Diastereoselective 1,2-Addition of Lithiated *N*-(Trialkylsilyl)methylphenylsulfoximines to Aldehydes: Preparation of 1,4,3-Oxathiazin-2(6*H*)-one 4-Oxides as Novel Cyclic Sulfoximines

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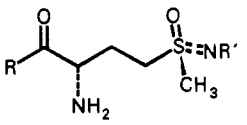
High field NMR and X-ray cryatallographic methods were used to elucidate the diastereoselectivity of 1,2-addition of lithiated *N*-(trialkylsilyl)methylphenylsulfoximines to aldehydes. The resulting (β-hydroxyalkyl)sulfoximines were readily cyclized with phosgene to yield the novel sulfoximine-derived 1,4,3-oxathiazin-2(6*H*)-one 4-oxides.

The sulfoximine as a functional group was unknown to organic chemistry until 1950, when Bentley and co-workers reported the structure elucidation of methionine sulfoximine, **1a**.[2,3] The latter, specifically as the 2*S*,5*S* isomer, is a potent inhibitor of the enzyme glutamine synthetase (EC 6.3.1.2)[4] and is responsible for the mammalian neurotoxicity associated with the ingestion of nitrogen trichloride bleached flour. Methionine sulfoximine was subsequently reported as a natural product in the form of the tripeptide N-phosphate **1b**,[5] the first naturally occurring sulfoximine to be discovered. Heterocyclic sulfoximines have also attracted considerable interest, because of a wide variety of physiological activities including spasmolytic, central nervous system depressant, antisecretory, antihistamine, bronchorespiratory, antiinflammatory, and antihypertensive properties.[6] The remarkable biological activity of many sulfoximines, as well as the interesting diversity of reactions associated with the functionality itself, has stimulated continued interest in sulfoximine chemistry.[7]

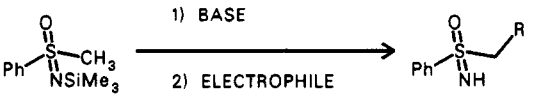


1a R=OH, R'=H

1b R=ala-ala

R'=PO_3H_2

Scheme I



2c

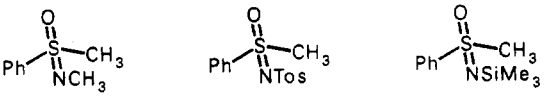
3a R=CH_2CH_2OH

3b R=$CH_2CH(OCH_3)_2$

3c R=$COCH_3$

3d R=$COOCH_3$

We have been interested for some time in the reactivity of α-sulfonimidoyl carbanions, particularly those obtained from methylphenylsulfoximines of the general type **2a–c**.



2a 2b 2c

Lithiation and alkylation were first described for **2a**,[8] and optically active methylcarbinols have been obtained from the reaction of resolved **2a** with carbonyl compounds, followed by desulfurization.[9] Carbanion alkylations have also been reported for the *N*-tosylsulfoximine **2b**.[8,10] More recently, one of us has described the lithiation and alkylation of *N*-(trimethylsilyl)methylphenylsulfoximine (**2c**);[11] in this instance lability of the silyl protecting group permits facile conversion of alkylation products to the free sulfoximines, in contrast with the use of **2a** and **2b** as precursors.

This paper describes our studies on the 1,2-addition of the lithium salt of **2c** to aldehydes and ketones. Desilylation of the resulting addition products afforded free (β-hydroxyalkyl)sulfoximines, which could be readily cyclized to the previously unknown 1,4,3-oxathiazin-2(6*H*)-one 4-oxide ring systems. Structure elucidation of the latter, using proton NMR and single-crystal X-ray diffraction methods, has permitted unequivocal assignment of the stereochemistry of the 1,2-addition products. We have also

(1) Present address: Korea Research Institute of Chemical Technology, Daeduk-Danji, South Korea.

(2) (a) Oae, S.; Furukawa, N. *Sulfilimines and Related Derivatives*, ACS Monograph 179; American Chemical Society: Washington, D. C., 1983; p 297. (b) Kennewell, P. D.; Taylor, J. B. *Chem. Soc. Rev.* **1980**, *9*, 477.

(3) Bentley, H. R.; McDermott, E. E.; Moran, T.; Pace, J.; Whitehead, J. K. *Proc. R. Soc. London, Ser. B* **1950**, *137*, 402.

(4) Meister, A. In *Enzyme-Activated Irreversible Inhibitors*; Seiler, N., Jung, M. J., Koch-Weser, J. Eds.; Elsevier: Amsterdam, 1978; p 187.

(5) (a) Preuss, D. L.; Scannell, J. P.; Ax, H. A.; Kellett, M.; Weiss, F.; Demny, T. C.; Stempel, A. *J. Antibiot.* **1973**, *26*, 261. (b) Scannell, J. P.; Pruess, D. L.; Demny, T. C.; Ax, H. A.; Weiss, F.; Williams, T.; Stempel A. In *The Chemistry and Biology of Peptides*; Meienhofer, J., Ed.; Ann Arbor Science: Ann Arbor, 1972; p 415.

(6) See references cited in 2b.

(7) (a) Johnson, C. R.; Barbachyn, M. R.; Meanwell, N. A.; Stark, C. J., Jr.; Zeller, J. R. *Phosphorus Sulfur* **1985**, *24*, 151. (b) Levenson, C. H.; Meyer, R. B., Jr. *J. Med. Chem.* **1984**, *27*, 228. (c) Dillard, R. D.; Yen, T. T.; Stark, P.; Pavey, D. E. *J. Med. Chem.* **1980**, *23*, 717. (d) Schaffner-Sabba, K.; Tomaselli, H.; Henrici, B.; Renfroe, H. B. *J. Org. Chem.* **1977**, *42*, 952. (e) Stoss, P.; Satzinger, G. *Chem. Ber.* **1976**, *109*, 2097; (f) **1975**, *108*, 3855.

(8) Johnson, C. R. *Acc. Chem. Res.* **1973**, *6*, 341.

(9) (a) Johnson, C. R.; Lockard, J. P. *Tetrahedron Lett.* **1971**, 4589. (b) Johnson, C. R.; Lockard, J. P.; Kennedy, E. R. *J. Org. Chem.* **1980**, *45*, 264. (c) Johnson, C. R.; Stark, C. J. Jr. *Ibid.* **1982**, *47*, 1193.

(10) Johnson, C. R.; Kirchhoff, R. A.; Reischer, R. J.; Katekar, G. F. *J. Am. Chem. Soc.* **1973**, *95*, 4287.

(11) Hwang, K.-J. *J. Org. Chem.* **1986**, *51*, 99.

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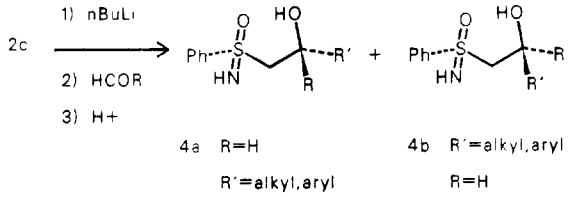
Table I. Condensation of *N*-(Trimethylsilyl)methylphenylsulfoximine (2c) with Aldehydes and Ketones



entry	R, R′	yield (%)[a]	ratio 4a/4b[b]
1	H, CH_3	69	2:1
2	H, $CH(CH_3)_2$	80	2:1
3	H, $CH_2CH(CH_3)_2$	79	2:1
4	H, $C(CH_3)_3$	91	2.5:1
5	H, Ph	81	2.8:1[c]
6	H, 2-thienyl	94	2.3:1[c]
7	H, H	41[d]	n.a.
8	CH_3CH_2, Ph	70	n.a.[e]
9	$CH_2(CH_2)_2CH_2$	83	n.a.
10	$CH_2(CH_2)_3CH_2$	97	n.a.

