-Phenylethyl)amino]-2-phenylethanol (24a and 24b)**. A solution of 0.63 g (1.55 mmol) of a 91:9 mixture of carbonates **23a** and **23b** in 50 mL of liquid ammonia and 11 mL of THF was stirred under reflux (−33 °C) as 64 mg (9.3 mmol) of lithium was added in two portions. After the blue color persisted for 1 min, it was discharged by addition of 3 mL of absolute ethanol and the solution was evaporated. The residue was dissolved in 15 mL of water and was extracted with ether (3 × 25 mL). The combined ether extracts were dried (K_2CO_3) and concentrated. Purification of the residue by flash chromatography (30–40% ethyl acetate in hexane) yielded 0.2 g (53%) of a 9:1 mixture of isomeric amino alcohols **24a:24b** as an oil. The mixture exhibited the following spectral properties: IR (neat) 3323, 3084, 3061, 3027, 2967, 2926, 2865, 1954, 1880, 1811, 1601, 1493, 1452, 760, 700 cm^{-1}. Amino alcohol **24a**: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.36 (d, 3 H, J = 6.8 Hz, $CHCH_3$), 2.38 (br s, 2 H, NH and OH), 3.49 (dd, 1 H, J = 8.0, 10.1 Hz, OCH_AH_B), 3.72 (dd, 1 H, J = 4.6, 10.1 Hz, OCH_AH_B), 3.75 (q, 1 H, J = 6.8 Hz, $CHCH_3$), 3.88 (dd, 1 H, J = 4.6, 8.0 Hz, $CHCH_2$), 7.1–7.5 (m, 10, 2 C_6H_5).

A 9:91 mixture of carbonates **23a:23b** was reduced according to the procedure described above to give 36 mg (49%) of a 1:9 mixture of amino alcohols **24a:24b**. The mixture exhibited the following spectral properties: IR (neat) 3320, 3061, 3027, 2924, 2867, 1954, 1880, 1811, 1603, 1493, 1453, 760, 700 cm^{-1}. Amino alcohol **24b**: ^1H NMR ($CDCl_3$, 300 MHz) δ 1.31 (d, 3 H, J = 6.0 Hz, $CHCH_3$), 2.35 (br s, 2 H, NH and OH), 3.48–3.60 (m, 3 H, $CHCH_2$), 3.63 (q, 1 H, J = 6 Hz, $CHCH_3$), 7.2–7.3 (m, 10 H, 2 C_6H_5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.05, 54.67, 61.33, 66.83, 126.80, 127.06, 127.19, 127.54, 128.51, 128.62, 140.58, 144.79. The identity of the major component (**24b**) was established by spectral comparisons with an authentic sample prepared by the literature procedure.[14]

(1′*R,1*R**)- and (1′*R**,1*S**)-*N*-(2′-Methoxy-1′-phenylethyl)-1-phenylethanamine (25a and 25b) and (1′*R**,1*R**)-*N*-(2′-Methoxy-1′-phenylethyl)-*N*-methyl-1-phenylethanamine (26)**. Methylation of a 9:1 mixture of amino alcohols **24a:24b** was carried out according to the procedure of Hogeveen and his co-workers[14] using potassium hydroxide as the base and dimethyl sulfoxide as the solvent. Purification by flash chromatography yielded two fractions: 87 mg (41%) of a 6:1 mixture of **25a:25b** and 52 mg (23%) of dimethylated product **26**. The

