mL of dry CH_2Cl_2 (distilled from CaH_2). Bromine (1.6 g, 0.01 mol) in 30 mL of CH_2Cl_2 was added dropwise at -78 °C over 45 min. The resulting orange solution was stirred for an additional 10 min and was warmed to room temperature. The solvent was removed to give a yellow powder. The crude product (4.5 g) was applied as a solid to the top of a silica gel column and eluted with cyclohexane. The product appeared as a white band in the translucent column while the colored impurities remained near the origin. The yield was 2.3 g (50%): mp 124-125 °C; ^1H NMR ($CDCl_3$), δ 2.46-2.52, 2.70-2.75, 3.21-3.26 (m, 4 H), 3.91-3.98, 4.28-4.35 (m, 2 H), 5.63-5.68, 6.17-6.26 (AA'BB', 4 H); TLC showed one spot at R_f = 0.32.

1,6-Dibromomethano[10]annulene (3).[14] In a 500-mL, two-necked, round-bottomed flask with an air condenser were dissolved 4.0 g (0.0087 mol) of the tetrabromo triene and 10.6 g (0.085 mol) of 1,5-diazobicyclo[4.3.0]non-5-ene in 170 mL of dry dimethylformamide (distilled over CaH_2 and stored under molecular sieves, 4 Å). The light yellow solution was magnetically stirred under N_2 at room temperature for 3 days. The resulting orange solution was poured into 100 mL of H_2O, and 100 mL of 3 N HCl was added. The mixture was extracted (5×) with ether, and the green-yellow ether layer was separated from the lower orange, cloudy aqueous layer. The combined ether layers were washed with H_2O and dried ($MgSO_4$), and the solvent was removed under vacuum. The crude product was purified on a silica gel column by elution with hexane. Crystallization from ether gave fluffy yellow crystals: 0.5 g (20%); mp 98 °C; ^1H NMR ($CDCl_3$) δ 6.76-6.94 (m, unresolved pattern); UV (cyclohexane) 387 (vw), 285 (w), 257 (s), 222 (m) nm; IR (KBr) 1559, 1311, 1238, 1181, 823, 757, 569, 564, 462, 417 cm^{-1}.

Phenyl(tribromomethyl)mercury[19] was prepared in 60-75% yield, mp 119-120 °C (lit.[19] mp 118-120 °C), as white needles from hexane/$CHCl_3$ solvent.

Reaction of Annulene 3 with the Dienes. The reaction at 10 mol % of diene **2** with 1 mol % of annulene **3** is given as an example. A stock solution of 0.07 g (3.93×10^{-4} mol) of diene **2** and 4.30 g (5.51×10^{-2} mol) of benzene was placed in a 5-mL volumetric flask. Into a tube containing 2.4 mg of annulene **3** (7.85×10^{-6} mol) was quickly added 1 mL of stock solution and 1 mL of benzene. The tube was stoppered and placed in dry ice. The reaction mixture was degassed by four repetitions of pumping, thawing, and refreezing on a vacuum line at 0.05 mmHg. After the final degassing cycle, the tube was carefully sealed. Individual reaction tubes were marked and stored at dry ice temperature until an entire set had been prepared and sealed. The tubes were then immersed in a bath at 70 °C for 3 h. At that time the tubes were removed from the bath and stored in a dry ice bath for processing, which consisted of thawing the solution, opening the tube, and analyzing the raw material by GC gas chromatography. From each sample, the solvent was removed under vacuum, $CDCl_3$ was added, and the NMR integration was performed. The ratio was established from integration of characteristic protons on the three- and five-membered rings of the product. The overall yield ranged from 50 to 65% based on a GC analysis of volatile materials. The products from **2** were **4** [^1H NMR ($CDCl_3$) δ 0.90, 0.93, 1.09, 1.19 (four s, 12 H), 1.12 (s, 6 H), 1.75 (s, 2 H), 4.65, 5.13 (m, 2 H)] and **5** [^1H NMR ($CDCl_3$) δ 0.86 (s, 6 H), 0.95 (s, 12 H), 3.36 (s, 4 H)]. The products from **1** were **7** [^1H NMR ($CDCl_3$) δ 1.7-2.0 (m, 8 H), 2.24 (td, 1 H), 2.45 (dt, 1 H), 4.64, 4.94 (d, 2 H)] and **8** [^1H NMR ($CDCl_3$) δ1.7-2.0 (m, 8 H) 3.45 (s, 4 H)].[21]

(21) Since the completion of this paper, stereochemical evidence in favor of a concerted, one-step mechanism has been reported for 1,4-addition. Kraakman, P. A.; de Wolf, W. H.; Bickelhaupt, W. *J. Am. Chem. Soc.* **1989**, *111*, 8534-8535. Also see: Le, A. N.; Jones, M., Jr.; Bickelhaupt, F.; de Wolf, W. H. *Ibid.* **1989**, *111*, 8491-8493.

Diastereoselectivity of Organometallic Additions to Nitrones Bearing Stereogenic N-Substituents[1]

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The diastereoselectivity of organometallic additions to nitrones bearing stereogenic α-arylethyl, β-methoxyalkyl, and β-(silyloxy)alkyl substituents on nitrogen has been investigated. High and complementary diastereoselectivity (90-94%) was observed in the additions of Grignard reagents to nitrones (e.g. **22** and **23**) bearing the potentially chelating β-methoxyalkyl group. However, the opposite selectivity resulted from the reaction of methylmagnesium bromide with the corresponding silyl ether (**27**). The relative stereochemistry of selected hydroxylamine adducts was established by reduction of their phosphate and carbonate derivatives to known amines (**37a,b** and **39**), by periodate cleavage of a β-hydroxy hydroxylamine (**41b**), and by various correlations (Scheme II). The high facial diastereoselectivity observed with the *N*-(β-methoxyalkyl)nitrones is explained by a simple chelation model (Scheme III).

Diastereoselective addition of organometallic reagents to the C=N bond of imines and their derivatives offers an attractive approach for asymmetric synthesis of amines.[3] High asymmetric induction has been observed in organometallic additions to imines,[4,5] oximes,[6] and hydrazones[7-9] bearing hydroxy, alkoxy, or carbonyl substit-

(1) (a) Portions of this work were presented at the joint American Chemical Society-Canadian Institute of Chemistry meeting in Toronto, Ontario, June 7, 1988. (b) Taken in part from the Ph.D. Thesis of Z.-Y. Chang, University of Illinois, Urbana—Champaign, 1988.

(2) University of Illinois Fellow, 1984-1986.

(3) For reviews on organometallic additions to imines and their derivatives, see: (a) Volkmann, R. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I. Eds.; Pergamon Press: Oxford, 1990; Vol. 1, Schreiber, S. L., Ed. (b) Kleinman, E.; Volkmann, R. A. In *Ibid.*Vol. 2, Heathcock, C. H., Ed. We wish to thank Dr. Volkmann for preliminary copies of these reviews.

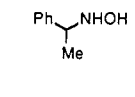
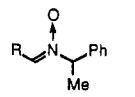
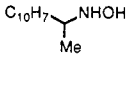
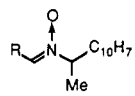
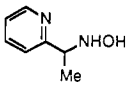
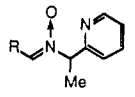
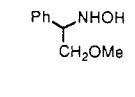
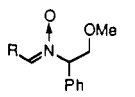
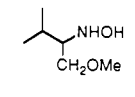
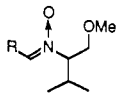
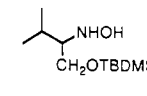
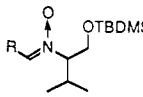
(4) (a) Takahashi, H.; Suzuki, Y.; Inagaki, H. *Chem. Pharm. Bull.* **1982**, *30*, 3160-3166. (b) Suzuki, Y.; Takahashi, H. *Ibid.* **1983**, *31*, 31-40 and 2895-2898. (c) Takahashi, H.; Suzuki, Y.; Hori, T. *Ibid.* **1983**, *31*, 2183-2191. (d) Takahashi, H.; Chida, Y.; Suzuki, T.; Yanaura, S.; Suzuki, Y.; Masuda, C. *Ibid.* **1983**, *31*, 1659-1665.

(5) (a) Fuganti, C.; Grasselli, P.; Pedrocchi-Fantoni, G. *J. Org. Chem.* **1983**, *48*, 909-910. (b) Davis, F. A.; Mancinelli, P. A. *Ibid.* **1977**, *42*, 398-399. (c) Emmert, P.; Meyer, J.; Stucki, C.; Schneebeli, J.; Obrecht, J.-P. *Tetrahedron Lett.* **1988**, *29*, 1265-1268.

(6) Hoffmann, R. W.; Eichler, G.; Endesfelder, A. *Justus Liebigs Ann. Chem.* **1983**, 2000.

0022-3263/90/1955-3464$02.50/0

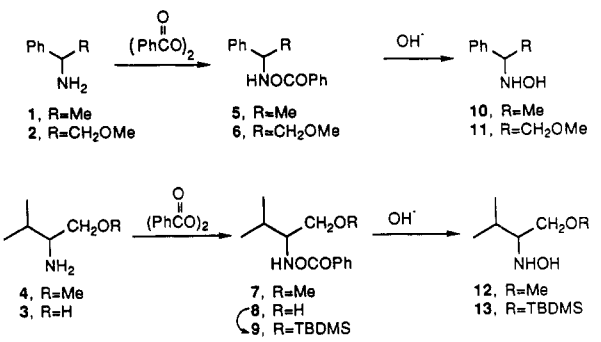
Table I. Preparation of Nitrones by Condensation of *N*-Alkylhydroxylamines with Benzaldehyde, Acetaldehyde, and Propionaldehyde

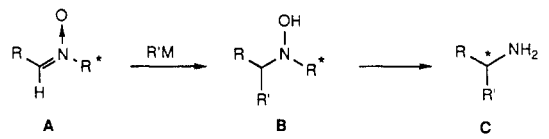
hydroxylamine	no.	nitrone	R	no.	yield, %
	10		Ph	16	86
			Me	17	74
	14		Ph	18	88
			Me	19	69
	15		Ph	20	74
			Me	21	48
	11		Ph	22	63
			Me	23	82
			Et	24	82
	12		Ph	25	84–91
			Me	26	45–67
	13		Ph	27	91
			Me	28	88

uents on the α carbon or on nitrogen, presumably owing to metal chelation in the transition state.[10] The use of organocerium reagents has extended substantially the scope and efficiency of additions to SAMP hydrazones.[9b] Chiral chromium tricarbonyl complexes of diaryl imines undergo Grignard reactions with a high degree of asymmetric induction.[11]

In contrast to the usually sluggish reactivity of imines, nitrones readily undergo addition of organometallic reagents and other carbon nucleophiles.[12-15] Although nitrones bearing stereogenic N-substituents have been employed in asymmetric synthesis via 1,3-dipolar cycloadditions to olefins,[16,17] the stereochemistry of their organometallic additions has not been investigated for this purpose. However, the high stereoselectivity reported for phosphite additions to carbohydrate-linked nitrones[17d,18] may be regarded as favorable precedent.

Scheme I





We report the results of a study on the diastereoselectivity of the reactions of Grignard and organolithium reagents with nitrones bearing stereogenic α-arylethyl and β-methoxyethyl groups on nitrogen. The high facial discrimination observed with *N*-(β-alkoxy)nitrones has lead

(7) (a) Takahashi, H.; Tomita, K.; Otomasu, H. *J. Chem. Soc., Chem. Commun.* **1979**, 668. (b) Takahashi, H.; Tomita, K.; Noguchi, H. *Chem. Pharm. Bull.* **1981**, *29*, 3387. (c) Takahashi, H.; Inagaki, H. *Ibid.* **1982**, *30*, 922–926. (d) Takahashi, H.; Suzuki, Y. *Ibid.* **1983**, *31*, 4295–4299.

(8) Claremon, D. A.; Lumma, P. K.; Phillips, B. T. *J. Am. Chem. Soc.* **1986**, *108*, 8265.

(9) (a) Enders, D.; Schubert, H.; Nübling, C. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1109–1110. (b) Denmark, S. E.; Weber, T.; Piotrowski, D. W. *J. Am. Chem. Soc.* **1987**, *109*, 2224–2225.

(10) For reviews addressing the chelation and chelation-controlled additions to α- or β-alkoxy compounds, see: (a) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556–569. (b) Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357–386. (c) Eliel, E. L. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Part A, pp 125–155.

(11) Solladie-Cavallo, A.; Tsamo, E. *J. Organomet. Chem.* **1979**, *172*, 165–169.

(12) For reviews on nitrone chemistry, see: (a) Rundel, W. In Houben-Weyl's Methoden der Organischen Chemie; Müller, E. Ed.; G. Thieme: Stuttgart, 1968; Vol. 10/4, pp 309–448. (b) Delpierre, G. R.; Lamchen, M. *Q. Rev.* **1965**, *19*, 329–348. (c) Hamer, J.; Macaluso, A. *Chem. Rev.* **1964**, *64*, 473–495. (d) Stamm, H. In C–N compounds. Zymalkowsky, F., Ed.; Vol. 6 of *Methodicum Chimicum*; Korte, F., Ed.; Academic Press: New York, 1975; pp 333–351. (e) Sandler, S. R.; Karo, W. *Organic Functional Group Preparations*; Academic Press: New York, 1972; Vol. 3, pp 351–376. (f) Breuer, E. In *The Chemistry of Amino, Nitroso and Nitro Compounds and their Derivatives*, Supplement F; Patai, S., Ed.; Wiley: New York, 1982; Part 1, Chapter 13.

