Synthesis of 2-Phenyl-, 3-Phenyl-, *cis*-2,3-Diphenyl-, and *trans*-2,3-Diphenyl-1,4-thiazanes and Derivatives (*N*-Methyl, *N*-Alkoxycarbonyl, *S*-Oxides, and *S*,*S*-Dioxides)

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The syntheses of the title 1,4-thiazanes (thiamorpholines) by reduction of the 5-oxa-1,4-thiazanes resulting from the lactamization of the appropriate acyclic phenyl derivatives of 5-amino-3-thiapentanoic acid are reported. The oxidation reactions at sulfur yielded the corresponding sulfoxides and sulfones. The stereochemistry of all these compounds was unequivocally established from their ^{1}H-NMR spectroscopic parameters.

Introduction

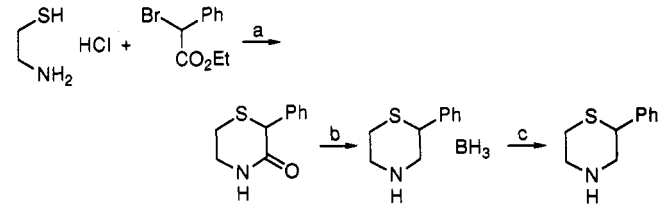
In previous publications we have reported on the conformational analysis of several acyclic β-oxygenated[2] and β-nitrogenated[3] thio derivatives. The vicinal coupling constants used in these reports as standards to estimate the populations of the different rotamers were obtained by calculation. In order to determine the value of these constants experimentally in rigid model compounds as well as to evaluate the magnitude of the gauche interactions between the sulfur functions, in different oxidation states, and other heteroatomic groups, we have undertaken the synthesis of a series of saturated heterocyclic compounds. We and others have already reported the synthesis and conformational behavior of (i) thianes and oxanes with exocyclic β-heteroatomic functions,[4] (ii) 2,3-dimethyl-1,4-oxathianes[5], and (iii) methyl- and 2,3-dimethyl-substituted 1,4-thiazanes.[6] The present paper is concerned with the synthesis and characterization as well as determination of the conformation and, where pertinent, configuration of the 2-phenyl, 3-phenyl, *cis*-2,3-diphenyl, and *trans*-2,3-diphenyl-1,4-thiazanes. A detailed spectroscopic study of these compounds will be published separately elsewhere.

The numbering used for the compounds studied is shown in Table I. In addition to thiazanes, we have also prepared their corresponding sulfoxides and sulfones. Synthesis of the *N*-methyl derivatives served to evaluate interactions involving the lone electron pair on nitrogen and the role of hydrogen bonding in the conformational behavior of the parent (NH) thiazanes. Finally, spectroscopic study of some *N*-alkoxycarbonyl derivatives which had been obtained as intermediates in some of the syntheses showed interesting conformational properties which induced us to prepare and study the complete series of these derivatives.

Results and Discussion

The synthesis of 2-phenyl-1,4-thiazane, 1 (Scheme I), was carried out by reaction of 2-aminoethanethiol hydrochloride with ethyl α-bromophenylacetate.[7] Reduction of lactam **65** with $LiAlH_4$ (described in the original reference) was unsuccessful; therefore, sodium borohydride/acetic acid in dioxane[8] (1:10 ratio substrate/reducing agent) was employed to obtain the aminoborane complex **66**, which was subsequently hydrolyzed to thiazane **1** with HCl (10%)/MeOH.[9]

Scheme I[a]



65 **66** **1**

[a] Key: (a) K_2CO_3; (b) $NaBH_4$/AcOH/dioxane; (c) 10% HCl/MeOH.

The 3-phenyl-1,4-thiazane (**17**) was synthesized in two different ways involving reduction of lactam **70** or imine **72** (Scheme II), respectively. Reaction of iodoisocyanate **67**[10] with *t*-BuOH gave iodocarbamate **68** whose reaction with methyl α-mercaptoacetate in basic medium[11] yielded **69** which was quantitatively transformed into lactam **70** upon acid hydrolysis of the carbamate group and subsequent treatment with K_2CO_3/MeOH. Reduction of **70** with $NaBH_4$/AcOH in dioxane yielded an equimolecular mixture of thiazane **17** and its amino–borane complex **71** which were easily separated by chromatography. Compound **71** was easily transformed to pure **17** by hydrolysis.

A one-pot synthesis of the 1,4-thiazane **17** was achieved, in 85% yield, by reaction of phenacyl bromide with 2-aminoethanethiol hydrochloride in basic medium, followed by treatment with HCl in methanol (to form imine hydrochloride **72**) and subsequent reduction with $NaBH_4$.[12] All attempts to isolate the intermediate free imine **72** were unsuccessful.

Synthesis of *cis*- and *trans*-2,3-diphenyl-1,4-thiazanes (**33** and **49**) required the use of acyclic precursors with the

(1) (a) UAM. (b) UNC.
(2) García Ruano, J. L.; Pedregal, C.; Rodríguez, J. H. *Tetrahedron* **1987**, *43*, 4407 and references cited therein.
(3) Brunet, E.; Carreño, M. C.; Gallego, M. T.; García Ruano, J. L.; Alcudia, F. *J. Chem. Soc., Perkin Trans. 2* **1983**, 937. Brunet, E.; Gallego, M. T.; García Ruano, J. L.; Alcudia, F. *Tetrahedron* **1986**, *42*, 1423.
(4) Brunet, E.; Eliel, E. L. *J. Org. Chem.* **1986**, *51*, 677. García Ruano, J. L.; Rodríguez, J.; Alcudia, F.; Llera, J. M.; Eliel, E. L.; Olefirowicz, E. M. *J. Org. Chem.* **1987**, *52*, 4099. Brunet, E.; Azpeitia, P. *Tetrahedron* **1988**, *44*, 1751. Alcudia, F.; Llera, J. M.; García Ruano, J. L.; Rodríguez, J. H. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1225.
(5) Carretero, J. C.; García Ruano, J. L.; Rodríguez, J. H. *Tetrahedron Lett.* **1984**, *25*, 3029.
(6) Brunet, E.; Gallego, M. T.; García Ruano, J. L.; Parellada, D.; Rodríguez, J. H.; Urbano, A. *Tetrahedron* **1988**, *44*, 1421. Gallego, M. T.; Brunet, E.; García Ruano, J. L.; Eliel, E. L. Manuscript in preparation.
(7) Ishikawa, Y.; Terao, Y.; Suzuki, K.; Shikano, N.; Sekiya, M. *Chem. Pharm. Bull.* **1984**, *32*(2), 438.
(8) Umino, N.; Iwakuma, T.; Itoh, N. *Tetrahedron Lett.* **1976**, 763.
(9) Similar conditions to those reported by: Lane, C. F. *Aldrichimica Acta* **1973**, *6*, 51.
(10) Obtained by addition of iodoisocyanate to styrene: Hassner, A.; Heathcock, C. *Tetrahedron* **1964**, *20*, 1037.
(11) With more basic thiolates like sodium methylmercaptide, these substrates usually gave a mixture of regioisomers, suggesting that an aziridinic intermediate must be involved.
(12) A similar method has been used to prepare some thiazane derivatives: Sakai, K.; Yoneda, N. *Chem. Pharm. Bull.* **1981**, *29*, 1554.