[a] Yields are given for purified products and are not optimized. [b] Estimated from integrated 400-MHz proton NMR spectra (see text). [c] Ratio based on separation of diastereomeric products. [d] Low yield caused by product solubility in water. [e] An unassigned 2.2:1 ratio of tertiary (β-hydroxyalkyl)sulfoximines was obtained.

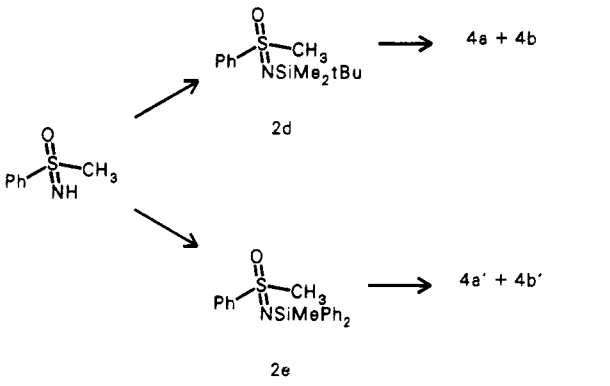
observed that the N-trialkylsilyl group can be utilized as a unique stereochemical control element to enhance the diastereoselectivity of the addition reaction. Possible mechanistic rationales for these observations will be considered.[12]

Results and Discussion

As reported previously,[11] the anion of **2c** may be readily condensed with oxiranes, halo acetals, acid chlorides, and alkyl chloroformates to produce, after methanolysis of the N-trimethylsilyl group, the corresponding sulfonimidoyl alcohols, acetals, ketones, and esters **3a–d** (Scheme I). Such products cannot be prepared directly by any other methodology. It was also of interest to investigate 1,2-additions of the anion of **2c** to aldehydes and ketones, particularly with the aim of elucidating the diastereoselectivity of such processes. Modest diastereoselectivity has been reported for addition of the lithium salt of *N*-methylmethylphenylsulfoximine (**2a**) to aldehydes and acyclic ketones, although structure assignment of the diastereomeric products was not reported.[9,13]

We have found that treatment of racemic *N*-(trimethylsilyl)methylphenylsulfoximine (**2c**)[11] with an equivalent of *n*-butyllithium in ether at −78 °C, followed by addition of aldehyde or ketone and workup with dilute aqueous hydrochloric acid, furnished the free (β-hydroxyalkyl)sulfoximines **4a** and **4b** in good yield (Table I). Product ratios were insensitive to reaction temperature over the range −78 °C to −10 °C. Most diastereomeric alcohols were inseparable chromatographically,[9] and ratios were estimated by integration of 400-MHz proton NMR spectra. However, the products arising from the reaction of **2c** with propiophenone (entry 8) could be separated on silica gel, while those obtained from benzaldehyde (entry 5) and 2-thiophenecarboxaldehyde (entry 6) were largely separated by fractional crystallization. Diastereomer structure assignments were based on spectroscopic analysis of the secondary alcohol products **4a** and **4b**, as well as the corresponding cyclized 1,4,3-oxathiazin-2(6*H*)-one 4-oxides; an X-ray structure determination was performed on one of the latter (vide infra).

Table II. Effect of N-Trialkylsilyl Group on Diastereoselectivity of Aldehyde 1,2-Additions



		diastereomer ratio 4a/4b[a]		
entry	R, R′	2c	2d	2e
1	H, CH_3	2:1	4:1	6:1[b]
2	H, $C(CH_3)_3$	2.2:1	8:1	8:1[b]

[a] Estimated from integrated 400-MHz proton NMR spectra. [b] Reaction products isolated as the *N*-(methyldiphenylsilyl)sulfoximines **4a′** and **4b′**.

As indicated in Table I, diastereoselectivity of the 1,2-addition process was relatively insensitive to the steric bulk of the reacting aldehyde. However, it occurred to us that variations in the size of the N-trialkylsilyl group might influence the stereochemical course of the reaction; *tert*-butyldimethylsilyl and methyldiphenylsilyl substituents were chosen to explore this idea. Thus, racemic *N*-(*tert*-butyldimethylsilyl)methylphenylsulfoximine (**2d**) was quantitatively prepared by treatment of methylphenylsulfoximine[14a] with *N*-methyl-*N*-(*tert*-butyldimethylsilyl)trifluoroacetamide (MTBSTFA),[14b] followed by vacuum distillation (Table II); attempted quenching of the *N*-lithiosulfoximide with *tert*-butyldimethylchlorosilane failed to give any **2d**. However, the latter procedure afforded the corresponding *N*-(methyldiphenylsilyl)-methylphenylsulfoximine (**2e**) in good yield. 1,2-Additions of lithiated **2d** and **2e** to acetaldehyde and pivalaldehyde were performed in the manner previously described. The remarkable hydrolytic stability of the N-methyldiphenylsilyl group permitted direct chromatographic purification of the N-silylated (β-hydroxyalkyl)sulfoximines **4a/4b**. As indicated in Table II, the use of larger N-silyl groups enhances the diastereoselectivity of 1,2-addition, particularly when a sterically bulky aldehyde is used. The possible origin of this remarkable directing effect will be considered later.

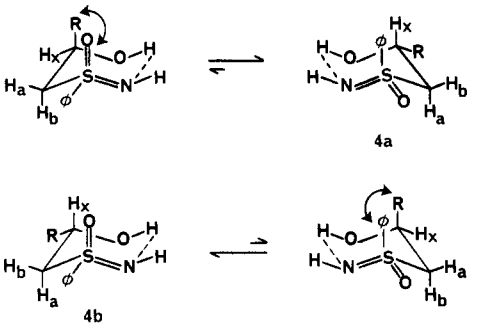
Tentative structure assignments of the diastereomeric secondary alcohols **4a** and **4b** were made in the following manner. In deuteriochloroform such compounds would likely adopt internally hydrogen-bonded conformations of some rigidity, permitting the coupling constants of H_A, H_B, and H_X to be analyzed according to the equation of Karplus.[15] Similar coupling constants in the ABX patterns

(12) All compounds reported in this paper are racemic, although single enantiomers are depicted for the sake of clarity.