6:1 mixture of **25a:25b** exhibited the following spectral properties: IR (neat) 3330, 3085, 3061, 3026, 2965, 2924, 2885, 2824, 1948, 1888, 1811, 1601, 1493, 1453, 760, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) amine **25a** δ 1.36 (d, 3 H, J = 6.8 Hz, $CHCH_3$), 2.01 (s, 1 H, NH), 3.32 (s, 3 H, OCH_3), 3.49 (m, 2 H, $CHCH_2$), 3.72 (q, 1 H, J = 6.8 Hz, $CHCH_3$), 4.01 (dd, 1 H, J = 5.2, 6.9 Hz, $CHCH_2$), 7.0–7.36 (m, 10 H, 2 C_6H_5); ^{13}C NMR ($CDCl_3$, 75 MHz) amine **25a** δ 22.03, 54.57, 58.74, 59.82, 77.27, 126.50, 127.12, 127.53, 128.13, 128.17, 141.20, 145.94. The spectral data of amine **25b** were given previously.[11] N-Methylated amine **26**: IR (neat) 3085, 3061, 3029, 2975, 2926, 2874, 2806, 1950, 1887, 1811, 1601, 1493, 1451, 762 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.29 (d, 3 H, J = 6.7 Hz, $CHCH_3$), 2.17 (s, 3 H, NCH_3), 3.28 (s, 3 H, OCH_3), 3.67 (dd, 1 H, J = 6.0, 9.9 Hz, OCH_AH_B), 3.77–3.85 (4-line, 2 H, OCH_AH_B and OCH_2CH), 3.91 (q, 1 H, J = 6.7 Hz, $CHCH_3$), 7.18–7.43 (m, 10 H, 2 C_6H_5). The spectral data for **25a** and **25b** agree with the literature values.[14]

NMR Experiments with Magnesium Bromide Complex 29. The ^1H and ^{13}C NMR spectra of a solution of 23 mg of nitrone **4** in 0.5 mL of THF-d_8 gave the following spectral data: ^1H NMR (THF-d_8, 300 MHz) δ 3.67 (dd, 1 H, J = 3.5, 10.1 Hz, $CHCH_AH_BO$), 4.52 (dd, 1 H, J = 9.5, 10.1 Hz, $CHCH_AH_BO$), 4.56 and 4.60 (AB q, 2 H, J = 12.4 Hz, CH_2Ph), 5.30 (dd, 1 H, J = 3.5, 9.5 Hz, $CHCH_2O$), 7.15–7.40 (m, 11 H), 7.60 (m, 2 H), 7.78 (s, 1 H, =CH), 8.31 (m, 2 H); ^{13}C NMR (75 MHz, THF-d_8) δ 71.03, 73.88, 76.69, 127.97, 128.21, 128.57, 128.78, 128.95, 128.99, 129.13, 130.25, 132.68, 133.82, 137.06, 139.55.

The ^1H and ^{13}C NMR spectra data from a solution of 13 mg of nitrone **4** in 0.5 mL of CD_2Cl_2 are as follows: ^1H NMR (CD_2Cl_2, 300 MHz) δ 3.78 (dd, 1 H, J = 3.6, 10.2 Hz, $CHCH_AH_BO$), 4.54 (t, 1 H, J = 9.7 Hz, $CHCH_AH_BO$), 4.56 and 4.63 (AB q, 2 H, J = 12.0 Hz, CH_2Ph), 5.15 (dd, 1 H, J = 3.6, 9.4 Hz, $CHCH_2O$), 7.2–7.54 (m, 13 H), 7.58 (s, 1 H, =CH), 8.2–8.4 (m, 2 H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 70.13, 73.82; 79.62, 128.10, 128.03, 128.08, 128.21, 128.31, 128.41, 128.69, 128.86, 129.26, 130.41, 131.23, 134.29, 134.26, 135.50, 138.47.

The formation of complex **29** was carried out in a drybox to avoid exposure to the moisture. Solutions of 70 mg (0.21 mmol) of nitrone **4** in 1 mL of anhydrous ether and 54 mg (0.21 mmol) of magnesium bromide etherate in 1 mL of anhydrous ether were mixed and a solid precipitated. The precipitate was filtered and washed with 5 mL of ether to give 92 mg of **29** as a hygroscopic white solid. Anal. Calcd for $C_{22}H_{21}NO_2MgBr_2$: C, 51.25; H, 4.10; N, 2.72; Br, 31.00. Found: C, 51.61; H, 4.74; N, 2.52; Br, 27.27. The ether filtrate was evaporated to give 3 mg of nitrone **4**. The ^1H and ^{13}C NMR spectra of a solution of 10 mg of **29** in CD_2Cl_2 are as follows: ^1H NMR (300 MHz, CD_2Cl_2) δ 3.95 (dd, 1 H, J = 2.5, 12.6 Hz, $CHCH_AH_BO$), 4.83 (dd, 1 H, J = 9.0, 12.6 Hz, $CHCH_AH_BO$), 5.06 and 5.23 (2 d, 2 H, J = 13.1 Hz, CH_2Ph), 5.87 (br d, 1 H, J = 7.4 Hz, $CHCH_2O$), 7.2–7.55 (m, 13 H), 7.60 (s, 1 H, =CH), 8.23 (d, 2 H, J = 7.7 H); ^{13}C NMR (CD_2Cl_2, 75 MHz) δ 68.39, 73.82, 75.76, 131.34, 131.50, 132.72, 135.20, 136.15. The ^1H NMR spectra of complex **29** and nitrone **4** in THF-d_8 are the same.