(13) Lee, T. D.; Keana, J. F. W. *J. Org. Chem.* **1976**, *41*, 3237–3241.

(14) (a) Stamm, H.; Steud, H. *Tetrahedron* **1979**, *35*, 647–650. (b) Stamm, H.; Hoenicke, J. *Justus Liebigs Ann. Chem.* **1971**, *748*, 143–153. (c) Stamm, H.; Hoenicke, J. *Ibid.* **1971**, *749*, 146–152.

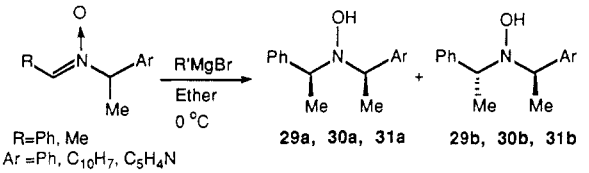
(15) Paetzold, P.; Schimmel, G. *Z. Naturforsch* **1980**, *35B*, 568–577.

(16) Tufariello, J. J. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; John Wiley and Sons, Inc.: New York, 1984; Vol. 2; pp 83–168.

(17) (a) Iida, H.; Kasahara, K.; Kibayashi, C. *J. Am. Chem. Soc.* **1986**, *108*, 4647–4648. (b) Kametani, T.; Nagahara, T.; Honda, T. *J. Org. Chem.* **1985**, *50*, 2327–2331. (c) Kametani, T.; Chu, S.-D.; Honda, T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1593–1597. (d) Bernet, B.; Krawczyk, E.; Vasella, A. *Helv. Chim. Acta* **1985**, *68*, 2299–2311. (e) DeShong, P.; Dicken, C. M.; Leginus, J. M.; Whittle, R. R. *J. Am. Chem. Soc.* **1984**, *106*, 5598–5602. (f) DeShong, P.; Leginus, J. M. *Ibid.* **1983**, *105*, 1686. (g) Tice, C. M.; Ganem, B. *J. Org. Chem.* **1983**, *48*, 5048. (h) Vasella, A.; Voeffray, R.; Pless, J.; Jugenin, R. *Helv. Chim. Acta* **1983**, *66*, 1241. (i) Vasella, A.; Voeffray, R. *Ibid.* **1982**, *65*, 1134, 1953. (j) Vasella, A.; Voeffray, R. *J. Chem. Soc., Chem. Commun.* **1981**, 97. (k) Wovkulich, P. M.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1981**, *103*, 3956. (l) Belzecki, C.; Panfil, I. *J. Org. Chem.* **1979**, *44*, 1212–1218. (m) Oppolzer, W.; Petrzilka, M. *Helv. Chim. Acta* **1978**, *61*, 2755. (n) Vasella, A. *Ibid.* **1977**, *60*, 426, 1273–1295.

(18) Huber, R.; Knierzinger, A.; Obrecht, J.-P.; Vasella, A. *Helv. Chim. Acta* **1985**, *68*, 1730–1747.

Table II. Addition of Grignard Reagents to *N*-(α-Arylethyl)nitrones 16–21



entry	nitrone	R'MgBr	product[a]	yield, %	isomer ratio
1	16	MeMgBr	29a,b	91	46:54
2	17	PhMgBr		92	46:54
3	18	MeMgBr	30a,b	71	42:58
4	19	PhMgBr		52	82:18
5	20	MeMgBr	31a,b	36	85:15
6	21	PhMgBr		39	48:52

[a] Relative stereochemistry of **30a,b** and **31a,b** tentatively assigned by ^{1}H NMR spectral correlations.

to the development of a new asymmetric synthesis of primary amines.[19]

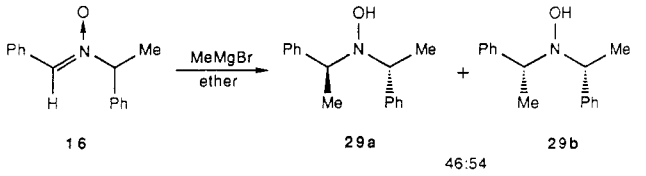
Preparation of *N*-Alkylhydroxylamines and Nitrones. The requisite chiral *N*-alkylhydroxylamines were prepared simply by N-oxygenation of primary amines with benzoyl peroxide[20] in tetrahydrofuran or benzene followed by hydrolysis of the resulting benzoate esters (Scheme I).[21] The yields in the benzoyl peroxide oxidations varied from 29 to 70%, owing to competing N-benzoylation. For example, oxidation of valinol (**3**) afforded hydroxyamino ester **8** in 59% yield while the yield of the corresponding methyl ether **7** was only 37%. Oxidation of phenyl glycinol benzyl ether with 2-chlorobenzoyl peroxide proceeded in somewhat better yield than with benzoyl peroxide (44% vs 29%).[19] The hydroxylamines are prone to undergo oxidation to oximes if too much exposure to air is permitted during basic hydrolysis in methanol. Conversion of the hydroxylamines to the nitrones was usually carried out soon after purification to avoid air oxidation.

The *N*-(α-naphthylethyl)- and *N*-(α-pyridylethyl)-hydroxylamines (**14** and **15**) were prepared by reduction of the corresponding oximes with sodium cyanoborohydride in methanol.[22] These reactions proved to be quite slow, and appreciable amounts of the unreacted oximes were recovered after long reaction times (50% after 21 h and 39% after 4 days, respectively).

Condensations of the hydroxylamines with benzaldehyde, acetaldehyde, and propionaldehyde (CH_2Cl_2, anhydrous Na_2SO_4, 25 °C)[23] afforded the nitrones shown in Table I. Only one isomer was isolated in all cases, and the *Z* configuration is assumed.[12] All hydroxylamines and nitrones were racemic except for **10** and the silyloxy derivatives **13** and **27** which were prepared in both racemic and optically active form of *S* configuration.

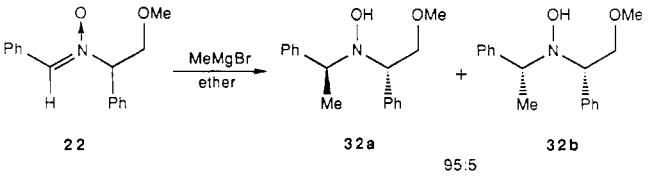
Diastereoselectivity of Organometallic Additions. The reactions of the nitrones with Grignard and organolithium reagents afforded pairs of diastereomeric hydroxylamine adducts (Tables II–IV). The isomer ratios were determined by analysis of their ^{1}H NMR spectra before and/or after purification.

N-(α-Phenylethyl)nitrones **16** and **17** furnished chromatographically separable 46:54 mixtures of meso and racemic adducts (**29a** and **29b**) upon reaction with methyl- and phenylmagnesium bromides in ether. The isomer ratio was only slightly affected by changing the solvent to THF or by lowering the temperature to −78 °C.[1b] The reactions of *C*-phenyl **16** were quite slow at −78 °C (45 and 67% conversion after 24 h).



In contrast to the Grignard reagents, methyllithium did not add efficiently to nitrone **16**. In this case the nitrone was converted to a dimer via benzylic lithiation, double bond rearrangement, and addition to a second nitrone molecule.[1b] The selectivity observed in the Grignard additions to the corresponding α-naphthyl nitrones **18** and **19** remained unsatisfactory, although the isomer ratio from the latter increased to 82:18. The α-pyridyl nitrones **20** and **21** were investigated with the hope that the chelating effect of the heterocycle might lead to enhanced selectivity. Unfortunately the improved ratio (85:15) resulting from reaction of the *C*-phenylnitrone **20** with methylmagnesium bromide was not maintained in the complementary case of the *C*-methyl analogue (**21**).

Since potentially chelating alkoxy groups often enhance the stereoselectivity of organometallic additions to carbonyl compounds,[10] we also examined nitrones substituted with β-methoxyethyl groups on nitrogen (Tables III and IV). The introduction of the methoxy group resulted in high (90:10 to 97:3) and complementary selectivity in all cases except the reaction of methylmagnesium bromide with valinol-derived nitrone **25** (64:36, entry 1, Table IV). However, high selectivity was retrieved in this case by use of methyllithium. Thus, the configuration of the major isomer can be controlled simply by the order in which the groups are introduced.



The use of THF as solvent usually resulted in somewhat lower isomer ratios compared to ether (e.g. entries 6 and 8 in Table III) whereas the ratio was often improved slightly in dichloromethane.[19] The effect of temperature proved to be inconsistent. For example, the diastereoselectivity in the addition of ethylmagnesium bromide to nitrone **23** in ether was greater at 25 °C than at reflux temperature (7:93 vs 12:88); however, the ratio resulting from the chloro Grignard was more favorable at 0 °C than at −25 °C (10:90 vs 21:79).

The high selectivity associated with the additions to the β-methoxyethyl nitrones was diminished in the corresponding silyloxy nitrones **27** and **28**, although the predominant isomer (61–70%) is the same.[24] An exception

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

(20) (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.

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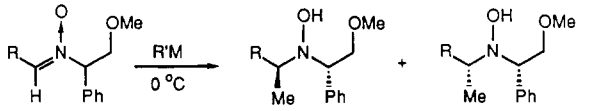
(23) (a) Torssell, K.; Zeuthen, O. *Acta Chem. Scand. Ser. B* **1978**, *B32*, 118–124. (b) Coates, R. M.; Cummins, C. H. *J. Org. Chem.* **1986**, *51*, 1383–1389.

(24) Similar low diastereoselectivities (61:39 and 72:28, respectively) resulted from addition of CH_3Li and CH_3MgBr to the *N*-(β-hydroxyethyl)nitrone corresponding to **27**.

Table III. Addition of Organometallic Reagents to Nitrones 22–24



22, R=Ph
23, R=Me
24, R=Et

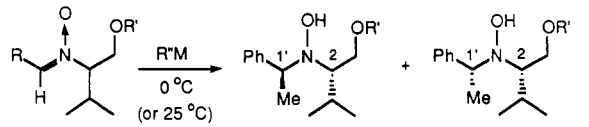
32a, R=Ph
33a, R=Et

32b, R=Ph
33b, R=Et

entry	nitrone	R'M	solvent	yield, %	product[a]	a:b ratio
1	**22**	MeMgBr	ether	96	**32a,b**	95:5
2	**23**	PhMgBr	ether	79		3:97
3		PhLi	ether	20		9:91
4		EtMgCl	ether	55	**33a,b**	10:90
5		EtMgCl	ether (−25 °C)	86		21:79
6		EtMgBr	ether (25 °C)	91[b]		7:93
7		EtMgBr	ether (reflux)	90[b]		12:88
8		EtMgBr	THF	73[b]		33:67
9	**24**	MeMgBr	ether	79		90:10

[a] Relative stereochemistry of **33a** and **33b** assigned by analogy, see text. [b] Yield of crude product.

Table IV. Addition of Organometallic Reagents to Nitrones 25–28



25,26 (R'=Me)
27,28 (R'=TBDMS)[a]

34a (R'=Me)
35a (R=TBDMS)[a]

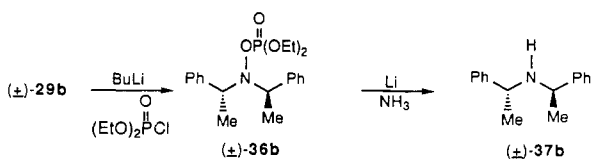
34b (R'=Me)
35b (R'=TBDMS)[a]

entry	nitrone	R"M	solvent	product	yield %	a:b ratio
1	**25** (R = Ph)	MeMgBr	ether	**34a,b**	61	64:36
2		MeLi	ether		87	96:4
3		MeLi	THF		60	97:3
4	**26** (R = Me)	PhMgBr	ether (25 °C)		43[b]	5:95
5		PhLi	ether (25 °C)		37	6:94
6	**27** (R = Ph)	MeMgBr	ether	**35a,b**	94	8:92
7		MeMgBr	ether		88	20:80[c]
8		MeMgBr	THF		62	68:32
9		MeLi	ether (25 °C)		48	61:39
10	**28** (R = Me)	PhMgBr	ether		80	33:67
11		PhLi	ether		11	30:70

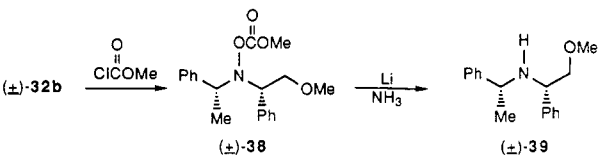
[a] TBDMS abbreviation stands for *tert*-butyldimethylsilyl. [b] 18% of starting nitrone was recovered. [c] Enantiomerically pure nitrone (*S*)-**27** was used.

to this generalization is the reaction of (±)-**27** with methylmagnesium bromide in ether which gave high but reversed diastereoselectivity (8:92). The decrease of this ratio to 20:80 with (*S*)-nitrone **27** reveals that aggregation phenomena can influence the diastereoselectivity.