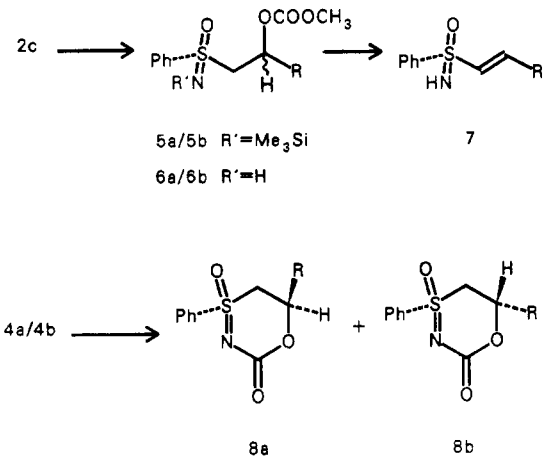
(13) High diastereoselectivity has been noted in the 1,2-addition of lithiated **2a** to sterically congested cyclic ketones: (a) Johnson, C. R.; Zeller, J. R. *Tetrahedron* **1984**, *40*, 1225; (b) *J. Am. Chem. Soc.* **1982**, *104*, 4021. (c) Johnson, C. R.; Meanwell, N. *Ibid.* **1981**, *103*, 7667. For an imaginative preparation of oxetanes via 1,2-addition of the anion derived from **2b**, see: Welch, S. C. Prakasa Rao, A. S. C.; Lyon, J. T.; Assercq, J. M. *J. Am. Chem. Soc.* **1983**, *105*, 252.

(14) (a) Johnson, C. R.; Haake, M.; Schroeck, C. W. *J. Am. Chem. Soc.* **1970**, *92*, 6594. (b) Mawhinney, T. P.; Madson, M. A. *J. Org. Chem.* **1982**, *47*, 3336.

Scheme II



Scheme III



of both diastereomers suggest predominant conformations in which similar bond angles are maintained for protons H_A, H_B, and H_X (Scheme II). Ring inversion to maintain hydrogen bonding with the more basic sulfoximine nitrogen and the resulting 1,3-diaxial relationship between the sulfoximine phenyl ring and H_X would cause significant shielding and therefore an upfield shift of the latter.[16] Structure **4a** was thus assigned to the major diastereomer, which exhibits a consistent upfield shift for H_X of approximately 0.6 ppm in the 400-MHz proton NMR spectra of all the (β-hydroxyalkyl)sulfoximines **4a** and **4b**. However, the inferential nature of these arguments underscored the desirability of obtaining an X-ray crystal structure. Neither of the crystalline (β-hydroxyalkyl)sulfoximines **4a** that could be isolated largely as a single diastereomer (entries 5 and 6, Table I) was suitable for X-ray structure determination, and it was hoped that a cyclic derivative of these compounds would be more amenable to such analysis.

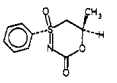
Bridging the sulfoximine nitrogen and β-hydroxyl functionalities of the sulfoximines **4a/4b** with a carbonyl group would provide entry to the previously unknown 6-membered 1,4,3-oxathiazin-2(6*H*)-one 4-oxide ring system. It was found that quenching the 1,2-addition reaction of **2c** and aldehydes with methyl chloroformate resulted in formation of the diastereomeric *N*-trimethylsilyl carbonates **5a/5b**, which could be readily hydrolyzed to the free sulfoximines **6a/6b** (Scheme III). All attempts to effect thermal or base-catalyzed cyclization of **6a/6b** led to formation of the olefins **7** (*E* isomer only), which also resulted from treatment of (β-hydroxyalkyl)sulfoximines **4a/4b** with the phosgene equivalent carbonyldiimidazole.[17]

(15) For a discussion of hydrogen bonding in sulfoximines, see p 304 of ref 2a.
(16) (a) Waugh, J. S.; Fessenden, R. W. *J. Am. Chem. Soc.* **1957**, *79*, 846; (b) **1958**, *80*, 6697.

Table III. Preparation of 1,4,3-oxathiazin-2(6*H*)-ones 8a/8b from (β-Hydroxyalkyl)sulfoximines 4a/4b

entry	R	yield (%)[a]
1	CH_3	81
2	$CH(CH_3)_2$	71
3	$CH_2CH(CH_3)_2$	49
4	Ph	66
5	2-thienyl	48
6	H	47

[a] Combined yield of both diastereomers.



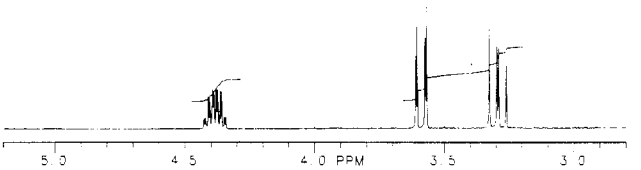


Figure 1. 400-HMz ABX spectrum ($CDCl_3$) of **9** (Table III, entry 1, major diastereomer).

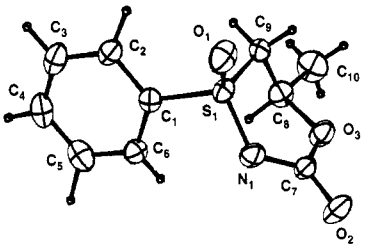
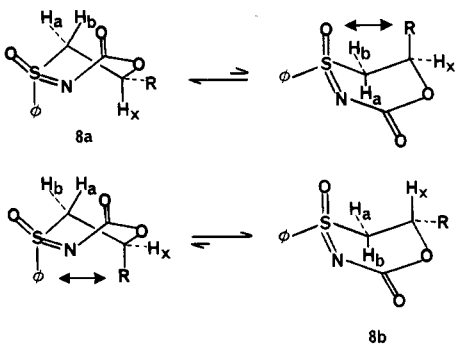


Figure 2. ORTEP perspective plot of **9**.

Scheme IV

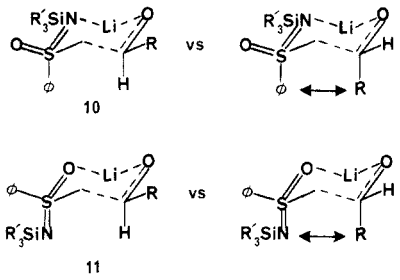


However, triethylamine-catalyzed reaction of **4a/4b** with phosgene[18] itself promoted smooth cyclization to the novel heterocyclic 1,4,3-oxathiazin-2(6*H*)-one 4-oxides **8a/8b**, the diastereomers of which were in most cases separable either by fractional crystallization or chromatography on silica gel. The results of these investigations are summarized in Table III.

Examination of models of the 1,4,3-oxathiazin-2(6*H*)-one 4-oxides **8a** and **8b** suggested that they would adopt twist-boat conformations, as depicted in Scheme IV. The product **8a** arising from the major (β-hydroxyalkyl)sulfoximine diastereomer **4a** would favor a conformation with H_X occupying an approximately 1,3 diaxial relationship with the sulfoximine phenyl ring. This proton would

(17) Kutney, J. P.; Ratcliffe, R. H. *Synth. Commun.* **1975**, *5*, 47.
(18) Barnes, A. C.; Kennewell, P. D.; Taylor, J. B. *J. Chem. Soc., Chem. Commun.* **1973**, 776.

Scheme V



consequently display a resonance upfield from that of H_X in the minor diastereomer **8b**. The proton NMR spectra of the diastereomers exhibit consistent H_X shift differences of approximately 0.6 ppm throughout the series. The 400-MHz ABX spectrum of the major methyl-substituted diastereomer **9** (Table III, entry 1, **8a**) is displayed in Figure 1.

The configuration and specific conformation of **9** were determined by X-ray crystallographic analysis. A computer-generated ORTEP perspective plot is illustrated in Figure 2. A single enantiomer (S_R,C_R) is depicted, although this compound crystallizes as a racemic mixture to which was assigned the noncentrosymmetric and nonenantiomorphous space group C_c, based on various statistical indicators calculated with normalized structure factors.[19] Crystallographic, positional, and thermal parameters are satisfactory, and interatomic distances and angles agree well with accepted values. No unreasonably short inter- or intramolecular contacts are apparent.