Competitive Reactions of Nitrones 30 and 4 with Methylmagnesium Bromide. A solution of 100 mg (0.3 mmol) of nitrone **4** and 68 mg (0.3 mmol) of nitrone **30** in 20 mL of ether was stirred and cooled at −78 °C as 0.6 mL of methylmagnesium bromide (0.5 M in ether) was added. The solution was then warmed to room temperature with stirring, hydrolyzed with saturated ammonium chloride, and extracted with ether (2 × 10 mL). The ether layers were combined, dried (K_2CO_3), and concentrated to give 0.180 g of a crude oil. TLC analysis of the oil showed the presence of the starting nitrones and their reaction products. The ratio of hydroxylamine adducts **31a–b:8a–b** was determined to be 3:2 by ^1H NMR ($CDCl_3$, 200 MHz) analysis. Separation by flash chromatography (20–30% of ethyl acetate in hexane) afforded 43 mg of a 3:2 mixture of hydroxylamines **31a–b:8a–b**, 70 mg of nitrone **4**, and 43 mg of nitrone **30**. The same experiment was carried out in dichloromethane starting with 30 mg of nitrone **4** and 20 mg of nitrone **30**. After separation by flash chromatography, 10 mg of a 1:2 mixture of hydroxylamines **31a–b:8a–b**, 20 mg of nitrone **4**, and 17 mg of nitrone **30** were obtained.

Synthesis of Chiral Amines. Optically active phenylglycinol was used as the starting material for the synthesis of optically active amines **34** and **36**. The whole sequence was developed using racemic materials and essentially no difference existed between the racemic and optically active series.

(*S*)-1-Phenylethanamine (34). A mixture of carbonates (1′*S*,1*S*)-**23a** and (1′*S*,1*R*)-**23b** was obtained in 95% yield by reaction of 1.28 g (3.68 mmol) of (*S*)-nitrone **4** with methylmagnesium bromide and subsequent treatment with methyl chloroformate as described before (see procedures for the preparation of **8a,b** and **23a,b**). Lithium–ammonium reduction of this mixture in the same way described for the racemic material before afforded 0.4 g (50%) of a 94:6 mixture of amino alcohols (1′*S*,1*S*)-**24a**:(1′*S*,1*R*)-**24b** by NMR analysis. (See the procedure for the preparation of **24a,b**.)