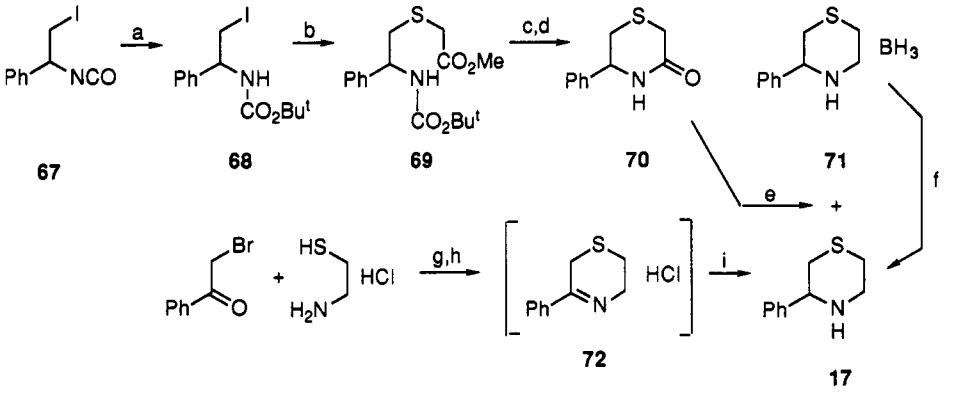
0022-3263/92/1957-4215$03.00/0

Table I. Structure and Numbering of the Prepared 2-Phenyl-, 3-Phenyl-, and 2,3-Diphenyl-(*cis* and *trans*)-1,4-thiamorpholines and Derivatives[a]

			Y =				Y =				Y =				Y =			
R^1	R^2	R^3	H	Me	EC	BC	H	Me	EC	BC	H	Me	EC	BC	H	Me	EC	BC
2-phenyl																		
Ph	H	H	1				2				3				4			
Ph	H	H		5				6				7				8		
Ph	H	H			9				10				11				12	
Ph	H	H				13				14				15				16
3-phenyl																		
H	Ph	H	17				18				19				20			
H	Ph	H		21				22				23				24		
H	Ph	H			25				26				27				28	
H	Ph	H				29				30				31				32
cis-2,3-diphenyl																		
Ph	Ph	H	33				34				35				36			
Ph	Ph	H		37				38				39				40		
Ph	Ph	H			41				42				43				44	
Ph	Ph	H				45				46				47				48
trans-2,3-diphenyl																		
Ph	H	Ph	49				50				51				52			
Ph	H	Ph		53				54				55				56		
Ph	H	Ph			57				58				59				60	
Ph	H	Ph				61				62				63				64

[a] EC ethyl carbamate; BC *tert*-butyl carbamate.

Scheme II[a]

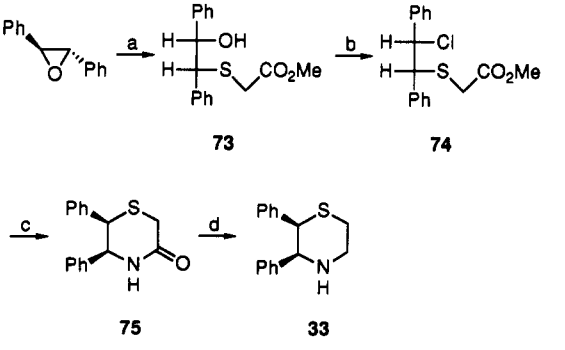


[a] Key: (a) *t*-BuOH, rt (4 d); (b) $MeO_2CCH_2SH/NaOMe/MeOH$; (c) HCl/AcOEt; (d) $K_2CO_3/MeOH$; (e) $NaBH_4/AcOH$/dioxane; (f) 10% HCl/MeOH; (g) KOH/MeOH; (h) HCl/MeOH; (i) $NaBH_4$.

correct stereochemistry. The *cis*- and *trans*-stilbene oxides[13] proved to be suitable starting materials.

Reaction of *trans*-stilbene oxide with methyl α-mercaptoacetate in the presence of a catalytic amount of NaOMe (0.15 equiv)[14] quantitatively yielded the *erythro*-hydroxy thio ether **73** (Scheme III). This product was transformed to the *erythro*-chloro thio ether **74** by treatment with HCl (quantitative yield) or Cl_2SO (80% yield).[15] The reaction of **74** with NH_4OH (20%) in acetonitrile afforded lactam **75**, whose reduction with $NaBH_4$/AcOH/dioxane yielded thiazane **33**. In this case, the corresponding amine–borane complex was not detected.

Scheme III[a]



[a] Key: (a) $MeO_2CCH_2SH/NaOMe$ (0.15 equiv)/MeOH; (b) HCl(g) or $SOCl_2$; (c) 20% NH_4OH/CH_3CN; (d) $NaBH_4$/AcOH/dioxane.

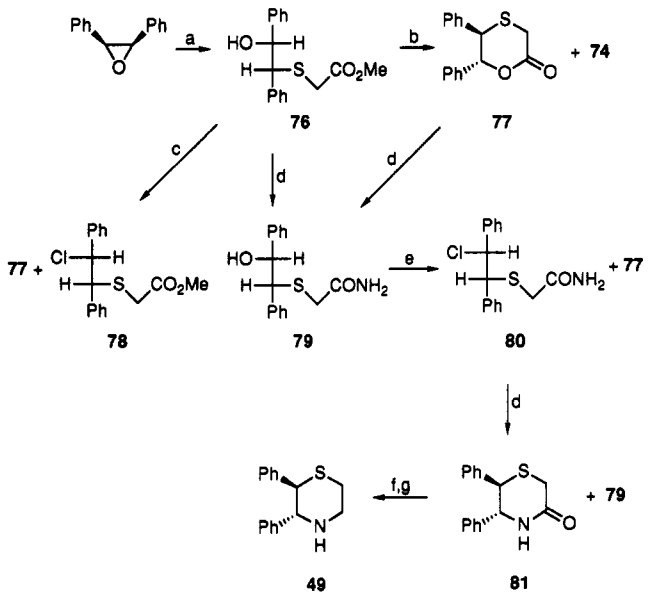
Synthesis of the *trans*-2,3-diphenyl-1,4-thiazane **49** was carried out in a similar way using *cis*-stilbene as starting material (Scheme IV). Its reaction with methyl α-mercaptoacetate and NaOMe (0.15 equiv)/MeOH quantita-

(13) The opening of the *cis*-2,3-diphenylaziridine with methyl thioglycolate might have yielded lactam **75** (Scheme III) in a single step. However, the low yields reported for the synthesis of the diphenylaziridines (Darapsky, A.; Spannagel, H. J. *Prakt. Chem.* **1915**, *92*, 272) encouraged us to explore alternative procedures avoiding the carcinogenic aziridines.

(14) The use of larger amounts of NaOMe (stoichiometric or excess) yielded the hydroxy acid corresponding to compound **73** (88% yield), which evolved into mixtures of cis lactone and erythro chloro thio ether by reaction with Cl_2SO or HCl(g).

(15) The observed total retention of configuration is a consequence of the anchimeric assistance of the sulfenyl sulfur (Carretero, J. C.; García Ruano, J. L.; Martínez, M. C.; Rodríguez, J. H. *J. Chem. Res., Synop.* **1985**, 6; *J. Chem. Res., Miniprint* 0172).

Scheme IV[a]

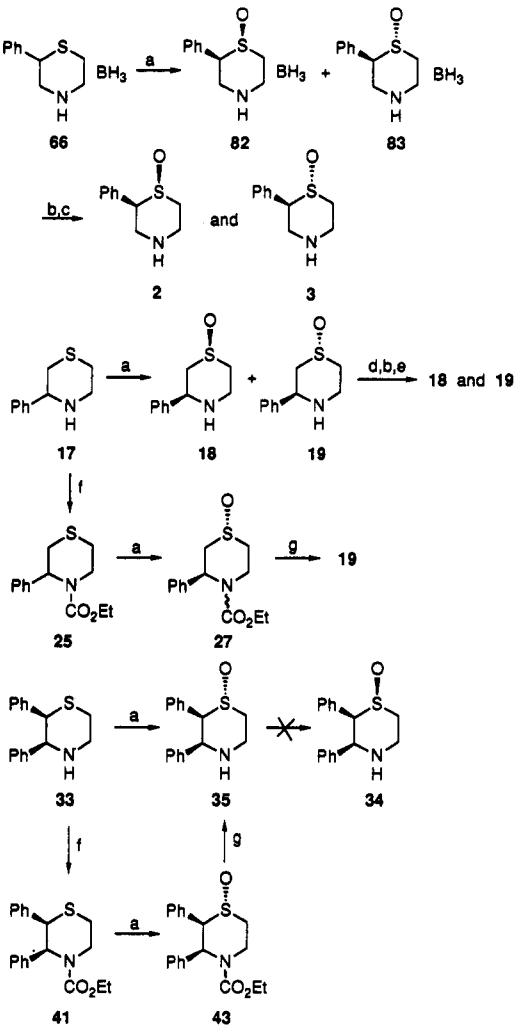


[a] Key: (a) $MeO_2CCH_2SH/NaOMe$ (0.15 equiv)/MeOH; (b) HCl(g); (c) $SOCl_2$, rt (16 h); (d) 20% NH_4OH/CH_3CN; (e) $SOCl_2$, 0 °C (5 min); (f) $NaBH_4$/AcOH/dioxane; (g) 10% HCl/MeOH.

tively afforded the *threo*-hydroxy thio ether **76** which was transformed into an equimolar mixture of the lactone **77** and the *erythro*-chloro thio ether **74** with HCl as chlorination agent.[16] The reaction of **76** with Cl_2SO yielded a 9:1 mixture of **77** and the desired *threo*-chloro thio ether **78**. Presumably, the trans disposition of the phenyl groups in lactone **77** makes its formation from **76** much easier than lactonization of **73**. In order to decrease the lactonization rate, ester **76** (or lactone **77**) was transformed into the amide **79** which reacted with Cl_2SO[17] to give a 9:1 mixture of *threo*-chloro derivative **80** and lactone **77**. The reaction of this mixture with NH_4OH/acetonitrile yielded a 9:1 mixture of lactam **81** and carbinol **79**, the former being easily separated by crystallization. The reduction of **81** with $NaBH_4$/AcOH/dioxane, followed by hydrolysis of the so-formed amino–borane complex (which was not isolated) afforded thiazane **49**.