Proof of Stereochemistry. The identity of *meso* and *d,l* hydroxylamines **29a** and **29b** was established by lithium–ammonia reduction of their diethyl phosphate derivatives (**36a** and **36b**) to the known *meso* and *d,l* *N,N*-bis(α-phenylethyl)amines (**37a** and **37b**)[25a] in 57–64% overall yield.[25b] The relative configurations of the related α-naphthyl and α-pyridyl hydroxylamines (**30a,b** and **31a,b**) shown in Table II are tentative assignments based on ^{1}H NMR spectral and polarity correlations with **29a,b**.



In a similar fashion hydroxylamine **32b** was converted to the carbonate **38** (71%), which was reduced by lithium in ammonia to the known methoxyamine **39** (80%). Comparison of ^{1}H NMR spectral data with the literature values[26] established the relative stereochemistry of **39** and therefore that of **32a** and **32b**. The configurational assignments for **33a** and **33b** are based on analogy with those of the corresponding benzyl ethers.[1b,19]

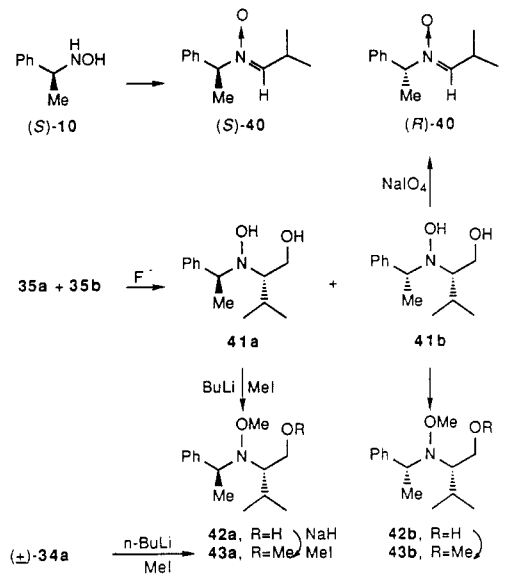


The configurations of the valinol-derived hydroxylamines **34a,b** and **35a,b** were determined by the correlations summarized in Scheme II. (*S*)-Nitrone **27**, prepared from (*S*)-valinol, underwent reaction with methylmagnesium bromide to give a 1:4 mixture of optically active hydroxylamines **35a** and **35b**. Cleavage of the silyl group (*n*-Bu_4NF, THF, 25 °C) provided a chromatographically

(25) (a) Murahashi, S.-I.; Yoshimura, N.; Tsumiyama, T.; Kojima, T. *J. Am. Chem. Soc.* **1983**, *105*, 5002–5011. (b) Catalytic hydrogenolysis of phosphate **36b** (Pd/C, EtOH, 1 atm, 25 °C) gave **37b** in 90% yield but was accompanied by 10% isomerization to **37a**.

(26) Eleveld, M. B.; Hogeveen, H.; Schudde, E. P. *J. Org. Chem.* **1986**, *51*, 3635–3642.

Scheme II



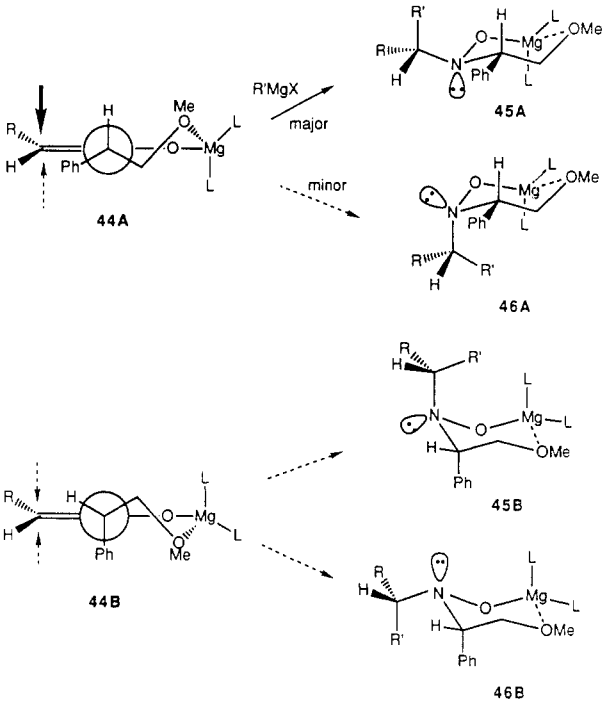
separable mixture of hydroxyamino alcohols **41a** and **41b**. Oxidation of the latter with sodium periodate in aqueous methanol effected cleavage to (*R*)-nitrone **40**. A reference sample of enantiomerically pure (*S*)-nitrone **40** was prepared from (*S*)-hydroxylamine **10** and isobutyraldehyde. The enantiomeric relationship of the two nitrones was established by ^{1}H NMR spectra of (*R*)-**40**, (*S*)-**40**, and (*R*,*S*)-**40** in the presence of the chiral shift reagent, (*R*)-2,2,2-trifluoro-1-(9-anthryl)ethanol.

Conversion of hydroxyamino alcohols **41a** and **41b** to dimethyl ethers **43a** and **43b** was carried out in two stages. Lithiation of **41a** and **41b** with *n*-butyllithium (5 equiv) in THF–hexane at −78 °C followed by addition of methyl iodide effected selective O-methylation of the hydroxylamine to give **42a** (58%) and **42b** (64%). The hydroxyl groups of **42a** and **42b** were methylated with sodium hydride and methyl iodide in THF. Methylation of (±)-**34a** afforded racemic dimethyl ether **43a**, which was spectrally identical with enantiomerically pure **43a** and spectrally distinguishable from enantiomerically pure **43b**.

Chelated Transition-State Model. The major isomers formed in the organometallic additions to the (β-methoxyethyl)nitrones shown in Tables III and IV can be rationalized in terms of a chelated transition-state model (Scheme III, **44A** → **45A**). Two half-chair conformations (**44A** and **44B**) are likely for a six-membered magnesium chelate of the methoxy nitrones. ^{1}H NMR spectral data for a magnesium bromide complex of the *O*-benzyl analogue of nitrone **22** in CD_2Cl_2 (but not in THF-d_8) are consistent with formation of a chelate having the ring phenyl group pseudoequatorial (**44A**) rather than pseudoaxial (**44B**).[19] Furthermore, nucleophilic addition to iminium ions is known to be subject to stereoelectronic control.[27]

If the transition state resembles the magnesio hydroxylamine product, then the pathway leading to adduct conformer **45A** would appear to be sterically more favorable than **45B** (R′···CH_2OMe interaction), **46A** (R′···CH_2OMe interaction), or **46B** (R′···Ph interaction). Alternatively if the transition state is early and nitrone-like, the pathway **44A** → **45A** should also be favored since the pseudoequatorial phenyl group is positioned somewhat below the nitrone plane and should interfere to some extent with approach of the organometallic nucleophile from below (i.e. **44A** → **46A**).

Scheme III



The chelated transition-state model can explain some trends in the results noted above. Enhanced stereoselectivity in dichloromethane[19] may be attributed to tighter chelation and larger steric interactions. The stronger coordinating ability of tetrahydrofuran relative to ether would diminish chelate stability, lessen steric interactions, and lower the facial discrimination. The decrease or reversal of stereoselectivity with the *N*-(β-(silyloxy)alkyl)-nitrones **27** and **28** is consistent with recent reports indicating loss of chelation control in additions to α- and β-silyloxy carbonyl compounds.[28-30]

It is also appropriate to make some cautionary comments concerning this chelation model. The reasons for the low selectivity observed in Grignard additions to nitrones **21** (pyridine chelator) and **25** (methoxy chelator) are not clear, since the complementary reactions with **20** and **26** proceed with good selectivity. Attenuated steric interactions might be expected in the transition state for addition to pyridyl nitrones **20** and **21** owing to flattening of the chelate ring from incorporation of the two sp^2 centers of the heterocycle. The appreciable difference in selectivity observed in additions to silyloxy-substituted (*R*,*S*)- and (*S*)-nitrones **27** must arise from reaction via nitrone–nitrone or nitrone–adduct aggregates.

Experimental Section

General Aspects. Melting points are uncorrected. Oven temperature and pressure are given for Kugelrohr distillations. All shifts reported for ^{1}H NMR spectra are values downfield from tetramethylsilane or the methyl signal of the dimethyl-*tert*-butylsilyl group if present.

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Silica gel chromatographic purifications were performed by flash chromatography[31] with Woelm 32–63-mm silica gel packed in glass columns. The weight of silica gel was approximately 100 times that of the substance unless noted otherwise. The eluting solvent indicated in parentheses for each purification was determined by thin-layer chromatography (TLC), which was performed on Merck glass plates coated with 0.25-mm silica gel 60 F_{254}. TLC plates were visualized with UV light and/or in an iodine chamber. The chromatographic solvents were distilled from bulk solvents prior to use.

All reactions were carried out under nitrogen. Organometallic reactions were conducted in flame- or oven-dried glassware under nitrogen using anhydrous ether or tetrahydrofuran (THF) freshly distilled from sodium benzophenone ketyl. Methyl-, butyl-, and phenyllithium were purchased from Aldrich Chemical Co. and were titrated with diphenylacetic acid prior to use.[32] Commercially available Grignard reagents were purchased from either Alfa or Aldrich Chemical Co. and were used without titration. All other reagents were commercially available reagent-grade quality and used without further purification.

(±)-2-Amino-2-phenylethanol was prepared by esterification[33] of (±)-phenylglycine to its ethyl ester [yield, 40.7 g (92%); bp 102–104 °C (0.9 mm); lig.[34] bp 114–115 °C (5 mm)] followed by reduction iwth $LiAlH_4$.[35] The yield was 15.5 g (72%); mp 70–74 °C (lit.[36] mp 76–77 °C).

2-Methoxy-1-phenylethanamine (2) was prepared according to Meyers' procedure.[37] Distillation under reduced pressure gave 1.38 g (72%) of **2** as a colorless liquid estimated to be 90% pure by ^1H NMR analysis: bp 81–82 °C (1.5 mm) [lit.[37] bp 47–50 °C (0.02 mm)]; IR (neat) 3380, 3302, 3061, 2886, 1603, 1493 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.80 (s, 2 H, NH_2), 3.39 (s, 3 H, OCH_3), 3.39 (dd, 1 H, J = 8.7, 10.4 Hz, OCH_AH_B), 3.51 (dd, 1 H, J = 4.0, 10.4 Hz, OCH_AH_B), 4.19 (dd, 1 H, J = 4.0, 8.7 Hz, CHN), 7.25–7.40 (m, 5 H, C_6H_5). The product was used in the preparation of **6** without further purification.

(±)- and (*S*)-2-amino-3-methyl-1-butanol [(±)-3 and (*S*)-3] were prepared by esterification[33] of valine to its ethyl ester [yield of (±)-ester, 21.2 g (86%); bp 73–74 °C (9 mm); lit.[38] bp 68 °C (10 mm)] followed by reduction with $LiAlH_4$[35] yields: 4.44 g (82% for (±)-**3**), bp 57–58 °C (0.8 mm); lit.[39] bp 62–67 °C (2.5 mm); 5.13 g (69% for (*S*)-**3**), bp 65 °C (1.5 mm).

1-Methoxy-3-methyl-2-butanamine (4) was prepared according to Meyers' procedure[35] from valinol, sodium hydride, and methyl iodide. Kugelrohr distillation at 75 °C (34 mm) gave 1.98 g (43%) of a colorless liquid estimated to be 90% pure by ^1H NMR analysis: IR (neat) 3380, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (d, 6 H, J = 6.8 Hz, $CH(CH_3)_2$), 1.64 (m, 1 H, $CHCHN$), 1.95 (br s, 2 H, NH_2), 2.74 (m, 1 H, NCH), 3.19 (dd, 1 H, J = 7.9, 9.4 Hz, OCH_AH_B), 3.36 (s, 3 H, OCH_3), 3.42 (dd, 1 H, J = 3.9, 9.4 Hz, OCH_AH_B). The product from the competing N-methylation reaction accounted for about 10% of the material by analysis of the NMR spectrum which shows a singlet at 2.42 ppm (N-CH_3). The product was used directly in the preparation of **7** without further purification.

***N*-(Benzoyloxy)-1-phenylethanamine hydrochloride (5·HCl)** was prepared according to the procedure of Zinner:[20a-b] yield (crude), 16 g (66%); mp 117–121 °C (lit.[20a] mp 119–121 °C).

***N*-(Benzoyloxy)amines (*S*)-5, 6, 7, (±)-8, and (*S*)-8** were prepared according to Ganem's procedure[20c] by N-oxygenation of the corresponding amines with benzoyl peroxide in THF using Na_2HPO_4 (3–5 equiv) as a heterogeneous buffer. The reactions were conducted at 25 °C for 3 h (except for (*S*)-5: 25 °C, 30 min; reflux, 2 h). The suspended salts were filtered, the filtrate was evaporated, and the remaining crude products were purified by flash chromatography. If crystals formed (unreacted benzoyl peroxide and/or benzamide) after evaporation of the filtrate, the solid was washed thoroughly with hexane and removed by filtration before the chromatography.

(*S*)-*N*-(Benzoyloxy)-1-phenylethanamine [(*S*)-5]. Purification by flash chromatography (5% ethyl acetate in hexane) afforded 1.11 g (44%) of (*S*)-**5** as an oil: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.54 (d, 3 H, J = 6.7 Hz, CH_3), 4.32 (quintet, 1 H, J = 6.7 Hz, CH), 7.45 (m, 7 H), 7.5 (m, 1 H), 7.95 (m, 3 H).