A solution of 0.36 g (1.49 mmol) of the amino alcohols **24a,b** in 9 mL of methanol was stirred at room temperature as 1 mL of 40% aqueous methylamine, and then a solution of 0.89 g (3.90 mmol)e of periodic acid in 8 mL of water were added. After 3 h the solution was extracted with ether (3 × 10 mL). The ether extracts were combined and mixed with 3 mL of 4 N hydrochloric acid. The water–ether mixture was concentrated, stirred for 30 min to ensure complete hydrolysis of the imine, and concentrated further to remove methanol present in the solution. The remaining aqueous solution was washed with ether (3 × 10 mL) to remove benzaldehyde, neutralized with 6 N NaOH at 0 °C, and extracted with ether (3 × 10 mL). The ether extracts were combined, dried (K_2CO_3), and concentrated. Distillation of the remaining yellow oil in a Kugelrohr appratus at 75 °C (6 mm) afforded 0.13 g of amine **34** as a colorless liquid estimated to be 98% pure by ^1H NMR analysis: $[\alpha]^{25}_D$ −36.0° (*c* 1.26, benzene) [lit.[22] $[\alpha]$ −34.6° (*c* 4.5, benzene)]. The optical purity was determined to be 94% ee by HPLC analysis of the 3,5-dinitrobenzamide derivative of the amino using an analytical Pirkle covalent D-naphthylalanine HPLC column. The DNB derivative was prepared by mixing 10 mg of the amine and 40 mg of 3,5-dinitrobenzoyl chloride in 4 mL of dichloromethane and 0.5 mL of 15% of NaOH solution. The two-phase mixture was stirred for 15 min. The precipitate formed was filtered, and the dichloromethane layer in the filtrate was separated and dried (K_2CO_3). Evaporation gave benzamide **35** as a white solid, which was then analyzed with a Pirkle covalent D-naphthylalanine column (450 psi, 0.7 mL/min, 10% isopropyl alcohol). The *R* enantiomer is known to be the most retained isomer.[16] The ratio of the two enantiomers was 97:3 in favor the less retained *S* enantiomer (retention time: *S*, 41 min; *R*, 56 min). Amide **35**: IR ($CHCl_3$) 3434, 3347, 3100, 3015, 1671, 1547, 1346, 1080 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.65 (d, 3 H, J = 6.9 Hz, CH_3), 5.30 (quintet, 1 H, J = 7.1 Hz, CH), 6.93 (d, 1 H, J = 1.1 Hz, NH), 7.2–7.4 (m, 5 H, C_6H_5), 8.94 (d, 2 H, J = 1.7 Hz, *o*-H of C_6H_3), 9.12 (d, 1 H, J = 1.7 Hz, *p*-H of C_6H_3).

(1′*R,2*S**)- and (1′*R**,2*R**)-methyl *N*-[2′-(phenylmethoxy)-1′-phenylethyl]-*N*-(2-heptyl)amino carbonate (32a and 32b)** were prepared according to the procedure given for carbonates **23a,b**.

A. From a 9:91 Mixture of 19a:19b. Purification by flash chromatography (20% ethyl acetate in hexane) gave a mixture of **32a/32b** as an oil: yield, 1.66 g (97%); IR (neat) 3065, 3032, 2953, 2861, 1775, 1495, 1454, 1439, 1375, 1231, 1125, 1028, 735, 700 cm^{-1}. Carbonate **32b**: ^1H NMR ($CDCl_3$, 200 MHz) δ 0.84 (t, 3 H, J = 6.8 Hz, CH_2CH_3), 1.0–1.6 (m, 11 H, $CH_3CH(CH_2)_4$), 2.6–2.9 (br s, 1 H, $CHCH_3$), 3.63 (dd, 1 H, J = 5.5, 9.9 Hz, $CHCH_AH_BO$), 3.70 (s, 3 H, OCH_3), 4.00 (dd, 1 H, J = 6.6, 9.7 Hz, $CHCH_AH_BO$), 4.3–4.5 (m, 3 H, $CHCH_2O$ and CH_2Ph), 7.1–7.5 (m, 10 H, 2 C_6H_5). Anal. Calcd for $C_{24}H_{33}NO_4$: C, 72.15; H, 8.32; N, 3.51. Found: C, 72.24; H, 8.24; N, 3.48.

B. From a 82:18 Mixture of 19a:19b. Purification by flash chromatography (20% ethyl acetate in hexane) gave a mixture of **32a/32b** as an oil: yield, 0.14 g (90%). Carbonate **32a**: ^1H NMR ($CDCl_3$, 200 MHz) δ 0.87 (br t, 3 H, CH_2CH_3), 1.0–1.6 and 1.6–1.8 (2 m, 7 H and 1 H, $(CH_2)_4$), 1.11 (d, 3 H, J = 6.3 Hz, $CHCH_3$), 3.5–3.8 and 3.8–4.05 (2 m, 5 H and 1 H, $CHCH_3$, OCH_3, and $CHCH_2O$), 4.2–4.5 (m, 3 H, $CHCH_2O$ and CH_2Ph), 7.1–7.55 (m, 10 H, 2 C_6H_5).

(2*R,2′*S**)- and (2*R**,2′*R**)-2-(2′-heptylamino)-2-phenylethanol (33a and 33b)** were prepared according to the procedure given for alcohol **24a,b**.