The *N*-methyl derivatives of the thiazanes (**5**, **21**, **37**, and **53**) were easily obtained by methylation of the corresponding amines using the system $H_2CO/NaBH_4$. The ethoxycarbonyl (**9**, **25**, **41**, and **57**) and *tert*-butoxycarbonyl (**13**, **29**, **45**, and **61**) derivatives were prepared by reaction with ethyl chloroformate in basic medium and di-*tert*-butyl carbonate, respectively.

Scheme V[a]



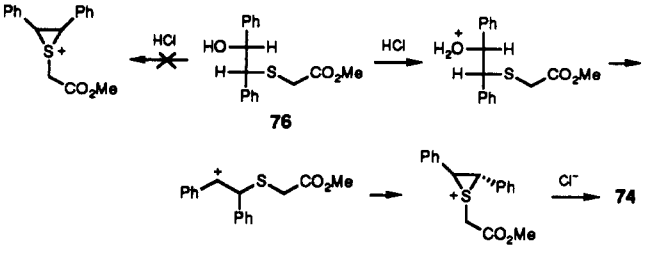
[a] Key: (a) $NaIO_4$ or *m*-CPBA; (b) separation; (c) 10% HCl/MeOH; (d) oxalic acid; (e) $NaHCO_3$; (f) $EtOCOCl/K_2CO_3$; (g) 10% KOH/MeOH, reflux, 6 h.

Thiazane *S*-oxides were in most cases prepared by oxidation of the corresponding thioethers. Mixtures of the two diastereomers (epimers at sulfur) were usually obtained requiring separation by chromatography or crystallization. These separations were not always successful, making it necessary in such cases to oxidize appropriate derivatives of the thiazanes in question; in other cases, oxidation yielded only one epimer making it necessary to use different methods to prepare the other. Such situations are discussed below.

Oxidation of **1** gave a mixture from which we could not isolate the desired sulfoxides **2** and **3**. Fortunately, the clean 3:1 mixture of amino–borano sulfoxides **82** and **83**, obtained from the corresponding thioether **66** and $NaIO_4$,[18] was easily separated by chromatography and transformed by hydrolysis to sulfoxides **2** and **3** (Scheme V).

In the case of compound **17** (whose amino–borane complex was not formed during the hydrolysis probably due to steric hindrance of the phenyl group next to the nitrogen) oxidation of free amine **17** was easily carried out, but separation of the epimeric sulfoxides formed was not possible. However, diastereomerically pure samples of

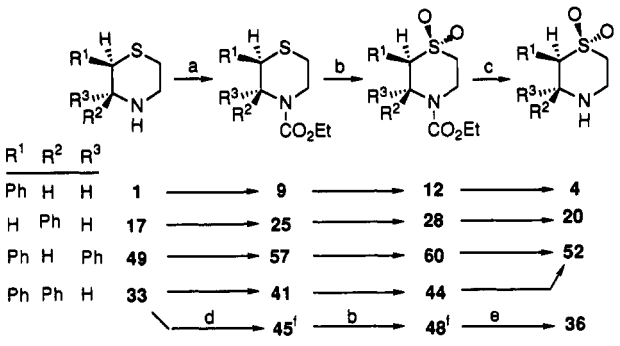
(16) The anchimeric assistance of the sulfenylic sulfur (resulting in retention of the configuration at the hydroxylic carbon) must be much more difficult in **76** than that in **73**, because in the first case the phenyl groups must adopt the very hindered cis arrangement in the episulfonium salt intermediate. The formation of **74** can be explained by assuming that anchimeric assistance takes place after the formation of the carbocation through an S_N1 process forming the most stable *trans*-diphenyl episulfonium salt.



(17) The conditions used in this chlorination reaction are critical; the best results were obtained in 5 min at 0 °C. Under other conditions major side products may result.

(18) Presumably the B–N association in **66** prevents oxidation of the nitrogen.

Scheme VI[a]



[a] Key: (a) $EtOCOCl/K_2CO_3$; (b) *m*-CPBA excess; (c) 10% KOH, $MeOH/H_2O$; (d) $(t\text{-}BuO_2C)_2O$; (e) 3 N HCl; $NaHCO_3$; (f) *tert*-butyl carbamate.

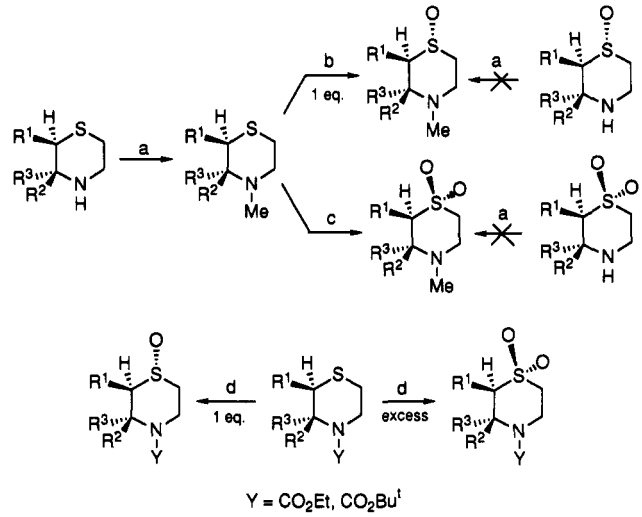
sulfoxides **18** and **19** were obtained by transformation of the oxidation mixture into the corresponding oxalate derivatives, separating the latter by crystallization and then hydrolyzing. In contrast, oxidation of **25** (the ethoxycarbonyl derivative of thioether **17**) with $NaIO_4$ or *m*-CPBA (1 equiv) yielded almost exclusively sulfoxide **27** (80% yield) whose basic hydrolysis afforded diastereomerically pure **19**.

The reaction of *cis*-2,3-dimethyl-1,4-thiazane (**33**) with $NaIO_4$ (1 equiv) yielded only one sulfoxide which was characterized as **35**. The use of other oxidizing agents such as *m*-CPBA or peroxytrifluoroacetic acid (PTFA) gave the same result. The transformation of **33** to its ethoxycarbonyl derivative **41** followed by oxidation again afforded only one sulfoxide whose structure was assigned as **43**. Hydrolysis of **43** yielded **35**. A final attempt to obtain the second diastereoisomer **34** involved equilibration of **35** in acidic medium (HCl/dioxane). However, this substrate remained unaltered under the conditions used; thus, compound **34** could not be obtained.

Attempted synthesis of the sulfones by direct oxidation of the amino thioethers (using excess of oxidizing agent) was unsuccessful (probably due to the competition between the NH and the SO groups, the latter being formed in the first step of the oxidation) and resulted in a complex mixture of products. Protection of the amino group as the ethoxycarbonyl derivative solved the problem. Thus, compounds **9**, **25**, **41**, and **57** were easily oxidized to the sulfones **12**, **28**, **44**, and **60**, respectively. Basic hydrolysis of **12**, **28**, and **60** led to the corresponding amino sulfones **4**, **20**, and **52**, but with the *cis*-2,3-diphenyl derivative **44** epimerization at C-2 was observed resulting in the formation of *trans*-sulfone **52** instead of the expected **36**. This problem was circumvented by using the *tert*-butoxycarbonyl derivative **45** (obtained from **33**) whose oxidation to **48** and subsequent acid hydrolysis yielded the desired **36** (without epimerization) in good yield (Scheme VI).