***N*-(Benzoyloxy)-2-methoxy-1-phenylethanamine (6).** Purification by flash chromatography (10% ethyl acetate in hexane) gave 1.84 g (29%) of the hydroxyamino ester as an oil: IR(neat) 3237, 3063, 2895, 1721, 1601 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.42 (s, 3 H, OCH_3), 3.60–3.75 (m, 2 H, CH_2O), 4.45 (dd, 1 H, J = 5.2, 8.1 Hz, CHN), 5.0–6.0 (br s, 1 H, NH), 7.3–7.5 (m, 8 H), 7.9 (m, 2 H).

***N*-(Benzoyloxy)-1-methoxy-3-methyl-2-butanamine (7).** Two large-scale flash chromatographies (10% ethyl acetate in hexane) afforded 3.96 g (37%) of hydroxyamino ester **7** as an oil: IR (neat) 3239, 3069, 1705, 1603, 1180 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.03 and 1.09 (2 d, 6 H, J = 7.0 and 7.0 Hz, $CH(CH_3)_2$), 2.02 (m, 1 H, J = 7.0 Hz, $CHCHN$), 3.08 (m, 1 H, NCH), 3.36 (s, 3 H, OCH_3), 3.38 (dd, 1 H, J = 7.6, 9.7 Hz, OCH_AH_B), 3.56 (dd, 1 H, J = 4.0, 9.7 Hz, OCH_AH_B), 7.45, 7.55, and 8.0 (3 m, 2 H, 1 H, and 2 H, C_6H_5), 8.19 (d, 1 H, NH). Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.91; H, 8.09; N, 6.16.

(–)-(*S*)- and (±)-2-[*N*-(Benzoyloxy)amino]-3-methyl-1-butanol [(*S*)-8 and (±)-8]. Purification by flash chromatography (30% ethyl acetate in hexane) afforded 2.2 g (59%) of hydroxyamino ester **8** as an oil: $[\alpha]^{25}_D$ –12.5° (c 1.77, $CHCl_3$). Racemic **8** was obtained as an oil: yield, 1.83 g (56%); IR (neat) 3410, 3067, 1722, 1583, 1179 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.02 and 1.15 (2 d, 6 H, J = 6.6 and 7.2 Hz, $CH(CH_3)_2$), 1.95 (m, 1 H, J = 7.0 Hz, $CHCHN$), 2.70 (br s, 1 H, OH), 2.88 (dt, 1 H, J = 3.4, 7.2 Hz, NCH), 3.64 (dd, 1 H, J = 7.2, 11.8 Hz, OCH_AH_B), 3.81 (dd, 1 H, J = 3.6, 11.8 Hz, OCH_AH_B), 7.45 (m, 2 H), 7.6 (m, 1 H), 8.0 (m, 3 H). Anal. Calcd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.33; H, 7.80; N, 6.13.

(+)-(*S*)- and (±)-*N*-(Benzoyloxy)-1-[[dimethyl(1,1-dimethylethyl)silyl]oxy]-3-methyl-2-butanamine [(*S*)-9 and (±)-9]. Optically active **9** was prepared according to Cook's procedure.[40] A solution of 2.1 g (9.4 mmol) hydroxyamino ester (*S*)-**8**, 1.67 g (11.1 mmol) of dimethyl-*tert*-butylchlorosilane, and 1.92 g (28.3 mmol) of imidazole in 20 mL of DMF was stirred at room temperature for 3.5 h. Sodium bicarbonate solution (20 mL, 5%) was added, and the aqueous solution was extracted with hexane (3 × 30 mL). The combined hexane extracts were washed with 10 mL of saturated sodium chloride solution, dried (K_2CO_3), and evaporated. Purification of the residue by flash chromatography (5% ethyl acetate in hexane) afforded 2.8 g (88%) of the silyl ether **9** as a colorless oil: $[\alpha]^{25}_D$ +24.5° (c 13.85, $CHCl_3$). Racemic **9** was prepared in the same way and obtained as an oil: yield, 2.36 g (87%); IR (neat) 3235, 3067, 1722, 1586, 1177 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.00 (s, 6 H, $Si(CH_3)_2$), 0.86 (s, 9 H, $C(CH_3)_3$), 0.99 and 1.06 (2 d, 6 H, J = 6.5 and 7.1 Hz, $CH(CH_3)_2$), 1.93 (m, 1 H, J = 6.6 Hz, $CHCHN$), 2.89 (m, 1 H, NCH), 3.54 (dd, 1 H, J = 7.0, 10.4 Hz, OCH_AH_B), 3.76 (dd, 1 H, J = 4.1, 10.4 Hz, OCH_AH_B), 7.4 (m, 2 H), 7.5 (m, 1 H), 7.96 (m, 2 H), 8.24 (d, 1 H, NH). Anal. Calcd for $C_{18}H_{31}NO_3Si$: C, 64.05; H, 9.26; N, 4.15. Found: C, 64.08; H, 9.37; N, 4.30.

***N*-Hydroxy-1-phenylethanamine (10)** was prepared as described by Zinner.[20b] To a solution of 2.68 g (9.65 mmol) of the crude salt **5**·HCl in 10 mL of methanol was added 3.2 mL (2 equiv) of 6 N sodium hydroxide solution at 60 °C. After 15 min, 10 mL of ice-cold water was added, and the aqueous solution was extracted with ether (3 × 25 mL). The combined ether extracts were acidified with 1 N hydrochloric acid to pH <1. The acidic aqueous layer was basified with 1 N sodium hydroxide solution to pH >10 and extracted with ether (3 × 25 mL). The combined

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ether extracts were dried (Na_2SO_4) and concentrated to give, after recrystallization from petroleum ether, 1.00 g (75%) of (±)-**10**: mp 69–71 °C (lit.[20b] mp 68–70 °C); IR (Nujol) 3260, 3140, 3064, 1155, 1066 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.38 (d, 3 H, J = 6.6 Hz, $CHCH_3$), 4.09 (q, 1 H, J = 6.6 Hz, $CHCH_3$), 4.5–6.0 (br s, 2 H, NHOH), 7.31 (s, 5 H, C_6H_5). Anal. Calcd for $C_8H_{11}NO$: C, 70.07; H, 8.03; N, 10.22. Found: C, 69.79; H, 7.97; N, 10.17.

Hydroxylamines (*S*)-**10**, **11**, **12**, (±)-**13**, and (*S*)-**13** were obtained by hydrolysis of their *O*-benzoyl derivatives at 25 °C as described above.

(-)-(*S*)-*N*-Hydroxy-1-phenylethanamine [(*S*)-10]: yield, 0.255 g (40%) of (*S*)-**10** as a white solid; mp 97–98 °C; $[\alpha]^{25}_D$ −34.6° (*c* 4.93, $CHCl_3$) [lit.[17] $[\alpha]^{20}_{578}$ 43.5° (*c* 1, CH_2Cl_2)].

***N*-Hydroxy-2-methoxy-1-phenylethanamine (11).** Purification by flash chromatography (20–30% ethyl acetate in hexane) gave 0.15 g (78%) of the hydroxylamine as an oil: IR (neat) 3244, 2893, 1495 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.36 (s, 3 H, OCH_3), 3.5–3.6 (m, 2 H, CH_2O), 4.23 (dd, 1 H, J =5.1, 7.8 Hz, CHN), 4.5–6.0 (br s, 2 H, NHOH), 7.35 (m, 5 H, C_6H_5). Anal. Calcd for $C_9H_{13}NO_2$: C, 64.64; H, 7.84; N, 8.38. Found: C, 64.68; H, 7.71; N, 8.40.

***N*-Hydroxy-1-methoxy-3-methyl-2-butanamine (12).** Purification by flash chromatography (30% ethyl acetate in hexane) gave 0.42 g (78%) of hydroxylamine **12** as an oil: IR (neat) 3400, 3272, 1200, 1113 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.93 and 0.99 (2 d, 6 H, J = 7.0 and 7.0 Hz, $CH(CH_3)_2$), 1.89 (m, 1 H, J = 7.0 Hz, $CHCHN$), 2.77 (m, 1 H, NCH), 3.36 (s, 3 H, OCH_3), 3.41 (dd, 1 H, J = 7.3, 10.4 Hz, OCH_AH_B), 3.53 (dd, 1 H, J = 3.8, 10.4 Hz, OCH_AH_B), 5.65 (br s, 2 H, NHOH). Anal. Calcd for $C_6H_{15}NO_2$: C, 54.11; H, 11.35; N, 10.52. Found: C, 54.25; H, 11.07; N, 10.50.

(±)- and (+)-(*S*)-*N*-Hydroxy-1-[[dimethyl(1,1-dimethylethyl)silyl]oxy]-3-methyl-2-butanamine [(±)-13 and (*S*)-13]. Purification by flash chromatography (10% ethyl acetate in hexane) gave 0.78 g (83%) of the racemic hydroxylamine as an oil. Optically active (*S*)-**13** was prepared from (*S*)-**9** in the same way and obtained as an oil: yield, 0.80 g (80%); $[\alpha]^{25}_D$ +14.6° (*c* 13.2, $CHCl_3$); IR (neat) 3420, 3217, 1471, 1254, 1188 cm^{-1}; ^1H NMR ($CDCl_3$, 200: MHz) δ 0.00 (s, 6 H, $Si(CH_3)_2$), 0.83 (s, 9 H, $C(CH_3)_3$), 0.84 and 0.92 (2 d, 6 H, J = 7.0 and 6.5 Hz, $CH(CH_3)_2$), 1.81 (m, 1 H, J = 6.6 Hz, $CHCHN$), 2.56 (dt, 1 H, J = 3.8, 6.6 Hz, NCH), 3.52 (dd, 1 H, J = 6.8, 10.4 Hz, OCH_AH_B), 3.71 (dd, 1 H, J = 3.5, 10.4 Hz, OCH_AH_B), 5.8 (br s, 2 H, NHOH). Anal. Calcd for $C_{11}H_{27}NO_2Si$: C, 56.60; H, 11.66; N, 6.00. Found: C, 56.39; H, 11.38; N, 5.91.

1-(1-Naphthalenyl)ethanone oxime was prepared from 1-acetylnaphthalene according to Blicke's procedure:[41] yield, 8.5 g (66%); mp 136–138 °C (lit.[41] mp 134–135 °C): IR ($CHCl_3$) 3584, 3292, 1510, 1252, 1134 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.37 (s, 3 H, CH_3), 7.50, 7.86, 8.02 (3 m, 4 H, 2 H, and 1 H, $C_{10}H_7$). Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.78; H, 6.01; N, 7.51.

***N*-Hydroxy-1-(1-naphthyl)ethanamine (14)** was prepared according to the method of Borch.[22] The reaction was not complete after 4 days. The product was separated from the remaining oxime by the following procedure: methanol was evaporated and the residue was acidified with 1 N hydrochloric acid to pH <1, diluted with 200 mL of water, and extracted with ether (2 × 100 mL). The combined ether extracts were dried (Na_2SO_4) and concentrated to give 2.41 g (39%) of the starting oxime. The aqueous layer was basified with 6 N sodium hydroxide solution to pH >11 and extracted with ether (3 × 120 mL). The combined ether extracts were dried (Na_2SO_4) and concentrated to give 3.93 g of a crude solid. Recrystallization from hexane afforded 2.79 g (45%) of **14** as white crystals: mp 81–83 °C; IR ($CHCl_3$) 3586, 3265, 1178, 1143 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.55 (d, 3 H, J = 6.7 Hz, $CHCH_3$), 4.99 (q, 1 H, J = 6.7 Hz, $CHCH_3$), 5.3–6.5 (br s, 2 H, NHOH), 7.52, 7.77, 7.86, and 8.16 (4 m, 4 H, 1 H, 1 H, and 1 H, $C_{10}H_7$). Anal. Calcd for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.48. Found: C, 76.78; H, 7.29; N, 7.41.

1-(2-Pyridinyl)ethanone oxime was prepared according to the procedure given above from 2-acetylpyridine. Recrystallization from benzene afforded a white solid: yield, 17.8 g (80%); mp 118.5–120.5 °C (lit.[42] mp 120 °C); IR (Nujol) 3150, 1586, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3 H, CH_3), 7.3 (m, 1 H, H-C4), 7.7 (m, 1 H, H-C5), 7.85 (m, 1 H, H-C3), 8.65 (m, 1 H, H-C6), 9.87 (s, 1 H, OH). Anal. Calcd for $C_7H_8N_2O$: C, 61.75; H, 5.92; N, 20.58. Found: C, 61.54; H, 5.94; N, 20.53.

***N*-Hydroxy-1-(2-pyridyl)ethanamine (15)** was prepared by a modification of Borch's method.[22] A solution of 5.02 g (36.9 mmol) of the pyridyl oxime and a trace of methyl orange in 55 mL of methanol was stirred at room temperature as 2 N hydrochloric acid was added until the color turned orange-red. A solution of 4.14 g (65.9 mmol) of sodium cyanoborohydride in 20 mL of methanol was added. The solution was then maintained at pH 3 by addition of 2 N hydrochloric acid (orange-red transition point) and was stirred at room temperature for 21 h. Methanol was removed on a rotatory evaporator. The residue was dissolved in a minimum amount of water; the aqueous solution was basified with 6 N potassium hydroxide solution to pH 9 and extracted with ether (5 × 80 mL). The combined ether extracts were dried (K_2CO_3) and evaporated. Purification of the residue by flash chromatography (13% ethyl acetate in hexane) afforded 2.52 g (50%) of the starting oxime and 1.58 g (31%) of hydroxylamine **15**: mp 90–92 °C; IR (Nujol) 3270, 3100, 1594, 1149 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.40 (d, 3 H, J = 6.9 Hz, $CHCH_3$), 4.27 (q, 1 H, J = 6.9 Hz, $CHCH_3$), 6.18 (br s, 2 H, NHOH), 7.20 (m, 1 H, H-C4), 7.30 (d, 1 H, H-C5), 7.7 (m, 1 H, H-C3), 8.53 (m, 1 H, H-C6). Anal. Calcd for $C_7H_{10}N_2O$: C, 60.84; H, 7.30; N, 20.28. Found: C, 61.05; H, 7.45; N, 20.28.