A. From a 10:90 Mixture of 32a:32b. Purification by flash chromatography (30–70% ethyl acetate in hexane) gave 0.61 g (63%) of a 10:90 mixture of **33a:33b** as an oil: IR (neat) 3343, 3063, 3027, 2957, 2926, 2859, 1603, 1493, 1454, 1377, 1155, 1061, 758, 700 cm^{-1}. Amino alcohol **33b**: ^1H NMR ($CDCl_3$, 200 MHz) δ 0.85 (t, 3 H, J = 6.7 Hz, CH_2CH_3), 1.02 (d, 3 H, J = 6.0 Hz, $CHCH_3$), 1.1–1.5 (m, 8 H, $(CH_2)_4$), 2.0–2.5 (br s, 2 H, NH and OH), 2.53 (6-line, 1 H, J = 6.0 Hz, $CHCH_3$), 3.49 (dd, 1 H, J = 8.5, 10.7 Hz, $CHCH_AH_BO$), 3.68 (dd, 1 H, J = 4.4, 10.7 Hz, $CHCH_AH_BO$), 3.89 (dd, 1 H, J = 4.4, 8.5 Hz, $CHCH_2O$), 7.2–7.5 (m, 5 H, C_6H_5).

B. From a 82:18 Mixture of 32a:32b. Purification by flash chromatography (30–70% ethyl acetate in hexane) gave 38 mg (50%) of a mixture of **33a:33b** as an oil. The mixture provided the following ^1H NMR data for **33a** as follows: ($CDCl_3$, 300 MHz) δ 0.87 (t, 3 H, J = 6.9 Hz, CH_2CH_3), 0.97 (d, 3 H, J = 6.5 Hz, $CHCH_3$), 1.1–1.4 (m 8 H, $(CH_2)_4$), 1.8–2.6 (br s, 2 H, NH and OH), 2.8 (m, 1 H, J = 6.0 Hz, $CHCH_3$), 3.45 (dd, 1 H, J = 8.5, 10.4 Hz, $CHCH_AH_BO$), 3.66 (dd, 1 H, J = 4.6, 10.4 Hz, $CHCH_AH_BO$), 3.85 (dd, 1 H, J = 4.6, 8.5 Hz, $CHCH_2O$), 7.2–7.4 (m, 5 H, C_6H_5).

(*S*)-*N*-(2-Heptyl)-3,5-dinitrobenzamide (37). Optically active (*S*)-**7** was used for the preparation of amide **37** as described below. Reaction of 1.48 g (4.55 mmol) of nitrone (*S*)-**7** with methylmagnesium bromide according to the general procedure provided a 9:91 mixture of hydroxylamines **19a:19b**, which was converted to a mixture of amino alcohols **33a,b** in 57% overall yield (0.61 g) via carbonates **32a,b**. (See procedures for **19**, **32**, and **33**.) A solution of 0.25 g (1.06 mmol) of amino alcohols **33a,b** in 8 mL of methanol was stirred at room temperature as 0.5 mL of 40% aqueous methylamine and a solution of 0.5 g (2.46 mmol) of periodic acid in 5 mL of water were added. The solution was stirred for 2.5 h at room temperature and extracted with ether (2 × 15 mL and 10 mL). The aqueous layer containing iodate was discarded, and the ether layers were combined and extracted twice with 2 N hydrochloric acid (10 and 4 mL). The ether layer was discarded. The acidic aqueous extracts were combined, refluxed at 62 °C for 1.5 h, concentrated with a rotatory evaporator to remove methanol, washed with ether (3 × 10 mL), and concentrated again to remove a trace of methanol. Methanol was removed as much as possible because it would react with 3,5-dinitrobenzoyl chloride to form benzoate, which might interfere with the purification of dinitrobenzamide **37** later. The remaining acidic aqueous solution was washed with 5 mL of ether to remove a trace of benzaldehyde, cooled to 0 °C, neutralized with 6 N NaOH at 0 °C to pH 10, and extracted with dichloromethane twice (10 and 6 mL). The organic extracts were combined and mixed with 0.57 g (2.49 mmol) of 3,5-dinitrobenzoyl chloride and 4 mL of 15% of NaOH solution. The heterogeneous mixture was stirred for 2 h. The dichloromethane layer was separated, washed with 6 mL of water and 6 mL of 1 N hydrochloric acid, dried ($MgSO_4$), and concentrated to give 0.45 g of a crude solid. Purification by flash chromatography (15% ethyl acetate in hexane) afforded 0.223 g (68%) of the optically enriched benzamide **37** as a white solid; $[\alpha]^{25}_D$ +21.5° (*c* 0.72, $CHCl_3$). The absolute configuration and optical purity of the benzamide was determined to be 82% ee in favor of the *S* enantiomer by HPLC analysis of the amide using a preparative Pirkle covalent D-naphthylalanine column (400 psi, 2.0 mL/min, 10% isopropyl alcohol in hexane, t_R: *R*, 43 min; *S*, 50 min). The *S* enantiomer is the most retained isomer according to the chiral recognition model.[16] The spectral properties of this amide are as follows: IR ($CHCl_3$) 3434, 3337, 3100, 2932, 1671, 1547, 1346, 1227, 1078 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, 3 H, J = 6.5 Hz, CH_2CH_3), 1.30 (d, 3 H, J = 6.6 Hz, $CHCH_3$), 1.25–1.34 (m, 6 H, $(CH_2)_3CH_3$), 1.38–1.65 (m, 2 H, $CHCH_2$), 4.24 (7-line, 1 H, NCH), 6.30 (br d, 1 H, NH), 9.15 (d, 2 H, J = 1.9 Hz, *o*-H of C_6H_3), 9.16 (t, 1 H, J = 1.9 Hz, *p*-H of C_6H_3).