Attempted synthesis of *N*-methyl-1,4-thiazane *S*-oxides and *S*,*S*-dioxides by methylation of the corresponding NH derivatives with $HCHO/NaBH_4$ was unsuccessful. Therefore, these compounds were prepared by oxidation of the *N*-methyl sulfides with 1 equiv of PTFA or an excess of H_2O_2/TFA, respectively.[19] Oxidation of **37** (the *N*-methyl derivative of *cis*-2,3-diphenyl-1,4-thiazane (**33**)) once again afforded only one sulfoxide **39** whereas oxidation of **5**, **21**, and **53** afforded mixtures of diastereomers

Scheme VII[a]



[a] Key: (a) $HCHO/NaBH_4$; (b) PTFA; (c) H_2O_2/TFA; (d) *m*-CPBA.

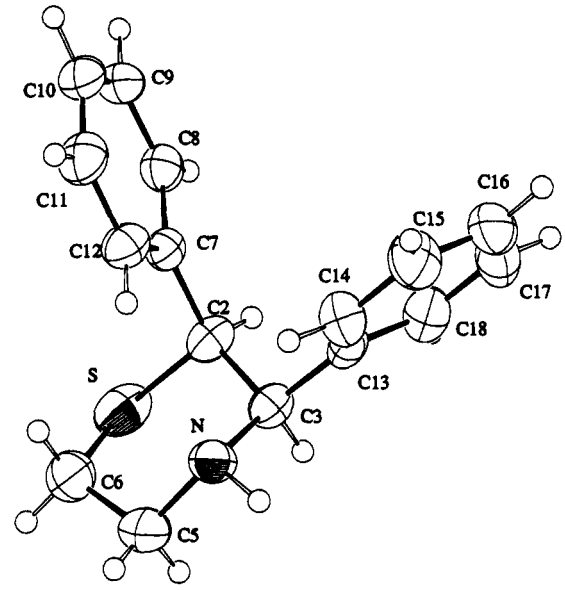


Figure 1.

which could not be separated.

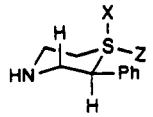
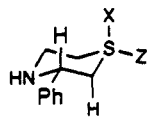
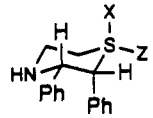
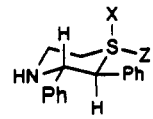
Oxidation of the *N*-ethoxycarbonyl and *N*-*tert*-butyoxycarbonyl derivatives of the thiazanes with *m*-CPBA generally afforded the corresponding sulfones or mixtures of sulfoxide epimers depending on the amount of oxidant used (Scheme VII). However, this reaction yielded only one of the two possible sulfoxides in those cases where the starting thiazane has a phenyl group at C-3. All these compounds exhibit a large preference for the conformation in which this phenyl group is axial[20] precluding axial approach of the oxidizing agent. Thus, the epimers obtained are always those with the phenyl at C-3 and the sulfoxide oxygen trans to each other.[21] This fact precluded synthesis of **26**, **30**, **42**, and **46** by this method (see Table I). Nevertheless, **30** was obtained by reaction of diastereomerically

(19) The use of $NaIO_4$ or *m*-CPBA yielded mixtures of amino sulfoxides, thio ether *N*-oxides (with 1 equiv of oxidant), and sulfoxide *N*-oxides (with 2 equiv), due to the similar ability of sulfur and nitrogen (which is easier to oxidize in tertiary than in secondary amines) to be oxidized by the reagent.

(20) The spectroscopic properties of these substrates unequivocally demonstrate this point and evidence ring deformations, which are more important in *trans*-2,3-diphenyl derivatives, where both phenyl groups adopt the axial arrangement. Although these points will be considered in detail in a subsequent paper, the ^{1}H-NMR parameters included in the experimental part of this work are evidence for this stereochemistry.

(21) Starting from **25** or **29**, compounds **26** and **30** respectively were identified in the epimeric mixtures obtained, but the low proportion of these compounds (<5%) prevented their isolation.

Table II. Significant Chemical Shifts and Coupling Constants To Assign the Relative Stereochemistry of the Sulfinyl Group

	compd (X,Z)	H_{3a} ($\Delta\delta$)[a]	$J_{2a,3a}$ (Hz)	H_{5a} ($\Delta\delta$)[a]	$J_{5a,6a}$ (Hz)
	**1** (:,:)	3.11	10.6		
	2 (O,:)	3.81 (+0.70)	11.7		
	3 (:,O)	3.05 (−0.06)	10.6		
	**17** (:,:)	3.92	10.6		
	19 (O,:)	4.64 (+0.72)	11.5		
	18 (:,O)	3.91 (−0.01)	11.6		
	**33** (:,:)	4.71	3.7[b]	2.73	9.9
	35 (O,:)	4.02 (+0.31)	3.2[b]	3.38 (+0.65)	12.7
	**49** (:,:)	4.05	9.6		
	50 (O,:)	4.85 (+0.80)	10.6		
	51 (:,O)	4.07 (+0.02)	10.4		

[a] $\delta_{sulfoxide} - \delta_{thioether}$. [b] $J_{2e,3a}$ (see text).

pure **18** with $(t\text{-}BuO_2C)_2O$ (a corresponding attempt to obtain **26** with ethyl chloroformate was unsuccessful). By contrast, the reaction of **57** and **61** yielded equimolar mixtures of the corresponding epimeric sulfoxides. This difference in behavior must be a consequence of the strong ring deformations in the starting thioethers.[20]

The X-ray crystal structure of *cis*-2,3-diphenyl-1,4-thiazane (**33**)[22] (Figure 1) showed the phenyl group at C-2 to be axial and that at C-3 to be equatorial. This is in accordance with the expected magnitude of their respective axial interactions, taking into account that the distance 2-Ph_a/H_{6a} is longer than 3-Ph_a/H_{5a} would be (a C–S bond is longer than a C–N bond). The structure of **33**[23] was determined not only to establish the conformation of the (axial) 2-phenyl and (equatorial) 3-phenyl moieties but also to check if the geometry of the thiazane would explain the anomalous reactivity of **33** (which was obtained as free amine instead of borane–amine complex and yielded only one of the two possible sulfoxides by oxidation).

The orientation of the axial phenyl ring at C-2 is such that it is perpendicular to the sulfur–C-2 bond, i.e., torsion angles $S\text{–}C_2\text{–}C_7\text{–}C_8 = -88.8°$ and $S\text{–}C_2\text{–}C_7\text{–}C_{12} = 90.0°$. Therefore, this phenyl substituent is almost in the axial parallel (or bisecting) conformation ($H_1\text{–}C_2\text{–}C_7\text{–}C_8 = 18.1°$, $H_1\text{–}C_2\text{–}C_7\text{–}C_{12} = -163.0°$) with respect to the heterocyclic ring (Figure 1). However, there is a slight rotation ($C_3\text{–}C_2\text{–}C_7\text{–}C_8 = 143.1°$ and $C_3\text{–}C_2\text{–}C_7\text{–}C_{12} = -38.2°$) toward the nitrogen side of the ring presumably to avoid the steric interaction between the axial hydrogen atom (H_6) on C_6 and the ortho C_{12} hydrogen atom (H_{12}).

The equatorial phenyl substituent on C-3 is oriented such that it is skewed from the normal[23] bisecting conformation by 33.3° ($H_2\text{–}C_3\text{–}C_{13}\text{–}C_{18}$) probably to minimize its steric interaction with the axial phenyl group on C-2 (see Figure 1).

The spatial orientation of both phenyl rings precludes axial approach of BH_3 to form an amine–borane complex. Equatorial approach of the reagent would require axial disposition of the hydrogen on nitrogen which must considerably increase the conformational energy of the axial and perhaps also of the equatorial phenyl substituent.