General Procedure for the Preparation of Nitrones. Nitrones were prepared according to the procedure of Torsell and Zeuthen.[23] Solutions of 1.2–2 equiv of the aldehyde and 1 equiv (0.3 M solution) of the approximate hydroxylamine in dichloromethane were stirred in the presence of 1.5 equiv of anhydrous sodium sulfate for 3–12 h. The reactions were followed by TLC. After filtration of sodium sulfate and evaporation of the solvent, the products were purified by recrystallization and/or flash chromatography using ethyl acetate–hexane as the eluent. One specific example is illustrated by the preparation of nitrone **16**.

***N*-Benzylidene-1-phenylethanamine *N*-Oxide (16).** A suspension of 2.1 g (22 mmol) of anhydrous sodium sulfate, 2.47 g (18.0 mmol) of hydroxylamine **10**, and 2.65 g (25.0 mmol) of benzaldehyde in 22 mL of dichloromethane was stirred under nitrogen at room temperature for 7 h. Sodium sulfate was filtered, and the filtrate was evaporated to give an oil which solidified. The solid was washed once with cold petroleum ether and recrystallized from hexane to afford 2.85 g (70%) of white crystals: mp 85–87 °C. (lit.[17] oil). Concentration of the mother liquor and washings followed by purification by flash chromatography (30% ethyl acetate–hexane) afforded another 0.63 g of a white solid. The combined yield was 3.48 g (86%). The IR spectral data agree with the literature values.[17] The ^1H NMR ($CDCl_3$, 200 MHz) spectral data are as follows: δ 1.88 (d, 3 H, J = 6.8 Hz, $CHCH_3$), 5.17 (q, 1 H, J = 6.8 Hz, $CHCH_3$), 7.40, 7.52 and 8.22 (m, 6 H, 3 H, 2 H, N=CH and 2 C_6H_5). Anal. Calcd for $C_{15}H_{15}NO$: C, 80.00; H, 6.67; N, 6.22. Found: C, 79.69; H, 6.53; N, 6.15.

***N*-Ethylidene-1-phenylethanamine *N*-Oxide (17).** Recrystallization of the product from hexane gave 1.91 g (74%): mp 73–75 °C; IR (Nujol) 3075, 1590, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.80 (d, 3 H, J = 7.0 Hz, $PhCHCH_3$), 1.97 (d, 3 H, J = 6.0 Hz, $=CHCH_3$), 4.99 (q, 1 H, J = 7.0 Hz, $PhCHCH_3$), 6.85 (q, 1 H, J = 6.0 Hz, $=CHCH_3$), 7.35 (m, 3 H, ArH), 7.45 (m, 2 H, ArH); MS (70 eV) *m/e* (rel int) 163 (M^+, 3), 105 (100), 77 (9). Anal. Calcd for $C_{10}H_{13}NO$: C, 73.62; H, 7.98; N, 8.59. Found: C, 73.44; H, 7.83; N, 8.55.

***N*-Benzylidene-1-(1-naphthyl)ethanamine *N*-Oxide (18).** Recrystallization from ethyl acetate–hexane yielded 1.71 g (88%): mp 124–126 °C; IR ($CHCl_3$) 3068, 1585, 1124 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.08 (d, 3 H, J = 6.6 Hz, $CHCH_3$), 5.93 (q, 1 H, J = 6.6 Hz, $CHCH_3$), 7.20 (s, 1 H, =CH), 7.33 (m, 3 H), 7.55 (m, 3 H), 7.84 (m, 3 H), 8.13 (m, 3 H). Anal. Calcd for $C_{19}H_{17}NO$: C, 82.88; H, 6.22; N, 5.09. Found: C, 83.04; H, 6.21; N, 5.07.

***N*-Ethylidene-1-(1-naphthyl)ethanamine *N*-Oxide (19).** The polar nitrone was purified by flash chromatography using 50% ethyl acetate–hexane and 10% methanol–ethyl acetate as

(41) Blicke, F. F.; Maxwell, C. E. *J. Am. Chem. Soc.* **1939**, *61*, 1780–1782.

(42) Bower, J. D.; Ramage, G. R. *J. Chem. Soc.* **1955**, 2834–2837.

the eluents. The product was obtained as an oil and used soon after purification because of its instability; yield, 0.29 g (69%). The ^{1}H NMR ($CDCl_3$, 200 MHz) spectral data are as follows: δ 1.85 (d, 3 H, J = 6.1 Hz, NCHCH_3), 1.97 (d, 3 H, J = 6.7 Hz, =CHCH_3), 5.76 (q, 1 H, J = 6.1 Hz, NCHCH$_3$), 6.51 (q, 1 H, J = 6.7 Hz, =CHCH$_3$), 7.48 (m, 3 H, H-C3-C6, and -C7), 7.71 (d, 1 H, J = 7.3 Hz, H-C2), 7.81 (m, 2 H, H-C5 and H-C8), 8.05 (d, 1 H, J = 7.8 Hz, H-C4).

***N*-Benzylidene-1-(2-pyridyl)ethanamine *N*-Oxide (20).** Recrystallization from petroleum ether gave 1.87 g (74%): mp 77.5–79.5 °C; IR (Nujol) 1583, 1136 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.95 (d, 3 H, J = 7.2 Hz, CHCH_3), 5.34 (q, 1 H, J = 7.2 Hz, CHCH$_3$), 7.24 (m, 1 H), 7.38 (m, 3 H), 7.72 (m, 3 H), 8.25 (m, 2 H), 8.55 (m, 1 H). Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.32; H, 6.24; N, 12.37. Found: C, 74.19; H, 6.30; N, 12.30.

***N*-Ethylidene-1-(2-pyridyl)ethanamine *N*-Oxide (21).** Purification by repeated flash chromatography (13% methanol in ethyl acetate) afforded 0.22 g (74%) of the nitrone as an oil estimated to be 90% pure by ^{1}H NMR analysis: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.85 (d, 3 H, J = 7.0 Hz, NCHCH_3), 2.02 (d, 3 H, J = 6.2 Hz, =CHCH_3), 5.16 (q, 1 H, J = 7.0 Hz, NCHCH$_3$), 7.07 (q, 1 H, J = 6.2 Hz, =CHCH$_3$), 7.25 (m, 1 H), 7.68 (m, 2 H), 8.56 (m, 1 H).

***N*-Benzylidene-2-methoxy-1-phenylethanamine *N*-Oxide (22).** Recrystallization from hexane gave 0.14 g (63%): mp 106.5–108.5 °C; IR (Nujol) 2916, 1584, 1566 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.43 (s, 3 H, OCH_3), 3.72 (dd, 1 H, J = 3.6, 10.2 Hz, OCH_AH_B), 4.50 (dd, 1 H, J = 9.2, 10.2 Hz, OCH_AH_B), 5.15 (dd, 1 H, J = 3.6, 9.2 Hz, CHCH$_2$), 7.33–7.46, 7.5–7.6, and 8.2–8.3 (3 m, 6 H, 3 H, and 2 H, 2 C_6H_5 and =CH). Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.12; H, 6.61; N, 5.42.

***N*-Ethylidene-2-methoxy-1-phenylethanamine *N*-Oxide (23).** Purification by flash chromatography (50–90% ethyl acetate–hexane) afforded 0.25 g (82%) of the polar nitrone as an oil which eventually crystallized. Recrystallization from petroleum ether gave 0.13 g (43%) of a white solid: mp 83–85 °C; IR (neat) 3410, 3086, 3031, 1653, 1596, 1497, 1454, 768, 706 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.03 (d, 3 H, J = 5.6 Hz, CHCH_3), 3.42 (s, 3 H, OCH_3), 3.65 (dd, 1 H, J = 3.9, 10.2 Hz, CH_AH_BO), 4.40 (apparent t, 1 H, J = 9.4 Hz, CH_AH_BO), 4.95 (dd, 1 H, J = 3.5, 8.9 Hz, NCH), 6.95 (q, 1 H, J = 5.6 Hz, CHCH$_3$). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.28; H, 7.92; N, 7.30.

***N*-Propylidene-2-methoxy-1-phenylethanamine *N*-Oxide (24).** Purification by flash chromatography (70% ethyl acetate in hexane) gave 0.102 g (81%) of the nitrone as an oil: IR (neat) 3433, 3066, 1588, 1496, 1455, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.09 (t, 3 H, J = 7.6 Hz, CH_2CH_3), 2.40–2.62 (m, 2 H, CH_2CH_3), 3.42 (s, 3 H, OCH_3), 3.63 (dd, 1 H, J = 3.6, 10.1 Hz, OCH_AH_B), 4.40 (dd, 1 H, J = 9.1, 10.1 Hz, OCH_AH_B), 4.91 (dd, 1 H, J = 3.6, 9.1 Hz, NCH), 6.81 (t, 1 H, J = 5.4 Hz, =CHCH$_2$), 7.35 and 7.50 (2 m, 3 H and 2 H, C_6H_5). Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.05; H, 8.01; N, 6.79.

***N*-Benzylidene-1-methoxy-3-methyl-2-butanamine *N*-Oxide (25).** Purification by flash chromatography (30% ethyl acetate in hexane) afforded 0.38 g (91%) of the nitrone as an oil: IR (neat) 1578, 1146 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.98 and 1.03 (2 d, 6 H, J = 6.7 and 7.0 Hz, $CH(CH_3)_2$, 2.26 (m, 1 H, CHCHN), 3.34 (s, 3 H, OCH_3), 3.60 (m, 2 H, CH_2O), 4.00 (t-like, 1 H, J = 11.2 Hz, NCH), 7.4 and 8.28 (2 m, 4 H and 2 H, =CHC_6H_5). Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.55; H, 8.65; N, 6.33. Found: C, 70.49; H, 8.74, N, 6.56.

***N*-Ethylidene-1-methoxy-3-methyl-2-butanamine *N*-Oxide (26).** Purification by flash chromatography (10–20% methanol in ethyl acetate) gave 0.17 g (69%) of the nitrone as an oil: IR (neat) 3421, 3089, 1598, 1457, 1116 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.93 and 0.98 (2 d, 6 H, J = 5.7 and 6.1 Hz, $CH(CH_3)_2$), 2.04 (d, 3 H, J = 6.2 Hz, =CHCH_3), 2.15 (m, 1 H, CHCHN), 3.35 (s, 3 H, OCH_3), 3.48 (m, 2 H, OCH_2), 3.93 (m, 1 H, NCH), 6.77 (q, 1 H, J = 6.2 Hz, =CHCH$_3$). Anal. Calcd for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.30; H, 10.68; N, 8.87.

(±)- and (+)-(*S*)-*N*-Benzylidene-1-[[dimethyl(1,1-dimethylethyl)silyl]oxy]-3-methyl-2-butanamine *N*-Oxide [(±)-27 and (*S*)-27]. Purification by flash chromatography (20% ethyl acetate in hexane) afforded 0.79 g (93%) of racemic **27** as a white solid: mp 64.5–66.5 °C; IR (KBr) 3400, 3080, 1582, 1180 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ –0.08 and 0.00 (2 s, 6 H, $Si(CH_3)_2$), 0.78 (s, 9 H, $C(CH_3)_3$), 0.96 and 1.00 (2 d, 6 H, J = 6.6 and 6.5 Hz, $CH(CH_3)_2$), 2.20 (m, CHCHN), 3.49 (dt, 1 H, J = 2.8, 9.2 Hz, NCH), 3.82 (dd, 1 H, J = 3.0, 10.5 Hz, OCH_AH_B), 4.10 (dd, 1 H, J = 8.9, 10.5 Hz, OCH_AH_B), 7.35 (m, 4 H), 8.23 (m, 2 H). Anal. Calcd for $C_{18}H_{31}NO_2Si$: C, 67.24; H, 9.72; N, 4.36. Found: C, 67.55; H, 9.83; N, 4.33.

Optically active (*S*)-**27** was prepared from (*S*)-**13** in the same way. Purification by flash chromatography (10% ethyl acetate in hexane) gave 0.92 g (91%) of the nitrone as an oil: $[\alpha]^{25}_D$ +64.3° (c 10.3, $CHCl_3$).