The X-ray structure determination of **9** thus confirms the diastereoselectivity inferred for the 1,2-addition to aldehydes of lithiated sulfonimidoyl carbanions derived from sulfoximines **2c**, **2d**, and **2e**. While only one other study on the 1,2-addition of α-sulfonimidoyl carbanions to aldehydes has appeared,[9] the analogous reaction of carbanions derived from alkylphenylsulfoxides has been investigated extensively.[20] Attempts have been made to rationalize the modest diastereoselectivity observed for such reactions on the basis of a cyclic six-membered transition state,[21] although the applicability of such a transition-state model for α-sulfinyl carbanions is unclear.[22] A cyclic transition state **10** involving nitrogen–lithium chelation can be visualized for sulfonimidoyl carbanion additions (Scheme V). However, orientation of the N-trialkylsilyl group away from the aldehyde makes it difficult to explain the diastereoselectivity enhancement observed for bulky silyl groups. The oxygen-coordinated model **11**, on the other hand, provides for interaction of the silylated sulfoximine nitrogen with the R group of the incoming aldehyde.[23] Even so, the precise orientation of the N-trialkylsilyl group relative to the sulfur center is uncertain, since few N-substituted sulfoximine structures are known. Another objection to such cyclic transition-state models arises from positioning the metal cation between two heteroatoms and far from the α-carbanionic center. This seems implausible for the transition state of an exothermic reaction, whose geometry should in principle resemble that of starting materials more than products.[24] Finally, the extent of aggregation of the reacting α-sulfonimidoyl carbanion is unknown and may not involve monomeric species at all. It would thus appear that simple visualization of the transition-state geometry of sulfoximine carbanion additions to carbonyl groups remains problematic, given our current state of knowledge. Nevertheless, the remarkable influence on reaction diastereoselectivity of the N-trialkylsilyl group of **2c–e** and its implications for developing a transition-state model for the 1,2-addition process merit further investigation.

Conclusion

Elucidation of the diastereoselectivity of addition of α-sulfonimidoyl carbanions to aldehydes has made possible, for the first time, the preparation of secondary (β-hydroxylalkyl)sulfoximines of predictable stereochemistry. Such compounds can serve as intermediates for the preparation of cyclic sulfoximine derivatives of defined stereochemistry, an area of considerable interest to medicinal chemistry. Since carbon–sulfur bond cleavage provides a route to methylcarbinols,[9] a highly stereoselective preparation of (β-hydroxyalkyl)sulfoximines offers access to secondary methylcarbinols of predictable chirality, starting with the requisite enantiomer of N-trialkylsilyl sulfoximines such as **2d** and **2e**. Finally, mechanistic investigations of the reaction diastereoselectivity, and the origin of N-trialkylsilyl group's stereochemical directing effect, may yield a better understanding of the transition-state geometry for such 1,2-addition processes, as well as methods for obtaining even greater diastereoselectivity. Further study of this area offers interesting new directions for developing the chemistry of the sulfoximine group.

Experimental Section

General Experimental Details. Reactions were routinely performed in flame-dried apparatus under a positive pressure of nitrogen. All solvents and reagents were used as received from Aldrich Chemical Co. A solution of 1.9 M phosgene in toluene was purchased from Fluka Chemical Co. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Varian EM-360L (60 MHz) and XL400 (400 MHz) spectrometers. ^{13}C NMR spectra were recorded on a Bruker 360 (90 MHz) spectrometer. Shifts are reported as ppm downfield from tetramethylsilane. Analytical thin-layer chromatography (TLC) was performed on precoated Merck glass plates with a 0.25-mm layer of silica gel containing a 254-nm fluorescent indicator. Chromatographic separations were performed either on a Waters Prep-500 instrument or by using the flash column technique. Gas chromatography (GC) was performed on a Hewlett-Packard 5790 instrument equipped with a flame ionization detector; glass columns were packed with OV101 silicone gum coated on WHP (80/100 mesh). GC analyses were run over 150–300 °C, with a heating rate of 15°/min. Elemental analyses were performed by Atlantic Microlab Inc., Atlanta, GA (certain β-hydroxy sulfoximines **4a/4b** and 1,4,3-oxathiazin-2(6*H*)-one 4-oxides **8a/8b** showed a tendency to retain solvent, thus affecting accuracy).

General Procedure for the Synthesis of β-Hydroxy Sulfoximines 4a/4b. An equivalent of *n*-butyllithium in hexane was added over 10 min to vigorously stirred solution of **2c** in ether (1 mmol/mL) at −78 °C, and the reaction mixture was allowed

(19) See crystallographic experimental description.

(20) (a) Farnum, D. G.; Veysoglu, T.; Carde, A.; Duhl-Emswiler, B.; Pancoast, T. A.; Reitz, T. J.; Carde, R. T. *Tetrahedron Lett.* **1977**, 4009. (b) Kunieda, N.; Kinoshita, M.; Nokami, J. *Chem. Lett.* **1977**, 289. (c) Tsuchihashi, G.; Iriuchijima, S.; Ishibashi, M. *Tetrahedron Lett.* **1972**, 4605.

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to warm to 0 °C. The resulting white suspension was stirred at 0 °C for 0.5 h and was recooled to −78 °C, whereupon 1.1 equiv of aldehyde was added. The reaction mixture was stirred at ambient temperature for 3–4 h, and then 2 equiv of 3 N aqueous HCl was added (*CAUTION*! exothermic reaction). After stirring at 20 °C for 0.5 h, the phases were separated and the ether phase was washed with a small amount of aqueous 3 N HCl. The aqueous washes were combined, extracted with hexane, and then basified with aqueous 50% NaOH. The resulting suspension was extracted several times with dichloromethane. The dichloromethane was washed with brine, filtered through $MgSO_4$, and concentrated in vacuo to yield crude products, which usually contained some methylphenylsulfoximine. Unless otherwise stated, silica gel chromatography (Waters Prep 500) of the crude products using 3/2 EtOAc/hexane as eluent gave pure **4a**/**4b** as a mixture of diastereomers.

1-(*S*-Phenylsulfonimidoyl)-2-propanol (Table I, entry 1) was obtained in 69% yield from the reaction of **2c** with acetaldehyde: t_R 4.7 min; ^1H NMR ($CDCl_3$) δ 1.10 (d, J = 6.0 Hz) and 1.18 (d, J = 6.0 Hz) [(total 3 H; 1.10/1.18 = 2/1)], 3.03 (m) and 3.15 (m) (total 3 H), 3.90 (m, 1 H), 7.50 (m, 3 H), 7.88 (m, 2 H). Anal. Calcd for $C_9H_{13}NO_2S$: C, 53.24; H, 6.47. Found: C, 53.29; H, 6.75.