In order to establish the relative configuration of the different sulfoxides we have used several criteria, all of which confirm the assignments indicated in Scheme V.[24] The anisotropic effect of the sulfoxide oxygen, which leads to a strong deshielding of those protons adopting a syn-diaxial arrangement,[25] allowed us to assign the stereochemistry indicated in Table I. Taking into account that *N*-methyl- and *N*-alkoxycarbonyl derivatives have been obtained from or transformed into their corresponding N-unsubstituted thiazanes by reactions which do not affect the relative stereochemistry of the substrates, it is necessary only to justify assignment of configuration of the parent compounds.

In Table II are collected the chemical shifts of H_{3a} in thioethers and their corresponding axial and equatorial sulfoxides. In the cases of 2-phenyl, 3-phenyl, and *trans*-2,3-diphenyl derivatives the axial character of this proton is clearly inferred from the value of the vicinal coupling constant with H_{2a}. In contrast, the $J_{2,3}$ value observed in *cis*-2,3-diphenyl derivatives is compatible with two different relative spatial arrangements: H_{3a}/H_{2e} and H_{3e}/H_{2a}. Fortunately, H_2 exhibited a long-range coupling constant with one of the protons bonded to C-6 suggesting that these protons are in a W planar arrangement,[26] possible only when both are equatorial. Therefore, taking into account the cis disposition of the phenyl groups imposed by the synthetic route, H_3 must be axial and the small vicinal coupling constant observed for this proton must be assigned to $^3J_{2e,3a}$.

Once the signals corresponding to H_{3a} in the ^{1}H-NMR spectra of the thiazanes were identified and their axial

(22) A single colorless crystal of **33** was found to be triclinic with the $P\bar{1}$ space group. Two equivalent molecules are found in the unit cell with dimensions as follows: a = 9.095 (4) Å, b = 12.878 (9) Å, c = 6.228 (9) Å, α = 94.87 (6)°, β = 103.38 (6)°, γ = 74.91 (2)°, and the volume = 682 (2) Å^3. The calculated density is 1.243 g cm^{-1}, and the observed density is 1.25 (1) g cm^{-1}. The structure was refined to a final value of the weighted R factor of 0.0517 based on 1599 intensities (>3 σ).

(23) Normally this conformation (in axial phenylcyclohexane) is very high in energy: cf. Allinger, N. L.; Tribble, M. T. *Tetrahedron Lett.* **1971**, 3259. See also: Hodgson, D. J.; Rychlewska, U.; Eliel, E. L.; Manoharan, M. I.; Knox, D. E.; Olefirowicz, E. M. *J. Org. Chem.* **1985**, *50*, 4838. However, in the present case the replacement of one syn-axial hydrogen by a lone pair on nitrogen and the remoteness of the other syn-axial hydrogen on C(6) (resulting from the intervening sulfur atom) reduces the steric replusion in the phenyl-bisecting conformation; moreover, if the axial phenyl were perpendicular to the six-membered ring, it would clash with the adjacent equatorial phenyl group.

(24) A more detailed discussion about the NMR parameters of all these compounds, which unequivocally demonstrate the stereochemistry assigned to this paper and evidence other interesting stereochemical aspects will be published separately.

(25) Lett, R.; Marquet, A. *Tetrahedron* **1974**, *30*, 3379.

(26) Jochims, J. C.; Taigel, G.; Seeliger, A.; Lutz, P.; Driesen, H. E. *Tetrahedron Lett.* **1967**, 4363.

orientation confirmed, it was possible to study the effect of oxidation of sulfur (thioether to sulfoxide) on the chemical shifts of these signals. As can be seen in Table II the values of $\Delta\delta$ for H_{3a} ($\delta_{sulfoxide} - \delta_{thioether}$) when the sulfoxide oxygen adopts the equatorial conformation are very small (lower than ±0.1 ppm) whereas they are quite large ($\Delta\delta$ = +0.7–0.8 ppm) in the sulfoxides with axial oxygen. This strong deshielding effect of the axial sulfoxide oxygen of the syn-diaxial proton[25] allowed us to unambiguously demonstrate the relative stereochemistry of all substituents in those series where both sulfoxides were obtained. In the case of *cis*-2,3-diphenyl-1,4-thiazane *S*-oxide (**35**), the only sulfoxide obtained from **32** for the value of $\Delta\delta$ for H_{3a} (+0.3 ppm) may be considered ambiguous, but the syn-diaxial arrangement of H_{5a} and the sulfoxide oxygen was unequivocally established from the value of $\Delta\delta$ for this proton (+0.65 ppm). This suggests that the anomalous value observed for $\Delta\delta$ for H_{3a} is due to a substantial distortion of the substituted CH–CH fragment in the chair conformation.

Experimental Section

General. Unless otherwise noted routine workup was as follows: The crude mixtures were extracted with methylene chloride, dried over anhydrous sodium sulfate, and concentrated at reduced pressure (rotary evaporator). Column (flash) chromatography was performed with silica gel 60 (230–400 mesh). Melting points were measured in an electrothermal apparatus in open capillary tubes and are uncorrected (d = decomposition). Some distillations of crude liquid products were carried out in a Kugelrohr apparatus in which case oven temperatures (ot) refer to the air bath temperature. ^{1}H-NMR (200.1 MHz) spectra were measured in $CDCl_3$ solutions. Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad), and axial or equatorial arrangements of protons are indexed as a or e, respectively. *J* values are given in Hz. Infrared spectra (IR) (supplementary material) were measured as Nujol dispersions on NaCl plates, film, or in KBr pellets and are reported in cm^{-1}. Mass spectra (supplementary material) were recorded in the electron impact (EI) at 70 eV or chemical ionization (CI) (methane as the reagent gas) modes. High-resolution mass spectra (HRMS) were obtained in the electron impact (EI) mode at 70 eV. All compounds prepared were shown to be over 96% pure by NMR analysis.

General Methods. (a) Reduction of Lactams. A solution of the appropriate lactam (0.2 mol) and sodium borohydride (7.5 g, 0.2 mol) in dry dioxane (300 mL) was cooled to 0 °C, and glacial acetic acid (12 g, 0.2 mol) in dry dioxane (25 mL) was slowly added. The reaction mixture was warmed to reflux for 22 h and hydrolyzed with water (200 mL). Routine workup affored crude material.

(b) Hydrolysis of amine–borane complexes was carried out by treatment of 0.02 mol of the complex with 10% aqueous hydrochloric acid (25 mL) in methanol (25 mL) at room temperature for 10 h. The resulting mixture was neutralized with sodium bicarbonate, extracted with chloroform, dried, and concentrated to dryness.

(c) Chlorination of Hydroxy Esters. (i) With Thionyl Chloride. To a solution of 0.7 mmol of hydroxy ester in 20 mL of methylene chloride was added 166 mg (1.4 mmol) of thionyl chloride. The mixture was stirred at room temperature for 16 h, and the excess of thionyl chloride was evaporated at reduced pressure. **(ii) With Hydrogen Chloride.** Hydrogen chloride was bubbled through a well-stirred solution of the hydroxy ester in methylene chloride containing anhydrous sodium sulfate. After 30 min the reaction mixture was filtered and concentrated.

2-Phenyl-1,4-thiazane (1). 1. 2-Phenyl-3-oxo-1,4-thiazane (65). To a solution of 5 g (0.02 mol) of ethyl α-bromophenylacetate and 2.27 g (0.02 mol) of 2-aminoethanethiol hydrochloride in 150 mL of absolute ethanol was added 5.52 g (0.04 mol) of potassium carbonate. The reaction mixture was refluxed for 24 h and then was treated with water (100 mL), extracted, dried, and evaporated. The residue was washed with cold diethyl ether to yield 4 g (80%) of **65**, mp 152–153 °C (lit.[7] mp 153–154 °C).

2. 2-Phenyl-1,4-thiazane–Borane Complex (66). The above product **65** was reduced following the general method described above. Crystallization of the residue from carbon tetrachloride yielded 3.3 g (83%) of **66**: δ 2.03 (bs, 3 H, BH_3), 2.65–3.08 (m, 4 H), 3.48–3.59 (m, 2 H), 3.94 (dd, *J* = 2.6, 11.8, 1 H, H_{2a}), 4.20 (bs, 1 H, NH), 7.26 (m, 5H, aromatic).