***N*-Ethylidene-1-[[dimethyl(1,1-dimethylethyl)silyl]oxy]-3-methyl-2-butanamine *N*-Oxide (28).** Purification by flash chromatography (40% ethyl acetate in hexane) gave 0.56 g (88%) of the nitrone as an oil which formed a crystalline solid: mp 56–58 °C; IR (KBr) 3400, 2090, 1603, 1185 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ –0.02 and 0.00 (2 s, 6 H, $Si(CH_3)_2$), 0.81 (s, 9 H, $C(CH_3)_3$), 0.88 and 0.92 (2 d, 6 H, J = 6.7, 6.6 Hz, $CH(CH_3)_2$), 1.95 (d, 3 H, J = 5.6 Hz, =CHCH_3), 2.12 (m, 1 H, CHCHN), 3.28 (dt, 1 H, J = 3.2, 9.2 Hz, NCH), 3.70 (dd, 1 H, J = 3.2, 10.2 Hz, OCH_AH_B), 4.00 (dd, 1 H, J = 9.0, 10.2 Hz, OCH_AH_B), 6.68 (q, 1 H, J = 5.6 Hz, =CHCH$_3$). Anal. Calcd for $C_{13}H_{29}NO_2Si$: C, 60.28; H, 11.27; N, 5.40. Found: C, 60.15; H, 11.37; N, 5.39.

General Procedure for the Reactions of Organometallic Reagents with Nitrones. Three equivalents of the organometallic reagent was added to a solution of the nitrone in ether (or dichloromethane or THF) at 0 °C (or 25 °C, –78 °C). The reaction was followed by TLC, and the solution was hydrolyzed by adding saturated ammonium chloride solution. The resulting aqueous solution was extracted three times with ether. The combined ether extracts were dried (Na_2SO_4 or K_2CO_3) and evaporated. The ratio of the resulting diastereomeric hydroxylamines was determined by analysis of the ^{1}H NMR spectrum of the crude product if possible. If the ratio had to be determined after chromatographic purification, care was taken to be sure that no loss of either diastereomer occurred. Generally, the two diastereomeric hydroxylamines were purified as a mixture but not separated by flash chromatography.

One representative procedure for an organometallic reaction is described in detail below. Usually two or three reactions were performed under different conditions (solvent, temperature) as listed in Tables II–IV. The conditions and results for only one reaction of each nitrone are given below in abbreviated form.

(*R,*S**)- and (*R**,*R**)-*N*-Hydroxy-*N*-(1-phenylethyl)-1-phenylethanamine (29a and 29b). A. From Nitrone 16.** A solution of 2.01 g (8.94 mmol) of nitrone **16** in 95 mL of anhydrous ether was stirred and cooled at 0 °C under nitrogen as 5.77 mL (17.88 mmol) of 3.1 M methylmagnesium bromide in ether was added. The solution was refluxed for 1 h, after which saturated ammonium chloride solution (60 mL) was added slowly to destroy the unreacted Grignard reagent. The ether layer was separated, and the aqueous layer was extracted with ether (3 × 80 mL). The combined ether extracts were dried (K_2CO_3) and concentrated. Purification of the remaining oil (2.19 g) by flash chromatography on a 44-mm (i.d.) column packed with 200 g of silica gel with 30% ethyl acetate–hexane as the eluting solvent gave a mixture of the two isomers. The material was divided into smaller portions of 0.3–0.4 g each and separated by a series of nine flash chromatographies on 60 g of silica gel packed in a 24-mm column eluting with 45% ethyl acetate–hexane and collecting 30-mL fractions. Mixed fractions containing both isomers were combined and separated again to give more of the pure isomers. The less polar meso isomer (**29a**) was obtained as a pale yellow oil: yield, 1.07 g (50%); IR (neat) 3540, 3400, 3084, 3065, 3030, 2990, 2978, 2938, 2875, 1900, 1880, 1810, 1700, 1604, 1494, 1454, 1370, 1300, 1278, 1088, 1080, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.40 (d, 6 H, J = 6.6 Hz, $N(CHCH_3)_2$), 3.86 (q, 2 H, J = 6.6 Hz, $N(CHCH_3)_2$), 4.40 (s, 1 H, OH), 7.30 (m, 10 H, 2 C_6H_5); MS (70 eV) m/e (rel int) 241 (M^+, 14), 226 (5), 105 (100). Anal. Calcd for $C_{16}H_{19}NO$: C, 79.01; H, 7.82; N, 5.76. Found: C, 79.32; H, 8.02; N, 5.77. The more polar isomer **29b** was also obtained as a pale yellow oil: yield, 0.53 g (25%); The IR and mass spectral properties of **29b** are the same as those of **29a**. The ^{1}H NMR spectral properties of **29b** are as follows: ($CDCl_3$, 200 MHz) δ 1.40 (d, 6 H, J = 6.6 Hz, 2 CH_3), 3.80 (q, 2 H, J = 6.6 Hz, 2 CH), 4.0–4.3 (br s, 1 H, OH),

7.25 (m, 10 H, 2 C_6H_5). Anal. Calcd for $C_{16}H_{19}NO$: C, 79.01; H, 7.82; H, 5.76. Found: C, 79.06; H, 7.90; N, 5.72.

B. From nitrone 17: ether, 0 °C; flash chromatography (10% ether acetate in hexane); 117 mg (92%) of a 46:54 mixture of **29a:29b** as an oil.

The ratios of **29a:29b** shown in Table II were determined from the ^1H NMR spectra of the crude products. Decoupling of methyl protons at 1.40 ppm caused the two quartets from the methine protons of **29a** and **29b** to collapse to two singlets. Integration of the two resulting singlets gave the ratios.

(*R,*S**)- and (*R**,*R**)-*N*-Hydroxy-*N*-[1-(1-naphthyl)-ethyl]-1-phenylethanamine (30a and 30b). A. From nitrone 18**: ether, 0 °C; flash chromatography (5% ethyl acetate in hexane); 61 mg (71%) of a 42:58 mixture of **30a:30b** as an oil.

B. From nitrone 19: ether, 0 °C; flash chromatography (5% ethyl acetate in hexane); 56 mg (52%) of a 82:18 mixture of **30a:30b** as an oil.

The two isomeric adducts were separated by flash chromatography, but the relative stereochemistry of the isomers was not determined. The less polar isomer is tentatively assigned to be **30a** and the more polar isomer to be **30b** in analogy to the polarity of hydroxylamines **29a** and **29b**. Hydroxylamine **30a**: IR ($CHCl_3$) 3580, 3264, 3063, 3030, 1724, 1597, 1201 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.44 (d, 3 H, J = 6.7 Hz, $PhCHCH_3$), 1.58 (d, 3 H, J = 6.7 Hz, $C_{10}H_7CHCH_3$), 4.03 (q, 1 H, J = 6.7 Hz, PhCH), 4.32 (br s, 1 H, OH), 4.65 (q, 1 H, J = 6.7 Hz, $C_{10}H_7CH$), 7.4 (m, 8 H, C_6H_5 and 3 H of $C_{10}H_7$), 7.65 (d, 1 H, J = 6.0 Hz), 7.78 (d, 1 H, J = 8.4 Hz), 7.8 (m, 1 H), 8.1 (m, 1 H). Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.81. Found: C, 80.18; H, 7.57; N, 4.50.

Hydroxylamine **30b**: IR (same as those of **30a**); ^1H NMR ($CDCl_3$, 200 MHz) δ 1.53 (d, 3 H, J = 6.7 Hz, $PhCHCH_3$), 1.54 (d, 3 H, J = 6.7 Hz, $C_{10}H_7CHCH_3$), 4.03 (q, 1 H, J = 6.7 Hz, PhCH), 4.29 (br s, 1 H, OH), 4.63 (q, 1 H, J = 6.7 Hz, $C_{10}H_7CH$), 7.20 (m, 5 H, C_6H_5), 7.47 (m, 3 H), 7.65 (d, 1 H, J = 5.8 Hz), 7.76 (d, 1 H, J = 8.4 Hz), 7.83 (m, 1 H), 8.15 (m, 1 H). Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.81. Found: C, 82.39; H, 7.45; N, 4.74. The ratios of **30a:30b** shown in Table II were determined by integrating the doublets of the methyl groups in the ^1H NMR spectra of the purified product mixtures.

(*R,*S**)- and (*R**,*R**)-*N*-Hydroxy-*N*-[1-(1-pyridyl)-ethyl]-1-phenylethanamine (31a and 31b). A. From nitrone 20**: ether, 0 °C; flash chromatography (30% ethyl acetate in hexane); 0.200 g (36%) of a 85:15 mixture of **31a:31b** as an oil; IR ($CHCl_3$) 3570, 3200, 1586, 1143 cm^{-1}. Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 75.66; H, 7.25; N, 11.45. Major isomer: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.47 and 1.48 (2 d, 6 H, J = 6.7 Hz, $N(CHCH_3)_2$), 3.92 and 4.05 (2 q, 2 H, J = 6.7 Hz, $N(CHCH_3)_2$), 6.56 (s, 1 H, OH), 7.13–7.4 (m, 6 H), 7.63 (m, 2 H), 8.53 (m, 1 H). Minor isomer: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.47 and 1.53 (2 d, 6 H, J = 4.7 Hz, $N(CHCH_3)_2$), 3.68 and 3.83 (2 q, 2 H, J = 4.7 Hz, $N(CHCH_3)_2$).

B. From nitrone 21: ether, 25 °C; flash chromatography (30% ethyl acetate in hexane); 41 mg (45%) of a 48:52 mixture of **31a:31b** as an oil

The ratio of **31a:31b** shown in Table II were determined by taking the integral over the two quartets at δ 4.05 and 3.68.

(1*R,1′*R**)- and (1*R**,1′*S**)-*N*-Hydroxy-*N*-(2′-methoxy-1′-phenylethyl)-1-phenylethanamine (32a and 32b). A. From nitrone 22**: ether, 0 °C; flash chromatography (20% ethyl acetate in hexane); 56 mg (96%) of a 95:5 mixture of **32a:32b** as an oil; IR (neat) 3528, 3380, 3080, 3061, 2980, 2930, 2876, 2820, 1601, 1493, 1452, 763, 704 cm^{-1}; ^1H NMR for the less polar hydroxylamine **32a** ($CDCl_3$, 200 MHz) δ 1.36 (d, 3 H, J = 6.8 Hz, $CHCH_3$), 3.32 (s, 3 H, OCH_3), 3.70 (dd, 1 H, J = 6.0, 9.7 Hz, OCH_AH_B), 3.84 (q, 1 H, J = 6.8 Hz, $CHCH_3$), 4.01 (dd, 1 H, J = 6.0, 9.7 Hz, OCH_AH_B, 4.15 (t, 1 H, J = 6.0 Hz, NCH), 4.7 (s, 1 H, OH), 7.2–7.5 (m, 10 H, 2 C_6H_5). Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.45; H, 7.94; N, 5.01.

B. From nitrone 23: ether, 0 °C; flash chromatography (5–20% ethyl acetate in hexane); 58 mg (80%) of a 3:97 mixture of **32a:32b** as an oil: IR, same as those reported above; ^1H NMR for the more polar hydroxylamine **32b** ($CDCl_3$, 200 MHz) δ 1.47 (d, 3 H, J = 6.7 Hz, $CHCH_3$), 3.30 (s, 3 H, OCH_3), 3.58 (dd, 1 H, J = 5.1, 9.5 Hz, OCH_AH_B), 3.73 (q, 1 H, J = 6.7 Hz, $CHCH_3$), 3.87 (dd, 1 H, J = 5.1, 6.9 Hz, NCH), 4.01 (dd, 1 H, J = 6.9, 9.5 Hz, OCH_AH_B), 5.0 (s, 1 H, OH), 7.2–7.4 (m, 10 H, 2 C_6H_5). The ratios of **32a:32b** were determined by integrating the two doublets at δ 1.36 (**32a**) and 1.47 (**32b**).

(1*R*,1′*R)- and (1*R**,1′*S**)-*N*-Hydroxy-*N*-(2′-methoxy-1′-phenylethyl)-2-butanamine (33a and 33b). A. From nitrone 24**: ether, 0 °C; flash chromatography (10% ethyl acetate in hexane); 87 mg (79%) of a 90:10 mixture of **33a:33b** as an oil; IR (neat) 3420, 3010, 2990, 2952, 2895, 1455, 755, 705 cm^{-1}. Hydroxylamine **33a**: ^1H NMR ($CDCl_3$, 200 MHz) δ 0.83 (t, 3 H, J = 7.2 Hz, CH_2CH_3), 0.96 (d, 3 H, J = 6.3 Hz, $CHCH_3$), 1.22–1.43 (8-line m, 1 H, CH_AH_B), 1.6–1.8 (8-line m, 1 H, CH_AH_B), 2.5 (6-line m, J = 6.3 Hz, $CHCH_3$), 3.31 (s, 3 H, OCH_3), 3.65 (dd, 1 H, J = 5.5, 9.7 Hz, OCH_AH_B), 3.92 (dd, 1 H, J = 5.6, 9.7 Hz, OCH_AH_B), 4.09 (t, 1 H, J = 5.7 Hz, $CHCH_2$), 7.3 (m, 5 H, C_6H_5).