3-Methyl-1-(*S*-phenylsulfonimidoyl)-2-butanol (Table I, entry 2) was obtained in 80% yield from the reaction of **2c** with isobutyraldehyde: t_R 5.7 min; ^1H NMR ($CDCl_3$) δ 0.82 (d, J = 3.6 Hz) and 0.84 (d, J = 3.6 Hz) and 0.89 (d, J = 3.6 Hz) and 0.91 (d, J = 3.6 Hz) [(total 6 H; 0.82 and 0.84/0.89 and 0.91 = 2/1)], 1.70 (m, 1 H), 3.15 (m, 3 H, contains =N*H*), 3.55 (m) and 4.20 (m) (total 1 H), 5.00 and 5.20 (total 1 H, O*H*), 7.60 (m, 3 H), 7.95 (m, 2 H). Anal. Calcd for $C_{11}H_{17}NO_2S$: C, 58.11; H, 7.54. Found: C, 57.87; H, 7.67.

4-Methyl-1-(*S*-phenylsulfonimidoyl)-2-pentanol (Table I, entry 3) was obtained in 79% yield from the reaction of **2c** with isovaleraldehyde: t_R 6.28 min; ^1H NMR ($CDCl_3$) δ 0.72 (m) and 0.78 (m) (total 6 H), 0.85–0.90 (m, 3 H), 1.00–1.10 (m, 1 H), 2.95–3.20 (m, 3 H), 3.80 (m) and 4.40 (m) (total 1 H, O*H*), 7.55 (m, 3 H), 7.90 (m, 2 H). Anal. Calcd for $C_{12}H_{19}NO_2S$: C, 59.71; H, 7.94. Found: C, 59.14; H, 7.96.

3,3-Dimethyl-1-(*S*-phenylsulfonimidoyl)-2-butanol (Table I, entry 4) was obtained in 91% yield from the reaction of **2c** with pivalaldehyde: t_R 5.60 min; ^1H NMR ($CDCl_3$) δ 0.82 (s) and 0.88 (s) (9 H, 0.82/0.88 = 2.5/1). Anal. Calcd for $C_{12}H_{19}NO_2S$: C, 59.71; H, 7.93. Found: C, 59.48; H, 7.91.

α-[(*S*-Phenylsulfonimidoyl)methyl]benzenemethanol (Table I, entry 5) was obtained in 81% yield from the reaction of **2c** with benzaldehyde. The major diastereomer could be resolved by a fractional crystallization of the diastereomeric mixture from ethanol. The mother liquor consisted of a 1:2 mixture of the **4a** and **4b** diastereomers. Physical properties of the pure diastereomer **4a**: mp 119.0–119.5 °C; ^1H NMR ($CDCl_3$) δ 3.25 (dd, J = 16 Hz, 2 Hz, 1 H), 3.48 (dd, J = 16 Hz, 9 Hz, 1 H), 4.88 (dd, J = 9 Hz, 2 Hz, 1 H), 6.10 (s, 1 H, O*H*), 7.30 (m, 5 H), 7.70 (m, 3 H), 8.05 (m, 2 H). Anal. Calcd for $C_{14}H_{15}NO_2S$: C, 64.31; H, 5.79; N, 5.35. Found: C, 64.15; H, 5.81; N, 5.31.

α-[(*S*-Phenylsulfonimidoyl)methyl]-2-thiophenemethanol (Table I, entry 6) was obtained in 94% yield from the reaction of **2c** with 2-thiophenecarboxaldehyde. One diastereomer could be separated by a fractional crystallization of the diastereomeric mixture from ethanol. Physical properties of the pure diastereomer **4a**: t_R 8.60 min; mp 97–98 °C; ^1H NMR ($CDCl_3$) δ 3.10 (br s, 1 H, =N*H*), 3.35 (dd, J = 17.0 Hz, 3 Hz, 1 H), 3.60 (dd, J = 17.0 Hz, 10.8 Hz, 1 H), 5.15 (dd, J = 10.8 Hz, 3.0 Hz, 1 H), 6.10 (s, 1 H, O*H*), 6.85 (d, J = 3.0 Hz, 1 H), 6.95 (t, J = 3.0 Hz, 1 H), 7.25 (d, J = 3.0 Hz, 1 H), 7.70 (m, 3 H), 8.00 (d, J = 4.8 Hz, 2 H). Anal. Calcd for $C_{12}H_{13}NO_2S_2$: C, 53.91; H, 4.90; S, 23.98. Found: C, 54.02; H, 4.90; S, 23.98.

2-(*S*-Phenylsulfonimidoyl)ethanol (Table I, entry 7) was obtained in 41% yield from the reaction of **2c** with paraformaldehyde (would not elute on GC): ^1H NMR ($CDCl_3$) δ 3.18 (t, 2 H), 3.85 (m, 4 H, including O*H* and =N*H*), 7.50 (m, 3 H), 7.88 (m, 2 H). Anal. Calcd for $C_8H_{11}NO_2S$: C, 51.87; H, 5.98. Found: C, 51.87; H, 5.80.

α-Ethyl-α-[(*S*-phenylsulfonimidoyl)methyl]benzenemethanol (Table I, entry 8) was obtained from the reaction of **2c** with propiophenone. The diastereomers were separated by flash chromatography with 2/3 EtOAc/CH_2Cl_2 as eluent (70% yield). Physical properties of the faster eluting minor diastereomer: mp 90–91 °C; ^1H NMR ($CDCl_3$) δ 0.70 (t, J = 7.2 Hz, 3 H), 1.80 (dd, J = 7.2 Hz, 16.0 Hz, 1 H), 2.03 (t, 2, J = 7.2 Hz, 16.0 Hz, 1 H), 3.55 (d, J = 16.2 Hz, 1 H), 3.62 (d, J = 16.2 Hz, 1 H). Anal. Calcd for $C_{16}H_{19}NO_2S$: C, 66.40; H, 6.62. Found: C, 66.38; H, 6.65. Physical properties of the more slowly eluting major diastereomer: mp 137–138 °C; ^1H NMR ($CDCl_3$) δ 0.70 (t, J = 7.2 Hz, 3 H), 1.70 (td, J = 7.2 Hz, 16.0 Hz, 1 H), 1.85 (td, J = 7.2 Hz, 16.0 Hz, 1 H), 3.70 (d, J = 16.2 Hz, 1 H), 3.76 (d, J = 16.2 Hz, 1 H).

1-[(*S*-Phenylsulfonimidoyl)methyl]cyclopentanol (Table I, entry 9) was obtained in 83% yield from the reaction of **2c** with cyclopentanone (would not elute on GC): mp 86–88 °C; ^1H NMR ($CDCl_3$) δ 1.85 (m, 8 H), 2.87 (br s, 1 H), 3.15 (d, J = 14 Hz, 1 H), 3.50 (d, J = 14 Hz, 1 H), 5.80 (s, 1 H), 7.50 (m, 3 H), 7.94 (m, 2 H). Anal. Calcd for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16. Found: C, 59.30; H, 7.21.

1-[(*S*-Phenylsulfonimidoyl)methyl]cyclohexanol (Table I, entry 10) was obtained in 97% yield from the reaction of **2c** with cyclohexanone (would not elute on GC): mp 134–135 °C; ^1H NMR ($CDCl_3$) δ 1.50 (m, 10 H), 2.85 (br s, 1 H), 3.15 (br s, 2 H), 5.60 (s, 1 H), 7.50 (m, 3 H), 7.90 (m, 2 H). Anal. Calcd for $C_{13}H_{19}NO_2S$: C, 61.63; H, 7.56. Found: C, 61.55; H, 7.61.