3. 2-Phenyl-1,4-thiazane (1). Amino–borane complex **66** was hydrolyzed with hydrochloric acid to afford 2.5 g (89%) of thiazane 1, mp 59–60 °C; HRMS calcd for $C_{10}H_{13}NS$ 179.0768, found 179.0752; δ 2.45–2.62 (m, 1 H), 2.87–3.15 (m, 3 H), 3.28–3.40 (m, 2 H), 3.92 (dd, *J* = 2.9, 10.6, 1 H, H_{2a}), 7.32 (m, 5 H, aromatic).

3-Phenyl-1,4-thiazane (17). Method A. 1. Ethyl 5-[(*tert*-Butoxycarbonyl)amino]-5-phenyl-3-thiapentanoate (69). To a solution of 0.4 g (7.4 mmol) of sodium methoxide in 150 mL of dry methanol was added 0.75 g (7.1 mmol) of methyl thioglycolate. The mixture was stirred for 15 min, and then 2.3 g (6.6 mmol) of *tert*-butyl *N*-(2-iodo-1-phenylethyl)carbamate (**68**) (obtained from ethyl *N*-(2-iodo-1-phenylethyl)carbamate[10] and 2-methyl-2-propanol) dissolved in 50 mL of dry methanol was added dropwise. The reaction mixture was refluxed 14 h and cooled to room temperature and the solvent removed. The residue was filtered, and the filtrate was concentrated to yield 1.83 g (85%) of **69**. It was crystallized from hexane–chloroform (1:1), mp 77–79 °C; δ 1.40 (s, 9 H, *t*-Bu), 3.00 (m, 2 H, $CHCH_2S$), 3.13 (d, 2 H, SCH_2CO), 3.73 (s, 3 H, CH_3O), 4.85 (m, 1 H, CHPh), 5.15 (s, 1 H, NH), 7.20 (m, 5 H, aromatic).

2. 3-Oxo-5-phenyl-1,4-thiazane (70). Carbamate **69** (3 g, 9.2 mmol) was stirred with a saturated solution of hydrogen chloride in ethyl acetate at room temperature for 5 min, and then the solvent was removed at reduced pressure. The oil obtained was dissolved in 50 mL of dry methanol and stirred with 0.63 g (4.6 mmol) of potassium carbonate for 12 h at room temperature. The reaction mixture was concentrated to dryness and the residue extracted with chloroform. The organic layer was evaporated to afford 1.7 g (quantitative yield) of **70** which was recrystallized from ethyl acetate: mp 148–149 °C; δ 2.78 (dd, *J* = 9.2, 13.7, 1 H, H_{6a}), 2.92 (ddd, *J* = 1.5, 4.1, 13.7, 1 H, H_{6e}), 3.28 (dd, *J* = 1.6, 19.7, 1 H, H_{2e}), 3.46 (d, *J* = 19.7, 1 H, H_{2a}), 4.80 (ddd, *J* = 1.3, 4.1, 9.2, 1 H, H_{5a}), 6.27 (bs, 1 H, NH), 7.10 (m, 5 H, aromatic).

3. 3-Phenyl-1,4-thiazane (17). The reduction of lactam **70** following the general method yielded a 1:1 mixture of **17** and its amine–borane complex **71**. The two compounds were separated by column chromatography using chloroform–methanol (6:1) as eluent. Compound **71** [mp 140–142 °C; δ 0.8–1.9 (bs, 3 H, BH_3), 2.30 (bs, 1 H, NH), 2.50–3.10 (m, 4 H), 3.50–3.90 (m, 3 H), 6.90–7.20 (m, 5 H, aromatic)], was quantitatively transformed into **17** by hydrolysis with a saturated solution of hydrogen chloride in ethyl acetate, mp 62–64 °C. HRMS calcd for $C_{10}H_{13}NS$ 179.0768, found 179.0762; δ 2.10 (bs, 1 H, NH), 2.42 (dddd, *J* = 2.2, 2.3, 3.0, 13.5, 1 H, H_{6e}), 2.47 (ddd, *J* = 2.2, 2.3, 13.4, 1 H, H_{2e}), 2.83 (dd, *J* = 10.6, 13.4, 1 H, H_{2a}), 2.90 (ddd, *J* = 3.1, 11.9, 13.5, 1 H, H_{6a}), 3.15 (ddd, *J* = 2.3, 11.9, 12.1, 1 H, H_{5a}), 3.43 (ddd, *J* = 3.0, 3.1, 12.1, 1 H, H_{5e}), 3.92 (dd, *J* = 2.2, 10.6, 1 H, H_3), 7.20 (m, 5 H, aromatic).

Method B. To a solution of 2.2 g (0.04 mol) of potassium hydroxide in 50 mL of methanol cooled to 0–5 °C was added 2.3 g (0.02 mol) of 2-aminoethanethiol hydrochloride. To this mixture was added a solution of 4.0 g (0.02) mol of α-bromoacetophenone in 10 mL of methanol. The reaction mixture was stirred below 5 °C for 1 h and then acidified with 30% methanolic hydrochloric acid. After being stirred for an additional 1 h at 0 °C, 1.5 g (0.04 mol) of sodium borohydride was slowly added and the mixture was stirred 30 min. The hydrolysis was carried out with aqueous hydrochloric acid, the solvent was evaporated to dryness, and the residue was treated with water. The aqueous layer was made basic with a saturated solution of sodium bicarbonate and extracted with chloroform. The extracts were dried and the solvent removed at reduced pressure. Spectroscopic data and physical constants of the resulting product (3.0 g, 85%) were identical with those of the compound obtained from method A.

***cis*-2,3-Diphenyl-1,4-thiazane (33). 1. Methyl *erythro*-5-Hydroxy-4,5-diphenyl-3-thiapentanoate (73).** To a solution of 42.5 mg (0.79 mmol) of sodium methoxide in 20 mL of methanol was added 0.6 g (5.7 mmol) of methyl thioglycolate and then 1 g (5.1 mmol) of *trans*-stilbene oxide in 50 mL of methanol. The reaction mixture was refluxed for 2 h and stirred at room tem-

perature overnight. It was hydrolyzed with water (50 mL), extracted, and dried and the solvent evaporated to afford 1.7 g (quantitative yield) of **73** which was crystallized from cyclohexane, mp 44–46 °C; δ 2.43 (d, J = 3.0, 1 H, OH), 2.88 and 2.97 (d and d, J = 15.4 and 15.4, 1 H and 1 H, CH_2), 3.61 (s, 3 H, CH_3O), 4.31 (d, J = 6.9, 1 H, CHS), 5.02 (dd, J = 3.0, 6.9, 1 H, CHO), 7.35–7.55 (m, 10 H, aromatic).

2. Methyl *erythro*-5-Chloro-4,5-diphenyl-3-thiapentanoate (74). Treatment of **73** with thionyl chloride (80% yield) or hydrogen chloride (quantitative yield) following the general procedure for chlorination (vide supra) afforded **74** which was crystallized from cyclohexane, mp 74–76 °C; δ 2.74 (s, 2 H, CH_2), 3.60 (s, 3 H, CH_3O), 4.64 (d, J = 9.9, 1 H, CHS), 5.22 (d, J = 9.9, 1 H, CHCl), 7.30–7.50 (m, 10 H, aromatic).

3. *cis*-4,5-Diphenyl-3-thiapentanolide (75). To 0.5 g of chloroester **74** dissolved in 150 mL of acetonitrile was added 20 mL of 20% ammonium hydroxide. The resulting solution was stirred at room temperature for 60 h and then extracted with methylene chloride. The crude product (90% yield) obtained after evaporation of dried extracts was crystallized from carbon tetrachloride/ethyl acetate (2:1) to afford lactam **75**, mp 197–198 °C; δ 3.44 and 3.81 (dd and d, J = 0.8, 16.3, and 16.3, 1 H and 1 H, CH_2), 4.57 (d, J = 4.0, 1 H, CHS), 4.97 (dd, J = 4.0, 4.1, 1 H, CHN), 6.16 (bs, 1 H, NH) 6.85–7.45 (m, 10 H, aromatic).