B. From nitrone 23: ether, 0 °C; flash chromatography (20–30% ethyl acetate in hexane); 20 mg (57%) of a 8:92 mixture of **33a:33b** as an oil; IR (neat) 3415, 3063, 3030, 2968, 2934, 2874, 1602, 1494, 1454, 1112, 701 cm^{-1}. ^1H NMR of hydroxylamine **33b**: ($CDCl_3$, 200 MHz) δ 0.84 (t, 3 H, J = 7.5 Hz, CH_2CH_3), 1.10 (d, 3 H, J = 6.3 Hz, $CHCH_3$), 1.3–1.5 and 1.6–1.8 (2 m, 2 H, CH_2CH_3), 2.6–2.8 (m, 1 H, $CHCH_3$), 3.32 (s, 3 H, OCH_3), 3.60 (dd, 1 H, J = 4.8, 10.0 Hz, $CHCH_AH_BO$), 3.86 (dd, 1 H, J = 6.8, 10.0 Hz, $CHCH_AH_BO$), 4.17 (dd, 1 H, J = 5.4, 6.6 Hz, $CHCH_2O$), 7.2–7.5 (m, 5 H, C_6H_5). Anal. Calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48, N, 6.27. Found: C, 69.76; H, 9.20; N, 6.39. The ratios of **33a:33b** were determined by integrating the two doublets at δ 0.96 (**33a**) and 1.10 (**33b**).

(1′*R,2*R**)-*N*-Hydroxy-*N*-(1′-phenylethyl)-1-methoxy-3-methyl-2-butanamine (34a)**: nitrone **25**, methyllithium in ether, 0 °C for 2 h; flash chromatography (10% ethyl acetate in hexane); 0.22 g (87%) of a 97:3 mixture of **34a:34b** as an oil; IR (neat) 3400, 3063, 1601, 1197 cm^{-1}. Hydroxylamine **34a**: ^1H NMR ($CDCl_3$, 200 MHz) δ 0.83 and 0.99 (2 d, 6 H, J = 6.7 Hz, $CH(CH_3)_2$), 1.46 (d, 3 H, J = 6.4 Hz, $PhCHCH_3$), 2.04 (m, 1 H, $CHCHN$), 2.28 (m, 1 H, $NCHCH$), 3.31 (s, 3 H, OCH_3), 3.61 (dd, 1 H, J = 3.5, 10.40 Hz, OCH_AH_B), 3.73 (dd, 1 H, J = 4.1, 10.4 Hz, OCH_AH_B), 4.14 (q, 1 H, J = 6.4 Hz, PhCH), 4.97 (s, 1 H, OH), 7.30 (m, 5 H, C_6H_5). Anal. Calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.97; N, 5.90. Found: C, 70.64; H, 9.71; N, 5.96.

(1′*R,2*S**)-*N*-Hydroxy-*N*-(1′-phenylethyl)-1-methoxy-3-methyl-2-butanamine (34b)**: nitrone **26**, phenylmagnesium bromide in ether, 25 °C for 4 h; flash chromatography (10% ethyl acetate in hexane); 14 mg (43%) a 5:95 mixture of **34a:34b** as an oil. Hydroxylamine **34b**: ^1H NMR ($CDCl_3$, 200 MHz), δ 1.00 and 1.03 (2 d, 6 H, J = 6.7 Hz, $CH(CH_3)_2$), 1.31 (d, 3 H, J = 6.4 Hz, $PhCHCH_3$), 2.04 (m, 1 H, $CHCHN$), 2.74 (m, 1 H, $NCHCH$), 3.33 (s, 3 H, OCH_3), 3.47 (dd, 1 H, J = 3.5, 10.4 Hz, OCH_AH_B), 3.85 (dd, 1 H, J = 5.4, 10.4 Hz, OCH_AH_B), 4.17 (q, 1 H, J = 6.4 Hz, PhCH), 4.39 (s, 1 H, OH), 7.3 (m, 5 H, C_6H_5). The isomer ratios shown in Table IV were determined from the integration ratio over the two doublets at 1.46 (**34a**) and 1.31 (**34b**).

(1′*R,2*R**)- and (1′*R**,2*S**)-*N*-Hydroxy-*N*-(1′-phenylethyl)-1-[(dimethyl-*tert*-butylsilyl)oxy]-3-methyl-2-butanamine (35a and 35b). A. From nitrone 27**: methylmagnesium bromide, ether, 25 °C for 30 min; flash chromatography (2.5% ethyl acetate in hexane); 97 mg (94%) of a 8:92 mixture of **35a:35b** as an oil; IR (neat) 3684, 3536, 3456, 1089 cm^{-1}. Anal. Calcd for $C_{19}H_{35}NO_2Si$: C, 67.60; H, 10.45; N, 4.15. Found: C, 67.86; H, 10.09; N, 4.15.

B. Fron nitrone 28: phenylmagnesium bromide in ether, 0 °C for 30 min; flash chromatography (2% ethyl acetate in hexane); 97 mg (80%) of a 33:67 mixture of **35a:35b** as an oil.

Hydroxylamine **35a**: ^1H NMR ($CDCl_3$, 200 MHz) δ 0.00 and 0.02 (2 s, 6 H, $Si(CH_3)_2$), 0.73 and 0.93 (2 d, 6 H, J = 6.4 Hz, $CH(CH_3)_2$), 0.83 (s, 9 H, $C(CH_3)_3$), 1.39 (d, 3 H, J = 6.4 Hz, $PhCHCH_3$), 2.06 (m, 2 H, CHCH), 3.80 (dd, 1 H, J = 2.8, 11.0 Hz, OCH_AH_B), 3.91 (dd, 1 H, J = 2.7, 11.05 Hz, OCH_AH_B), 4.08 (q, 1 H, J = 6.4 Hz, PhCH), 5.44 (s, 1 H, OH), 7.21 (m, 5 H, C_6H_5). Hydroxylamine **35b**: ^1H NMR ($CDCl_3$, 200 MHz) δ 0.00 (s, 6 H, $Si(CH_3)_2$), 0.83 (s, 9 H, $SiC(CH_3)_3$), 0.90 and 0.96 (2 d, 6 H, J = 6.6, 6.7 Hz, $CH(CH_3)_2$), 1.22 (d, 3 H, J = 6.2 Hz, $PhCHCH_3$), 1.94 (m, 1 H, $CHCHN$), 2.60 (m, 1 H, $NCHCH$), 3.69 (dd, 1 H, J = 3.5, 10.3 Hz, OCH_AH_B), 3.98 (dd, 1 H, J = 5.7, 10.3 Hz, OCH_AH_B), 4.20 (q, 1 H, J = 6.2 Hz, PhCH), 4.42 (s, 1 H, OH), 7.20 (m, 5 H, C_6H_5). The isomer ratios shown in Table IV were determined from the ratio of the integral over the two doublets at 1.39 (**35a**) and 1.22 (**35b**) ppm.

(*R,*R**)-Diethyl *N*,*N*-Bis(1-phenylethyl)amino Phosphate (36b).** A solution of 0.32 g (1.31 mmol) of hydroxyamine **29b** in 12 mL of anhydrous THF was stirred and cooled at −78 °C as 1.1 mL (1.40 mmol) of 1.27 M *n*-butyllithium in hexane was added to reach the end point indicated by a color change to purple. Diethyl chlorophosphoridate (0.3 mL, 0.36 g, 2.08 mmol) was then added, and the solution was warmed to 0 °C and stirred at 0 °C for 2 h and at 25 °C for 20 min. Ice–water (10 mL) was added, and the aqueous mixture was saturated with sodium chloride. The organic layer was separated, and the aqueous layer was extracted with ether (3 × 15 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. Purification of the residue by flash chromatography (30% ethyl acetate in hexane) afforded 0.40 g (81%) of the phosphate as an oil: IR (neat) 3028, 2982, 2936, 1884, 1601, 1165, 922 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.40 (t-like, 6 H, J = 6.8 Hz, $P(OCH_2CH_3)_2$), 1.50 (d, 6 H, J = 6.6 Hz, $N(CHCH_3)_2$), 3.98 (q, 2 H, J = 6.6 Hz, $N(CHCH_3)_2$), 4.25 (m, 4 H, $P(OCH_2CH_3)_2$), 7.26 (s, 10 H, 2 C_6H_5); MS (70 eV) *m*/*e* (rel int) 377 (M^+, 1), 273 (19), 244 (19), 223 (100), 155 (23), 118 (90), 105 (16). Anal. Calcd for $C_{20}H_{28}NO_4P$: C, 63.66; H, 7.43; N, 3.71. Found: C, 63.50; H, 7.27; N, 3.77.

(*R,*S**)-Diethyl *N*,*N*-Bis(1-phenylethyl)amino Phosphate (36a)** was prepared from **29a** according to the procedure given for **36b**. Purification by flash chromatography (30% ethyl acetate in hexane) gave 0.1 g (20%) of the starting hydroxylamine **29a** and 0.49 g (60%) of the phosphate as an oil. The IR spectral data of phosphate **36a** are identical with those of phosphate **36b** given above. Phosphate **36a**: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.19 (t, 6 H, J = 7.2 Hz, $P(OCH_2CH_3)_2$), 1.42 (d, 6 H, J = 6.8 Hz, $N(CHCH_3)_2$), 3.89 (m, 4 H, $P(OCH_2CH_3)_2$), 4.26 (q, 2 H, J = 6.8 Hz, $N(CHCH_3)_2$), 7.3 (m, 10 H, 2 C_6H_5). Anal. Calcd for $C_{20}H_{28}NO_4P$: C, 63.66; H, 7.43; N, 3.71. Found: C, 63.62; H, 7.34; N, 3.85.

(*R,*S**)-*N*-(1′-Phenylethyl)-1-phenylethanamine (37a).** A solution of 0.44 g (1.16 mmol) of phosphate **36a** in 18 mL of ether and 30 mL of condensed ammonia was stirred at −78 °C as 24 mg (3 equiv) of lithium was added piece by piece. After the completion of the addition, the blue color was discharged by adding 8 mL of absolute ethanol. After evaporation of ammonia, the residue was dissolved in 10 mL of water and extracted with three 20-mL portions of ether. The combined ether layers were dried (K_2CO_3) and evaporated to give, after purification by chromatography (20% ethyl acetate in hexane), 0.20 g (76%) of amine **37a** as a liquid: IR (neat) 3322, 3061, 1601 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.35 (d, 6 H, J = 6.8 Hz, $N(CHCH_3)_2$), 1.54 (s, 1 H, NH), 3.76 (q, 2 H, J = 6.8 Hz, $N(CHCH_3)_2$), 7.28 (m, 10 H, 2 C_6H_5). Anal. Calcd for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22. Found: C, 85.26; H, 8.46; N, 6.32.

(*R,*R**)-*N*-(1′-Phenylethyl)-1-phenylethanamine (37b)** was prepared from **36b** according to the procedure given for amine **37a**. Purification by flash chromatography (20% ethyl acetate in hexane) gave 0.23 g (79%) of amine **37b** as an oil: IR (neat) 3323, 3061, 1603 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.26 (d, 6 H, J = 6.6 Hz, $N(CHCH_3)_2$), 1.57 (s, 1 H, NH), 3.49 (q, 2 H, J = 6.6 Hz, $N(CHCH_3)_2$), 7.29 (m, 10 H, 2 C_6H_5). Anal. Calcd for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22. Found: C, 84.98; H, 8.42; N, 6.30. The ^1H NMR spectral data for **37a** and **37b** agree with the literature values[24] reported for the *meso* and *d*,*l* amines, respectively.

(1*R,1′*S**)-Methyl *N*-(2′-Methoxy-1′-phenylethyl)-*N*-(1-phenylethyl)amino Carbonate (38).** A solution of 38 mg (0.140 mmol) of a 3:97 mixture of 32a:32b, 85 mg (1.07 mmol) of pyridine, and 4.5 mg (0.036 mmol) of 4-(dimethylamino)pyridine in 3 mL of anhydrous dichloromethane was stirred at 25 °C as 43 mg (0.45 mmol) of methyl chloroformate was added. After 5 min, the solution was diluted with 10 mL of dichloromethane, washed with water (2 × 3 mL), dried (K_2CO_3), and concentrated. Purification by flash chromatography (10% ethyl acetate in hexane) yielded 33 mg (71%) of carbonate **38** as an oil, which exhibited the following spectral properties: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.25–1.5 (m, 3 H, $CHCH_3$), 3.2 (br s, 3 H, $C(O)OCH_3$), 3.3–4.1 (m, 4 H), 3.87 (s, 3 H, OCH_3), 7.1–7.4 (m, 10 H, 2 C_6H_5).