***S*-Methyl-*N*-(*tert*-butyldimethylsilyl)-*S*-phenylsulfoximine (2d).** A heterogeneous mixture of methylphenylsulfoximine (22.5 g, 0.145 mol) and *N*-methyl-*N*-(*tert*-butyldimethylsilyl)-trifluoroacetamide (35 g, 0.145 mol) was heated at 90 °C for 20 min. The resulting clear homogeneous solution was subjected to short path vacuum distillation at 0.1 mmHg. A small forerun containing *N*-methyltrifluoroacetamide was discarded and the fraction boiling at 91 °C was collected as a colorless liquid (36.0 g, 92%). [*CAUTION*! The distillation condenser should not be cooled until all the *N*-methyltrifluoroacetamide (mp 52 °C) has been distilled out, to prevent blockage of the condenser.] ^1H NMR ($CDCl_3$): δ 0.02 (s, 6 H), 0.95 (s, 9 H), 2.90 (s, 3 H).

***S*-Methyl-*N*-(methyldiphenylsilyl)-*S*-phenylsulfoximine (2e).** *n*-Butyllithium (2.5 M in hexane, 20 mL, 50 mmol) was added over 10 min to a vigorously stirred solution of methylphenylsulfoximine (7.8 g, 50 mmol) in THF (70 mL) at 0 °C. The resulting white suspension was treated with methyldiphenylchlorosilane (11.64 g, 50 mmol). The mixture became a clear solution upon addition of all the silylating agent. After being stirred at ambient temperature for 0.5 h, the reaction mixture was concentrated in vacuo, taken up in ethyl acetate (50 mL), washed with water (15 mL), and filtered through $MgSO_4$. Evaporation of solvent in vacuo gave a clear liquid (18 g), which was subjected to vacuum distillation at 0.1 mmHg to provide pure **2e** (15 g, bp 195 °C): ^1H NMR ($CDCl_3$) δ 0.59 (s, 3 H), 2.87 (s, 3 H), 7.10–7.87 (m, 15 H). Anal. Calcd for $C_{20}H_{21}SNSiO$: C, 68.33; H, 6.02. Found: C, 68.30; H, 6.05.

1-[*N*-(Methyldiphenylsilyl)-*S*-phenylsulfonimidoyl]-2-propanol (Silylated Product of Table II, Entry 1). *n*-Butyllithium (2.5 M in hexane, 4 mL, 10 mL) was added over 10 min to a vigorously stirred solution of **2e** (3.51 g, 10 mmol) in ether (20 mL) at −78 °C, and the reaction mixture was allowed to warm to 0 °C. The resulting white suspension was stirred at 0 °C for 0.5 h and was recooled to −78 °C, whereupon acetaldehyde (0.52 g, 12 mmol) was added. The reaction mixture became a clear solution upon addition of acetaldehyde and was allowed to warm to ambient temperature over 2 h. Quenching with saturated aqueous ammonium chloride, followed by normal workup, gave the crude product as a yellow oil, which was purified by flash chromatography with 3/7 EtOAc/hexane as eluent to provide the pure product (2.28 g, 58% yield) as a colorless oil: ^1H NMR ($CDCl_3$) δ 0.55 (s) and 0.60 (s) (total 3 H, SiCH_3, 0.55/0.60 ≅ 1/6), 1.10 (d, J = 7.2 Hz) and 1.14 (d, J = 7.2 Hz, total 3 H, CH(O-H)CH_3, 1.14/1.10 ≅ 1/7). Anal. Calcd for $C_{22}H_{25}NO_2SiS$: C, 66.79; H, 6.37. Found: C, 66.15; H, 6.44.

3,3-Dimethyl-1-[*N*-(methyldiphenylsilyl)-*S*-phenylsulfonimidoyl]-2-butanol (Silylated Product of Table II, Entry 2). By the same procedure as just described, reaction of **2e** with pivaldehyde afforded the pure silylated product as a colorless oil in 82% yield: ^1H NMR ($CDCl_3$) δ 0.56 (s) and 0.63 (s) [(total 3 H, SiCH_3, 0.56/0.63 ≅ 1/8)], 0.80 (s) and 0.83 (s) (total 9 H, 0.83/0.80 ≅ 1/8). Anal. Calcd for $C_{25}H_{31}NSiO_2S$: C, 68.60;

H, 7.14. Found: C, 68.43; H, 7.23.

6-Methyl-4-phenyl-1,4,3-oxathiazin-2(6*H*)-one 4-Oxide (Table III, Entry 1). A solution of phosgene (1.93 M in toluene, 2 mL, 3.86 mmol) was added over 2 min to a solution of starting material (Table I, entry 1, 0.77 g, 3.86 mmol) and triethylamine (0.78 g, 7.5 mmol) in dichloromethane (15 mL) at 0 °C. The reaction was allowed to warm to ambient temperature over 2 h and was then treated with water (10 mL). The phases were separated and the organic phase was washed with water (5 mL), filtered through $MgSO_4$, and concentrated in vacuo to leave a viscous oil (0.8 g). The crude product was subjected to flash chromatography with ethyl acetate as eluent to give the product as a white solid (0.7 g, 81% yield) consisting of a 2:1 diastereomeric mixture. Fractional crystallization (CH_2Cl_2/hexane) provided pure diastereomer **8a** (0.32 g). The mother liquor consisted of a diastereomeric mixture of **8a** and **8b**. The pure diastereomer **8a** displayed the following characteristics: mp 125–126 °C; ^1H NMR ($CDCl_3$) δ 1.32 (d, J = 7.2 Hz, 3 H), 3.70 (dd, J = 18.0 Hz, 12.6 Hz, 1 H), 4.30 (dd, J = 18.0 Hz, 3.0 Hz, 1 H), 4.45 (m, 1 H), 7.75 (t, J = 7.2 Hz, 2 H), 7.85 (t, J = 7.2 Hz, 1 H), 8.08 (d, J = 7.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 19.2, 51.8, 68.7, 128.5, 129.8, 134.9, 136.7, 151.8. Anal. Calcd for $C_{10}H_{11}O_3NS$: C, 53.32; H, 4.92; N, 6.22. Found: C, 53.40; H, 4.95; N, 6.23.

6-(1-Methylethyl)-4-phenyl-1,4,3-oxathiazin-2(6*H*)-one 4-Oxide (Table III, Entry 2). The starting alcohol of Table I, entry 2 (2.27 g) was converted to 2.5 g of crude cyclized product, which was subjected to flash chromatography with 3/2 EtOAc/hexane as eluent to give 1.58 g (71% yield) of pure **8a/8b** as a diastereomeric mixture (diastereomer separation was not attempted): ^1H NMR ($CDCl_3$) δ 0.95 (d, J = 7.2 Hz) and 0.99 (d, J = 7.2 Hz) and 1.02 (d, J = 7.2 Hz) and 1.04 (d, J = 7.2 Hz) [(c total 6 H, 0.95 and 0.99/1.02 and 1.04 ≅ 2/1)]. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.89; H, 5.97. Found: C, 56.69; H, 6.09.