1,2-Dimethyl-3-phenyldiaziridine (40). A solution of 0.37 g (1.56 mmol) of amino alcohol **33a,b** in 5 mL of methanol was stirred at 25 °C as 1 mL of 40% of methylamine solution and a solution of 0.75 g (3.29 mmol) of periodic acid in 4 mL of water were added sequentially. After stirring for 1 h, another 0.56 g (2.46 mmol) of periodic acid was added to the reaction solution, which was then stirred overnight. The aqueous methanol solution was extracted with ether (3 × 10 mL), and the ether extracts were combined, dried (K_2CO_3), and distilled to remove solvent. The remaining solution was then distilled in a Kugelrohr apparatus at 100 °C (30 mm) to give, after treatment with HCl, 112 mg of the hydrochloride salt of 2-heptylamine. The pot residue was purified by flash chromatography (10–30% of ethyl acetate in hexane) to afford 111 mg (48%) of a colorless liquid: IR (neat) 3088, 3064, 2972, 2925, 2862, 2769, 1497, 1453, 1399, 1312, 1077, 750, 368 cm^{-1}; ^1H NMR $CDCl_3$, 300 MHz) δ 2.15 (s, 3 H, CH_3), 2.62 (s, 3 H, CH_3), 3.60 (s, 1 H, CH), 7.35 (m, 5 H, C_6H_5); mass *m/e* (rel int) 148 (M^+, 11), 147 (100), 133 (5), 132 (13), 118 (40), 91 (18), 77 (18). Anal. Calcd for $C_9H_{12}N_2$: C, 72.94; H, 8.16; N, 18.90. Found: C, 72.91; H, 8.22; N, 19.03. The ^1H NMR spectral data agree with the literature values.[17]

Diaziridine **40** was also prepared by reaction of benzaldehyde with methylamine and periodic acid. A solution of 0.318 g (3.00 mmol) of benzaldehyde in 7 mL of methanol was stirred at 25 °C as 1 mL of 40% aqueous methylamine solution and 0.686 g (3.01 mmol) of periodic acid in 7 mL of water were added in succession. The solution was stirred at 25 °C for another 19 h and extracted with ether (3 × 15 mL). The ether layers were combined, dried (K_2CO_3), and concentrated to give, after chromatographic purification (10, 30, and 50% of ethyl acetate in hexane), 0.175 g (39%) of diaziridine **40**.

Acknowledgment. This research was supported in part by a grant from the National Institutes of Health (CA 20436).

Supplementary Material Available: Copies of ^1H NMR spectra of compounds **13a,b** and **33a,b** (4 pages). Ordering information is given on any current masthead page.