(1*R,1′*S**)-*N*-(2′-Methoxy-1′-phenylethyl)-1-phenylethanamine (39).** A solution of 33 mg (0.100 mmol) of **38** in 10 mL of liquid ammonia and 2 mL of THF was stirred at −33 °C as 2 mg (0.3 mmol) of lithium was added. After the blue color persisted for 1 min, the blue solution was discharged by addition of 1 mL of absolute ethanol and evaporated. The residue was acidified with 1 N hydrochloric acid to pH <1. The acidic aqueous solution was washed with ether (1 mL) and then basified with 1 N sodium hydroxide solution to pH >10. The resulting basic suspension was extracted with ether (3 × 10 mL). The combined ether extracts were dried (K_2CO_3) and concentrated to give 20 mg (80%) of amine **39** as a colorless oil: IR (neat) 3330, 3083, 3061, 2924, 2888, 1603, 1493, 1453, 7608 700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.32 (d, 3 H, J = 6.8 Hz, $CHCH_3$), 2.3 (s, 1 H, NH), 3.27 (s, 3 H, OCH_3), 3.31 (dd, 1 H, J = 4.0, 9.5 Hz, OCH_AH_B), 3.41 (t, 1 H, J = 9.5 Hz, OCH_AH_B), 3.53 (q, 1 H, J = 6.8 Hz, $CHCH_3$), 3.63 (dd, 1 H, J = 4.0, 10.2 Hz, $CHCH_2$), 7.1–7.4 (m, 10 H, 2 C_6H_5); ^{13}C NMR ($CDCl_3$, 75 MHz), δ 24.79, 54.67, 58.59, 59.01, 77.72, 126.52, 126.71, 127.31, 127.75, 128.33, 128.38, 140.88, 145.43. The spectral data of **39** agree with the literature values.[26]

(−)-(*S*)-*N*-(2-Methylpropylidene)-1-phenylethanamine *N*-oxide [(*S*)-40] was prepared by condensation of isobutyraldehyde and optically active (*S*)-**10** according to the general procedure. Purification by flash chromatography (70% ethyl acetate in hexane) afforded 0.17 g (80%) of the nitrone as a solid: mp 61.5–63.5 °C; $[\alpha]^{25}_D$ −30.8° (*c* 4.12, $CHCl_3$); IR (neat) 3059, 1578, 1192 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.04 and 1.09 (2 d, 6 H, J = 7.0 and 6.6 Hz, $CH(CH_3)_2$), 1.79 (d, 3 H, J = 6.7 Hz, $PhCHCH_3$), 3.16 (m, 1 H, J = 7.0 Hz, =CHCH), 4.95 (q, 1 H, J = 6.7 Hz, PhCH), 6.57 (d, 1 H, J = 7.4 Hz, N=CH), 7.4 (m, 5 H, C_6H_5). Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.71; H, 9.32; N, 7.04.

(+)-(*R*)-*N*-(2-Methylpropylidene)-1-phenylethanamine *N*-Oxide [(R)-40]. A solution of 92 mg (0.41 mmol) of optically active hydroxylamine **41b** in 6 mL of methanol was stirred at 0 °C as 88 mg (0.41 mmol) of sodium periodate in 7 mL of water was added. After 7 min, the aqueous solution was extracted with three 20-mL portions of ether. The combined ether extracts were dried (K_2CO_3) and evaporated to give, after chromatographic purification (50% ethyl acetate in hexane), 35 mg (44%) of (*R*)-**40** as a solid, which was 98% pure by the ^1H NMR analysis. This solid exhibited the same ^1H NMR spectral properties as nitrone (*S*)-**40**.

(±)-*N*-(2-Methylpropylidene)-1-phenylethanamine *N*-oxide [(±)-40] was prepared according to the general procedure. Purification of flash chromatography (50% ethyl acetate in hexane) afforded 0.41 g (94%) of a white solid, mp 47–48.5 °C.

Differentiation of (*S*)- from (*R*)-**40** required 43 mg of chiral shift reagent, (*R*)-2,2,2-trifluoro-1-(9′-anthryl)ethanol in the presence of 21 mg of nitrone **40**. With 1 equiv of nitrone (*R*)-**40**, 0.5 equiv of (*S*)-**40** (total weight of the two enantiomers: 21 mg), and 43 mg of the chiral shift reagent, the ratio of the integral over the two doublets at 1.46 [(*R*)-**40**] and 1.54 [(*S*)-**40**] ppm is 2 to 1. This proves that the configuration of **41b** is 1′*R*,2*S*.

(1′*S*,2*S*)- and (1′*R*,2*S*)-2-[*N*-Hydroxy-*N*-(1′-phenylethyl)amino]-3-methyl-1-butanol (41a and 41b). A solution of 0.88 g (2.75 mmol) of nitrone (*S*)-**27** in 70 mL of ether was stirred at 0 °C as 2.7 mL (8.25 mmol) of 3.1 M of methylmagnesium bromide in ether was added. The solution was stirred at 0 °C for 2 h and hydrolyzed with saturated ammonium chloride solution. The ether layer was separated, and the aqueous layer was extracted with ether (2 × 20 mL). The ether layers were combined, dried (Na_2SO_4), and concentrated. Purification of the crude residue by flash chromatography (5% ethyl acetate in hexane) afforded 0.82 g (88%) of two isomeric hydroxylamines as an oil. ^1H NMR analysis showed that this oil is a 4:1 mixture of **35b**:**35a**. Desilylation of the oil was performed according to Corey's procedure.[43] A solution of 0.80 g (2.38 mmol) of the above oil in 25 mL of THF was stirred at 0 °C as 0.99 g (3.13 mmol) of tetrabutylammonium fluoride trihydrate was added. The solution was then stirred at room temperature for 45 min. Saturated sodium chloride solution (10 mL) and 10 mL of ether were added, and the organic layer was separated. The aqueous layer was extracted with ether (2 × 20 mL). The organic layers were combined, dried (K_2CO_3), and concentrated to give a mixture of **41a** and **41b**. Careful purification of the mixture by flash chromatography (10–20% ethyl acetate in hexane) on a 34-min

(43) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191.

column packed with 133 g of silica gel afforded 65 mg (12%) of the less polar **41a** as a solid and 306 mg (58%) of a mixture of **41a** and the more polar **41b** as a solid. Recrystallization of the mixture from 10 mL of petroleum ether gave 215 mg of pure **41b**.

Hydroxylamine (1′*S*,2*S*)-**41a**: mp 107–109 °C (racemic **41a**, mp 89.5–91.5 °C); IR (KBr) 3430 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.89 and 0.99 (2 d, 6 H, *J* = 6.0 and 6.4 Hz, $CH(CH_3)_2$), 1.44 (d, 3 H, *J* = 6.3 Hz, $PhCHCH_3$), 2.20 (m, 2 H, CHCH), 2.95 (s, 1 H, CH_2OH), 3.65 (dd, 1 H, *J* = 4.7, 12.1 Hz, OCH_AH_B), 4.09 (dd, 1 H, *J* = 2.0, 12.1 Hz, OCH_AH_B), 4.21 (q, 1 H, *J* = 6.3 Hz, PhCH), 5.02 (s, 1 H, NOH), 7.25 (m, 5 H, C_6H_5). Anal. Calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 69.97; H, 9.55; N, 6.19.

Hydroxylamine (1′*R*,2*S*)-**41b**: mp 66.5–68.5 °C (racemic **41b**, mp 119–121 °C); $[\alpha]^{25}_D$ + 15.2° (*c* 2.30, $CHCl_3$); IR, identical with that of **41a**; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.01 (2 d, 6 H, *J* = 6.6 Hz, $CH(CH_3)_2$), 1.31 (d, 3 H, *J* = 6.6 Hz, $PhCHCH_3$), 2.23 (m, 1 H, *J* = 7.0 Hz, CHCHN), 2.45 (m, 1 H, NCHCH), 2.9 (br s, 1 H, CH_2OH), 3.74 (dd, 1 H, *J* = 5.9, 12.0 Hz, OCH_AH_B), 3.92 (dd, 1 H, *J* = 2.2, 12.0 Hz, OCH_AH_B), 4.20 (q, 1 H, *J* = 6.6 Hz, PhCH), 4.9 (br s, 1 H, NOH), 7.3 (m, 5 H, C_6H_5). Anal. Calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 70.00; H, 9.38; N, 6.43.

(1′*S*,2*S*)-2-[(*N*-Methoxy-*N*-(1′-phenylethyl)amino]-3-methyl-1-butanol (42a). A solution of 42 mg (0.19 mmol) of **41a** in 3 mL of anhydrous THF was stirred at −78 °C as 0.65 mL (0.51 mmol) of 0.79 M *n*-butyllithium in hexane was added. After ca. 10 min a solution of 73 mg (0.51 mmol) of methyl iodide in 2 mL of THF was added in succession. The mixture was warmed to room temperature and stirred for 4 h. Saturated sodium chloride solution (5 mL) was added, and the resulting aqueous solution was extracted with three 8-mL portions of ether. The ether extracts were combined, dried (K_2CO_3), and concentrated. Purification by flash chromatography (5% ethyl acetate in hexane) gave 2.5 mg (5%) of the less polar **43a** as an oil and 26 mg (58%) of the more polar **42a** as an oil. *N*-Methoxy alcohol **42a**: ($CDCl_3$, 200 MHz) δ 0.90 and 1.03 (2 d, 6 H, *J* = 6.3 Hz, $CH(CH_3)_2$), 1.48 (d, 3 H, *J* = 6.2 Hz, $PhCHCH_3$), 2.15 (m, 2 H, CHCHN and CH_OH), 2.97 (dd, 1 H, *J* = 2.8, 8.8 Hz, NCHCH), 3.55 and 4.19 (2 m, 1 H and 2 H, OCH_2 and PhCH), 3.62 (s, 3 H, $NOCH_3$), 7.25 (s, 5 H, C_6H_5). The spectral data of **43a** are given below.

(1′*R,2*S**)-2-[*N*-Methoxy-*N*-(1′-phenylethyl)amino]-3-methyl-1-butanol (42b)** was prepared according to the procedure given for **42a** from hydroxylamine **41b**. Purification by flash chromatography (10% ethyl acetate in hexane) afforded 86 mg (61%) of *N*-methoxy alcohol **42b** as an oil and 10 mg (6%) of double methylated **43b** as an oil. *N*-Methoxy alcohol **42b**: IR (neat) 3460, 1157 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (d, 6 H, *J* = 7.2 Hz, $CH(CH_3)_2$), 1.37 (d, 3 H, *J* = 6.5 Hz, $PhCHCH_3$), 2.17 (m, 1 H, *J* = 6.6 Hz, CHCHN), 2.44 (m, 1 H, NCHCH), 2.88 (t, 1 H, *J* = 5.7 Hz, OCH_AH_B), 3.36 (br s, 3 H, OCH_3), 3.68–3.8 (m, 2 H, OCH_AH_B and OH), 4.14 (q, 1 H, *J* = 6.5 Hz, PhCH), 7.3 (m, 5 H, C_6H_5). The spectral data of **43b** are given below.

(1′*S*,2*S*)-*N*-Methoxy-*N*-(1′-phenylethyl)-1-methoxy-3-methyl-2-butanamine (43a). A suspension of 13 mg (0.54 mmol) of sodium hydride was stirred at room temperature as 26 mg (0.11 mmol) of *N*-methoxy alcohol **42a** in 5 mL of THF was added. After 1.5 h, 77 mg (0.54 mmol) of methyl iodide was added and stirring was continued for 7 h. Saturated sodium chloride solution (5 mL) was added, and the aqueous solution was extracted with three 8-mL portions of ether. The combined ether extracts were dried (K_2CO_3) and concentrated to give, after chromatographic purification (5% ethyl acetate in hexane), 17.4 mg (64%) of **43a** as an oil: IR (neat) 3063, 1603, 1197, 1111, 1041 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.83 and 0.98 (2 d, 6 H, *J* = 6.6 and 6.1 Hz, $CH(CH_3)_2$), 1.44 (d, 3 H, *J* = 6.2 Hz, $PhCHCH_3$), 1.85 (m, 1 H, CHCHN), 2.28 (m, 1 H, NCHCH), 3.26 (s, 3 H, CH_2OCH_3), 3.35 (dd, 1 H, *J* = 4.4, 9.5 Hz, OCH_AH_B), 3.60 (s, 3 H, $NOCH_3$), 3.78 (dd, 1 H, *J* = 4.1, 9.5 Hz, OCH_AH_B), 4.20 (q, 1 H, *J* = 6.2 Hz, PhCH), 7.3 (m, 5 H, C_6H_5); MS (70 eV) *m/e* (rel int) 206 ($M^+ - CH_2OCH_3$, 16), 105 (100). Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.65; H, 10.02; N, 5.59. Found: C, 72.19; H, 10.10; N, 5.64.

N-Methoxyamine (±)-**43a** was also prepared from a 96:4 mixture of hydroxylamines **34a**:**34b** according to the procedure given for **42a**. Chromatographic purification (10% ethyl acetate–hexane) gave 37 mg (20%) of **43a** and 80 mg (57%) of the starting material. The spectral data for the product (**43a**) are identical with those of **43a** given above.

(1′*R,2*S**)-*N*-Methoxy-*N*-(1′-phenylethyl)-1-methoxy-3-methyl-2-butanamine (43b)** was prepared from (±)-**41b** according to the procedure given for **43a**. Purification by flash chromatography (10% ethyl acetate in hexane) gave 45 mg (53%) of an oil: IR and mass spectral data of compound **43b** are identical with those of **43a** given above. The ^1H NMR spectral data of **43b** are as follows: ($CDCl_3$, 200 MHz) δ 0.96 and 1.01 (2 d, 6 H, *J* = 7.1 and 7.1 Hz, $CH(CH_3)_2$), 1.37 (d, 3 H, *J* = 6.7 Hz, $PhCHCH_3$), 1.99 (m, 1 H, *J* = 6.7 Hz, CHCHN), 2.66 (q-like, 1 H, *J* = 5.1 Hz, NCHCH), 3.18 (s, 3 H, $NOCH_3$), 3.29 (s, 3 H, CH_2OCH_3), 3.38 (dd, 1 H, *J* = 4.4, 10.3 Hz, OCH_AH_B), 3.72 (dd, 1 H, *J* = 5.4, 10.3 Hz, OCH_AH_B), 4.12 (q, 1 H, *J* = 6.7 Hz, $PhCHCH_3$), 7.3 (m, 5 H, C_6H_5).

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Supplementary Material Available: Copies of ^1H NMR spectra of compounds **6**, **19**, **21**, **34b**, **38**, **42a**,**b** and **43b** (10 pages). Ordering information is given on any current masthead page.