6-(2-Methylpropyl)-4-phenyl-1,4,3-oxathiazin-2(6*H*)-one 4-Oxide (Table III, Entry 3). The alcohol of Table I, entry 3 (2.41 g) was converted to 1.5 g of crude cyclized product. Flash chromatography with 3/2 EtOAc/hexane as eluent afforded 0.6 g of the major diastereomer **8a** and 0.7 g of a diastereomeric mixture (total 49% yield). Physical properties of the pure diastereomer **8a**: mp 42 °C; ^1H NMR ($CDCl_3$) δ 0.80 (d, J = 6.0 Hz, 3 H), 0.83 (d, J = 6 Hz, 3 H), 1.50 (m) and 1.85 (m) (total 3 H), 3.30 (dd, J = 16.3, 12.7 Hz, 1 H), 3.66 (dd, J = 16.3, 3.6 Hz, 1 H), 4.25 (m, 1 H), 7.65 (t, J = 7.2 Hz, 1 H), 7.75 (t, J = 7.2 Hz, 1 H), 8.00 (d, J = 7.2 Hz, 2 H); IR (film) 1700, 1460, 1380, 1250, 1100, 1080, 690 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.40; H, 6.41. Found: C, 58.74; H, 6.40.

4,6-Diphenyl-1,4,3-oxathiazin-2(6*H*)-one 4-Oxide (Table III, Entry 4). A diastereomerically pure sample (isomer **4a**) of the alcohol of Table I, entry 5 (2.61 g) was converted to 1.9 g of pure cyclized product (66% yield): mp 206–208 °C; ^1H NMR ($CDCl_3$) δ 4.25 (dd, J = 18.0, 12.6 Hz, 1 H), 4.60 (dd, J = 18.0, 3.0 Hz, 1 H), 5.50 (dd, J = 12.6, 3.0 Hz, 1 H), 7.43 (m, 3 H), 7.50 (m, 2 H), 7.85 (m, 3 H), 8.20 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 51.4, 73.3, 127.3, 128.6, 128.7, 129.2, 129.8, 135.0, 135.9, 136.5, 151.6. Anal. Calcd for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56. Found: C, 62.18; H, 4.63.

4-Phenyl-6-(2-thienyl)-1,4,3-oxathiazin-2(6*H*)-one 4-Oxide (Table III, Entry 5). A diastereomerically pure sample (isomer **4a**) of the alcohol of Table I, entry 6 (1.63 g) was converted to the pure cyclized product (0.7 g, 48% yield): mp 135–136 °C; ^1H NMR (Me_2SO) δ 4.22 (dd, J = 18.0, 12.6 Hz, 1 H), 4.75 (dd, J = 18.0, 3.0 Hz, 1 H), 5.80 (dd, J = 12.6, 3.0 Hz, 1 H), 7.00 (t, J = 3.0 Hz, 1 H), 7.25 (d, J = 3.0 Hz, 1 H), 7.65 (d, J = 3.0 Hz, 1 H), 7.75 (t, J = 4.8 Hz, 2 H), 7.85 (t, J = 4.8 Hz, 1 H), 8.20 (d, J = 4.8 Hz, 2 H); ^{13}C NMR (Me_2SO) δ 51.7, 69.2, 127.0, 127.2, 127.7, 128.8, 129.8, 135.1, 136.4, 138.0, 151.2. Anal. Calcd for $C_{13}H_{11}NO_3S_2$: C, 53.22; H, 3.78; S, 21.86. Found: C, 53.04; H, 3.85; S, 21.73.

4-Phenyl-1,4,3-oxathiazin-2(6*H*)-one 4-Oxide (Table III, Entry 6). The alcohol of Table II, entry 7 (1.85 g) was converted to the pure cyclized product (1.0 g, 47% yield): mp 136–137 °C; ^1H NMR ($CDCl_3$) δ 3.95 (dm, 1 H), 4.10 (dm, 1 H), 4.45 (dm, 1 H), 4.60 (dm, 1 H), 7.75 (t, J = 7.2 Hz, 1 H), 7.85 (t, J = 7.2 Hz, 1 H), 8.10 (d, J = 7.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 46.4, 60.5, 128.4, 129.9, 135.0, 136.4, 151.7; IR ($CHCl_3$) 1700, 1450, 1260, 1220 ($\nu_{S=N}$), 1110 ($\nu_{S=O}$), 690 (monosubstituted phenyl). Anal. Calcd for $C_9H_9NO_3S$: C, 51.17; H, 4.29. Found: C, 50.43; H, 4.24.

Methyl 1-Methyl-2-[*S*-phenyl-*N*-(trimethylsilyl)sulfonimidoyl]ethyl Carbonate (5a/5b, Scheme III, R = CH_3). A solution of **2c** (9.08 g, 40 mmol) in dry ether (100 mL was cooled to −78 °C and was treated with a solution of *n*-butyllithium (2.1 M in hexane, 19 mL, 40 mmol), and the reaction mixture was allowed to warm to 0 °C. The resulting white suspension was stirred at 0 °C for 0.5 h and was recooled to −78 °C, whereupon acetaldehyde (1.94 g, 88 mmol) was added. Cooling was removed and the clear yellow reaction mixture was stirred at ambient temperature for 0.5 h, recooled to −78 °C, and treated with methyl chloroformate (4.16 g, 88 mmol). The resulting heterogeneous mixture was stirred at ambient temperature for 1 h, diluted with water (40 mL), and extracted with ether several times. The combined ether extracts were washed with brine, filtered through $MgSO_4$ and concentrated in vacuo to give the crude product (13.0 g, 99% yield) as a clear liquid, which solidified (mp 63–65 °C) upon standing at room temperature. This material was essentially pure by NMR and could be used for the next experiment without further purification. An analytical sample was obtained by trituration with hexane. Attempted bulb-to-bulb distillation under high vacuum resulted in partial decomposition. Physical properties of the product: ^1H NMR ($CDCl_3$) δ 0.05 (s, 9 H), 1.31 (d, J = 7.2 Hz) and 1.38 (d, J = 7.2 Hz) (total 3 H), 3.10 (dd, J = 14.4, 4.0 Hz, 1 H), 3.46 (dd, J = 14.4, 7.5 Hz, 1 H), 3.65 (s, 3 H), 5.15 (m, 1 H), 7.55 (m, 3 H), 7.90 (m, 2 H). Anal. Calcd for $C_{14}H_{23}NO_4SiS$: C, 51.03; H, 7.03. Found: C, 50.56; H, 6.51.

Methyl 1-Methyl-2-(*S*-phenylsulfonimidoyl)ethyl Carbonate (6a/6b, Scheme III, R = CH_3). A solution of the above-described carbonate (3.8 g, 11.5 mmol) and CsF (20 mg) in methanol (10 mL) was stirred at 20 °C for 0.5 h and at 40 °C for 5 min. Low boiling volatiles were removed in vacuo and the residue was subjected to flash chromatography with 4/1 EtOAc/hexane as eluent to give the pure sulfoximine (2.6 g, 87.6% yield) as a clear liquid: ^1H NMR ($CDCl_3$) δ 1.32 (d, J = 7.2 Hz, 3 He, 3.00 (br s, 1 H), 3.30 (dd, J = 14.4, 4.0 Hz, 1 H), 3.55 (dd, J = 14.4, 7.6 Hz, 1 H), 3.60 (s, 3 H), 5.10 (m, 1 H), 7.55 (m, 3 H), 7.90 (m, 2 H). Anal. Calcd for $C_{11}H_{15}NO_4S$: C, 51.35; H, 5.88. Found: C, 51.49; H, 5.99.