4. *cis*-2,3-Diphenyl-1,4-thiazane (33). Reduction of lactam **75** with the sodium borohydride/acetic acid/dioxane system (vide supra) afforded **33** (90% yield) which was crystallized from carbon tetrachloride/ethyl acetate (1:1), mp 121–122 °C; δ 2.06 (bs, 1 H, NH), 2.76 (ddd, J = 2.9, 5.2, 13.5, 1 H, H_{6e}), 3.25 (ddd, J = 3.4, 9.9, 13.5, 1 H, H_{6a}), 3.38 (ddd, J = 2.9, 9.9, 12.4, 1 H, H_{5a}), 3.65 (ddd, J = 3.4, 5.2, 12.4, 1 H, H_{5e}), 4.15 (d, J = 3.7, 1 H, H_2), 4.71 (d, J = 3.7, 1 H, H_3), 7.01–7.43 (m, 10 H, aromatic). Anal. Calcd for $C_{16}H_{17}NS$: C, 75.25; H, 6.71; N, 5.49. Found: C, 75.14; H, 6.69; N, 5.31.

***trans*-2,3-Diphenyl-1,4-thiazane (49).** **1. Methyl *threo*-5-hydroxy-4,5-diphenyl-3-thiapentanoate (76)** was obtained as a syrup using *cis*-stilbene oxide as starting material following the method described above for its isomer **73**. It was purified by column chromatography using methylene chloride as eluent; δ 3.07 and 3.21 (d and d, J = 15.1 and 15.1, 1 H and 1 H, CH_2), 3.64 (s, 3 H, CH_3O), 4.27 (d, J = 8.3, 1 H, CHS), 4.97 (d, J = 8.3, 1 H, CHO), 7.15–7.30 (m, 10 H, aromatic).

2. Chlorination of hydroxy ester **76** with thionyl chloride afforded a 9:1 mixture of ***trans*-2,3-diphenyl-6-oxo-1,4-oxathiane (77)** and **methyl *threo*-5-chloro-4,5-diphenyl-3-thiapentanoate (78).** The use of hydrogen chloride yielded an equimolar mixture of lactone **77** and *erythro*-chloro ester **74**. Compound **77** (syrup); δ 3.38 and 4.05 (d and d, J = 14.8, and 14.8, 1 H and 1 H, CH_2), 4.41 (d, J = 10.7, 1 H, CHS), 5.44 (d, J = 10.7, 1 H, CHO), 6.90–7.15 (m, 10 H, aromatic). Compound **78** (syrup); δ 2.90 and 3.11 (d and d, J = 15.4, and 15.4, 1 H and 1 H, CH_2), 3.59 (s, 3 H, CH_3O), 4.66 (d, J = 8.7, 1 H, CHS), 5.21 (d, J = 8.7, 1 H, CHCl), 6.95–7.15 (m, 10 H, aromatic).

3. *threo*-5-Hydroxy-4,5-diphenyl-3-thiapentanamide (79) was obtained by treatment of a solution of 1 g (3.3 mmol) of methyl *threo*-hydroxy ester **76** or 1 g (3.7 mmol) of lactone **77** in 25 mL of acetonitrile with 10 mL of 20% ammonium hydroxide for 16 h at room temperature. The reaction mixture was diluted with water (25 mL), extracted, dried, and evaporated to give crude **79** in quantitative yield. It was crystallized from chloroform, mp 131–132 °C: δ 3.05 and 3.22 (d and d, J = 16.8, and 16.8, 1 H and 1 H, CH_2), 4.04 (d, J = 7.9, 1 H, CHS), 5.01 (d, J = 7.9, 1 H, CHO), 5.39 (bs, 1 H, OH), 6.44 (bs, 2 H, NH_2), 7.00–7.25 (m, 10 H, aromatic).

4. *threo*-5-Chloro-4,5-diphenyl-3-thiapentanamide (80). To a solution of 2.87 g (0.01 mol) of hydroxyamide **79** in 250 mL of methylene chloride at 0 °C was added 2.62 g (0.02 mol) of thionyl chloride. After 5 min at this temperature, the excess thionyl chloride was removed in a rotary evaporator below 20 °C to afford a 9:1 mixture of the *threo*-chloroamide **80** and lactone **77**. Compound **80**: δ 2.88 and 3.12 (d and d, J = 16.8, and 16.8, 1 H and 1 H, CH_2), 4.36 (d, J = 8.6, 1 H, CHS), 5.20 (d, J = 8.6, 1 H, CHCl), 6.90–7.15 (m, 10 H, aromatic).

5. *trans*-4,5-Diphenyl-3-thiapentanolide (81). To 0.5 g of the above mixture of **80** and **77** in 150 mL of acetonitrile was added 20 mL of 20% ammonium hydroxide. The resulting solution was stirred at room temperature for 16 h and extracted. The crude product obtained after concentration of the dried extracts was crystallized from carbon tetrachloride to afford lactam **81** in quantitative yield from **80**. Recrystallized from cyclohexane it melted at 110–112 °C: δ 3.44 and 3.74 (d and d, J = 16.8, and 16.8, 1 H and 1 H, CH_2), 4.05 (d, J = 9.7, 1 H, CHS), 4.92 (dd, J = 1.2, 9.7, 1 H, CHN), 6.14 (bs, 1 H, NH) 6.94–7.56 (m, 10 H, aromatic).

6. *trans*-2,3-Diphenyl-1,4-thiazane (49). The reduction of lactam **81** with the sodium borohydride/acetic acid/dioxane system, following the method described above for the reduction of lactam **65**, afforded thiazane **49** as borane complex which was hydrolyzed with 10% hydrochloric acid in methanol/water, yield 85%. Crystallized from cyclohexane, mp 85–86 °C: HRMS calcd for $C_{16}H_{17}NS$ 255.1081, found 255.1089; δ 2.14 (bs, 1 H, NH), 2.61 (ddd, J = 2.3, 3.1, 13.1, 1 H, H_{6e}), 3.19 (ddd, J = 3.2, 12.0, 13.1, 1 H, H_{6a}), 3.26 (ddd, J = 2.3, 11.9, 12.0, 1 H, H_{5a}), 3.48 (ddd, J = 3.1, 3.2, 11.9, 1 H, H_{5e}), 4.02 (d, J = 9.6, 1 H, H_2), 4.05 (d, J = 9.6, 1 H, H_3), 7.08 (m, 10 H, aromatic).

(d) General Method for Preparation of *N*-Methyl Derivatives. To a solution of 0.78 mmol of the appropriate amino compound in 25 mL of methanol was added 0.68 mL (35 mmol) of a 40% aqueous solution of formaldehyde. The mixture was stirred under reflux for 30 min and cooled to room temperature after which 400 mg (0.01 mol) of sodium borohydride was slowly added. The reaction mixture was stirred for 1 h at this temperature, diluted with 25 mL of water, extracted, dried, and concentrated.

***N*-Methyl-2-phenyl-1,4-thiazane (5)** was obtained in 98% yield by methylation of **1**, ot 130–140 °C (0.1 mmHg): HRMS calcd for $C_{11}H_{15}NS$ 193.0925, found 193.0939; δ 2.34 (m, 1 H, H_{5a}), 2.36 (s, 3 H, CH_3), 2.46 (dd, J = 10.8, 11.9, 1 H, H_{3a}), 2.64 (m, 1 H, H_{6e}), 3.11 (m, 1 H, H_{6a}), 3.18 (dd, J = 2.8, 11.9, 1 H, H_{3e}), 3.16 (m, 1 H, H_{5e}), 4.10 (dd, J = 2.8, 10.8, 1 H, H_2), 7.20–7.40 (m, 5 H, aromatic).

***N*-Methyl-3-phenyl-1,4-thiazane (21)** was obtained in 97% yield by methylation of **2**, ot 160–170 °C (0.05 mmHg): HRMS calcd for $C_{11}H_{15}NS$ 193.0925, found 193.0919; δ 2.01 (s, 3 H, CH_3), 2.45 (dd, J = 2.5, 13.5, 1 H, H_{2e}), 2.53 (m, 2 H, H_{5a} and H_{6e}), 2.90 (dd, J = 10.8, 13.5, 1 H, H_{2a}), 3.05 (ddd, J = 2.8, 12.0, 13.5, 1 H, H_{6a}), 3.14 (dd, J = 2.5, 10.8, 1 H, H_{3a}), 3.28 (ddd, J = 2.8, 3.2, 12.2, 1 H, H_{5e}), 7.20 (m, 5 H, aromatic).