X-ray Crystallographic Analysis of 9. Large well-shaped crystals of **9** were obtained from the slow evaporation of an ethyl acetate solution at ambient laboratory temperature. The crystals were monoclinic at 20 °C, with a = 11.066 (2) Å, b = 12.179 (3) Å, c = 8.549 (3) Å, β = 113.93°, V = 1053.1 (9) Å^3, Z = 4, and ρ_{calc} = 1.309 gm/cm^3 (formula weight of 206.24). The systematically absent reflections in the diffraction pattern were consistent with the noncentrosymmetric space group Cc—C_s^4 (No. 9) or with the centrosymmetric space group C_2/c—D_{2h}^6 (No. 15).[25] The choice of the noncentrosymmetric space group Cc was indicated by the various statistical indicators calculated with normalized structure factors; this choice was also fully supported by all stages of the subsequent structure determination and refinement. Intensity measurements were made on a Syntex (Nicolet) P_{21} autodiffractometer using the $\theta/2\theta$ scan technique and graphite-monochromated Mo Kα radiation. The crystal specimen, having the shape of a rectangular parallelepiped with dimensions 0.50 × 0.30 × 0.23 mm, was glued to the end of a thin glass fiber and mounted on a goniometer with its longest dimension nearly parallel to the ϕ axis of the diffractometer. A total of 2173 reflections were measured having $2\theta_{Mo\,K\alpha} < 50.7°$ (the equivalent of 0.70 limiting Cu Kα spheres). A scan rate of 4.0 deg/min was employed for all reflections; background counting time was equal to the total peak accumulation time. No absorption correction was applied.

All 15 crystallographically independent non-hydrogen atoms were located by using direct methods (MULTAN).[26] Cycles of isotropic unit-weighted full-matrix least-squares refinement for the structural parameters for the 15 highest peaks found in the E map (using appropriate atomic form factors) converged at conventional residuals R_1 (unweighted, based on F) = 0.154 and R_w (weighted, based on F) = 0.149 for the 835 reflections having

(25) *International Tables for X-Ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. I, pp 89, 101.

(26) All computer programs used for data reduction, solution, and structure refinement were contained in the "Structure Determination Package", Enraf-Nonius Co., Delft, Holland.

$2\theta < 50.7$ degrees and $I > 3.0\ \sigma(I)$.[27] Further refinement employed anisotropic thermal parameters for the 15 non-hydrogen atoms, and unit-weighting converging at $R_1 = 0.073$ and $R_w = 0.079$. Hydrogen atoms were generated by using idealized geometry and a 0.95-Å C–H bond distance and were included and refined isotropically. Final cycles of full-matrix least-squares refinement included a least-squares refineable isotropic extinction correction and a non-Poisson weight scheme, converging at $R_1 = 0.0354$ and $R_1 = 0.0407$, with an estimated error in the observation of unit weight of 1.519. The largest shift/error for a non-hydrogen atom in the final cycle was 0.06, and the average shift/error was 0.01. The largest peak present in the difference Fourier calculated from the fully refined model had a density of 0.30 e/Å^3 and together with the remaining less intense peaks could not be attributed to molecular disorder or lattice solvation.

(27) The R values are defined as $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $R_\omega = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$, where w is the weight given each reflection. The function which is minimized is $\Sigma w(|F_o| - K|F_c|)^2$, where K is the scale factor.

Supplementary Material Available: Tables of atomic fractional coordinates, anisotropic thermal parameters for non-hydrogen atoms, bond lengths, bond angles, and 400-MHz ABX spectra of **4a**/**4b** and **8a**/**8b** (6 pages); tables of observed and calculated structure factors (5 pages). Ordering information is given on any current masthead page.

Notes

Synthesis through the Interconversion of Methoxyboranes and Boron Hydrides: 9-BBN Systems

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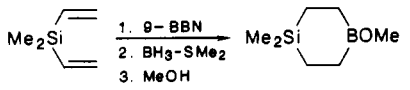
As a dialkylborane, 9-borabicyclo[3.3.1]nonane (9-BBN)[2] is unrivaled in both stability and selectivity.[3] Derivatives of 9-BBN are also both easily prepared from 9-BBN and have a variety of important synthetic applications.[4] Included in these applications is the preparation of isomerically pure boracycles, which are not available from the direct cyclic hydroboration process. This approach is outlined below for our recent synthesis of the silaborinane system.[5]



Thus, 9-BBN functions as a catalyst, first forming a diboryl adduct from α,ω-dienes, exchanging with BMS (borane–methyl sulfide) to equilibrate to the cyclic dialkylborane, and finally being converted to *B*-MeO-9-BBN with methanol. While several methods for effecting the separation of these organoborane products have been attempted by us and others, the best case found for the above example gives ca. 65% recovered 9-BBN. The remaining 9-BBN must be converted to its methoxy derivative and separated from the desired methoxyboracycle by fractional distillation. Thus, in a general sense, the difference in boiling points between cyclic borinate esters and *B*-MeO-9-BBN provides the basis of their isolation in pure form. Clearly, an efficient method for converting this byproduct back to 9-BBN would be desirable so that the true catalytic role of 9-BBN in the formation of boracycles could be realized.

Studies by Brown and Kulkarni[6] have revealed that exchange between BMS and *B*-MeO-9-BBN could be effected to give 9-BBN and $B(OMe)_3$ as the reaction products. We confirmed this finding by ^{11}B NMR, observing only **3** and **4**, together with minor (<10%) amounts of **1** and **2**, in the reaction mixture.

$$\underset{\mathbf{1}}{3[B\text{-MeO-9-BBN}]} + \underset{\mathbf{2}}{BH_3\text{–}SMe_2} \rightarrow {}^3/_2\underset{\mathbf{3}}{[9\text{-BBN}]_2} + \underset{\mathbf{4}}{B(MeO)_3}$$

Like Brown, we observed essentially pure methyl borate in the vaccum-removed volatiles. The solid 9-BBN residue contains ca. 10% of *B*-MeO-9-BBN and recrystallization as described from hexanes gives 9-BBN in 66% yield (mp 144–146 °C). The fact that 1,2-dimethoxyethane (MG) is now known to be a superior solvent for the recrystallization of 9-BBN[2] prompted us to repeat this procedure employing this solvent throughout. This change results in an increase in the yield of 9-BBN to 77% (mp 148–152 °C). Concerned as to the more quantitative aspects of the equilibration process, we examined the MG solution by ^{11}B NMR prior to the removal of the volatile components with the finding that 1:2:3:4 were observed in a ca. 23:5:53:19 ratio. While these ratios cannot be measured precisely due to some peak overlap, particularly between **3** and **4**, it is clear that the exchange does not go to completion. Distillation at atmospheric pressure (N_2) of the volatiles up to the boiling temperature of MG (85 °C) revealed that the major volatile boron components were **4** (53%), **2** (9%), and $(MeO)_2BH$ (38%). This result was surprising in light of the fact that only **4** was observed when the solvents were removed in vacuo! Clearly, this implied that the reaction mixture could further equilibrate to give the more volatile $(MeO)_2BH$ (bp 26 °C). 9-BBN (mp 150–152 °C) was isolated from MG in 46% yield with the supernatant containing only **1**. We interpret these results to mean that

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