***N*-Methyl-*cis*-2,3-diphenyl-1,4-thiazane (37)** was obtained in 96% yield by methylation of **33** and was purified by chromatography using methylene chloride/methanol (15:1) as eluent, mp 95–97 °C: HRMS calcd for $C_{17}H_{19}NS$ 269.1238, found 269.1226; δ 2.14 (s, 3 H, CH_3), 2.73 (ddd, J = 3.2, 8.0, 12.4, 1 H, H_{5a}), 3.25 (dddd, J = 0.5, 3.2, 7.6, 13.6, 1 H, H_{6e}), 3.19 (ddd, J = 2.9, 8.0, 13.6, 1 H, H_{6a}), 3.35 (ddd, J = 2.9, 7.6, 12.4, 1 H, H_{5e}), 3.89 (d, J = 3.7, 1 H, H_3), 4.18 (dd, J = 0.5, 3.7, 1 H, H_2), 7.08–7.33 (m, 10 H, aromatic).

***N*-Methyl-*trans*-2,3-diphenyl-1,4-thiazane (53)** was obtained in 95% yield by methylation of **49** and was purified by chromatography using methylene chloride as eluent, mp 119–120 °C: HRMS calcd for $C_{17}C_{19}NS$ 269.1238, found 269.1244; δ 2.03 (s, 3 H, CH_3), 2.63 (ddd, J = 2.4, 3.4, 13.5, 1 H, H_{6e}), 3.70 (ddd, J = 2.4, 12.1, 12.2, 1 H, H_{5a}), 3.23 (d, J = 9.7, 1 H, H_3), 3.24 (ddd, J = 2.9, 12.2, 13.5, 1 H, H_{6a}), 3.34 (ddd, J = 2.9, 3.4, 12.1, 1 H, H_{5e}), 3.96 (d, J = 9.7, 1 H, H_2), 6.95–7.37 (m, 10 H, aromatic).

(e) General Method of Preparation of Carbamates. *N*-Ethyl Carbamates. To a solution of 0.01 mol of the appropriate amino compound was added 0.02 mol of ethyl chloroformate and 0.04 mol of potassium carbonate. The reaction mixture was stirred under reflux for 12 h, and the solvent was removed at reduced pressure. The residue was treated with methylene chloride and filtered and the filtrate evaporated to dryness and purified as indicated for individual compounds. ***N*-*tert*-Butyl Carbamates**: A solution of 0.01 mol of the appropriate amino compound and 0.01 mol of di-*tert*-butyl dicarbonate in 50 mL of methylene chloride was stirred at room temperature for 12 h. The solvent was removed and the crude material purified as indicated in the individual preparations below.

***N*-(Ethoxycarbonyl)-2-phenyl-1,4-thiazane (9)** was obtained from **1** in quantitative yield, ot 140–145 °C (0.1 mmHg): HRMS calcd for $C_{13}H_{17}NO_2S$ 251.0980, found 251.0974; δ 1.30 (t, 3 H, CH_3), 2.54 (dd, J = 2.5, 13.1, 1 H, H_{6e}), 3.06 (m, 3 H, H_{3a}, H_{5a},

H_{6a}), 3.91 (dd, J = 2.9, 10.7, 1 H, H_{2e}), 4.13 (q, 2 H, CH_2O), 4.46 (m, 2 H, H_{3e}, H_{5e}), 7.20–7.40 (m, 5 H, aromatic).

***N*-(Ethoxycarbonyl)-3-phenyl-1,4-thiazane (25)** was obtained from **17** in quantitative yield, ot 150–155 °C (0.1 mmHg): HRMS calcd for $C_{13}H_{17}NO_2S$ 251.0980, found 251.0978; δ 1.15 (t, 3 H, CH_3), 2.29 (ddd, J = 2.5, 3.1, 12.3, 1 H, H_{6e}), 2.75 (ddd, J = 3.2, 12.2, 13.3, 1 H, H_{6a}), 2.99 (ddd, J = 1.6, 3.7, 14.2, 1 H, H_{2e}), 3.00 (ddd, J = 2.5, 12.2, 13.9, 1 H, H_{5a}), 3.13 (dd, J = 4.1, 14.2, 1 H, H_{2a}), 4.14 (q, 2 H, CH_2O), 4.21 (ddd, J = 3.1, 3.2, 13.9, 1 H, H_{5e}), 5.58 (dd, J = 3.7, 4.1, 1 H, H_{3e}), 7.20–7.40 (m, 5 H, aromatic).

***N*-(Ethoxycarbonyl)-*cis*-2,3-diphenyl-1,4-thiazane (41)** was obtained as a syrup from **33** in quantitative yield: HRMS calcd for $C_{19}H_{21}NO_2S$ 327.1293, found 327.1298; δ 1.26 (t, 3 H, CH_3), 2.79 (ddd, J = 2.8, 2.9, 13.5, 1 H, H_{6e}), 3.08 (ddd, J = 3.2, 12.4, 13.5, 1 H, H_{6a}), 3.38 (ddd, J = 2.8, 12.4, 14.3, 1 H, H_{5a}), 4.19 (dq, 2 H, CH_2O), 4.34 (ddd, J = 2.9, 3.2, 14.3, 1 H, H_{5e}), 4.62 (d, J = 4.1, 1 H, H_2), 5.81 (d, J = 4.1, 1 H, H_3), 6.89–7.43 (m, 10 H, aromatic).

***N*-(Ethoxycarbonyl)-*trans*-2,3-diphenyl-1,4-thiazane (57)** was obtained from **49** in quantitative yield and recrystallized from cyclohexane/carbon tetrachloride, mp 198–200 °C: HRMS calcd for $C_{19}H_{21}NO_2S$ 327.1293, found 327.1315; δ 1.16 (t, 3 H, CH_3), 2.75 (ddd, J = 2.2, 3.8, 12.3, 1 H, H_{6e}), 3.06 (ddd, J = 5.3, 12.3, 12.4, 1 H, H_{6a}), 3.44 (ddd, J = 3.8, 12.4, 14.1, 1 H, H_{5a}), 4.10 (q, 2 H, CH_2O), 4.41 (d, J = 7.1, 1 H, H_2), 4.47 (ddd, J = 2.2, 5.3, 14.1, 1 H, H_{5e}), 5.66 (d, J = 7.1, 1 H, H_3), 7.10–7.41 (m, 10 H, aromatic).

***N*-(*tert*-Butoxycarbonyl)-2-phenyl-1,4-thiazane (13)** was obtained from **1** as a syrup in quantitative yield and was purified by chromatography using methylene chloride as eluent: δ 1.47 (s, 9 H, *t*-Bu), 2.54 (ddd, J = 2.3, 2.8, 13.0, 1 H, H_{6e}), 2.90 (ddd, J = 2.5, 11.6, 13.0, 1 H, H_{6a}), 3.09 (ddd, J = 2.3, 11.6, 13.9, 1 H, H_{5a}), 3.18 (dd, J = 10.6, 13.0, 1 H, H_{3a}), 3.90 (dd, J = 2.8, 10.6, 1 H, H_{2a}), 4.40 (dd, J = 2.8, 13.0, 1 H, H_{3e}), 4.46 (ddd, J = 2.5, 2.8, 13.9, 1 H, H_{5e}), 7.40 (m, 5 H, aromatic).

***N*-(*tert*-Butoxycarbonyl)-3-phenyl-1,4-thiazane (29)** was obtained from **17** in quantitative yield. It was crystallized from cyclohexane: δ 1.43 (s, 9 H, *t*-Bu), 2.41 (ddd, J = 2.5, 2.9, 12.6, 1 H, H_{6e}), 2.84 (ddd, J = 3.0, 12.5, 12.6, 1 H, H_{6a}), 3.00 (dd, J = 3.8, 14.2, 1 H, H_{2e}), 3.05 (ddd, J = 2.5, 12.5, 13.6, 1 H, H_{5a}), 3.19 (dd, J = 4.3, 14.2, 1 H, H_{2a}), 4.27 (ddd, J = 2.9, 3.0, 13.6, 1 H, H_{5e}), 5.58 (dd, J = 3.8, 4.3, 1 H, H_3), 7.20–7.50 (m, 5 H, aromatic).

***N*-(*tert*-Butoxycarbonyl)-*cis*-2,3-diphenyl-1,4-thiazane (45)** was obtained as a syrup from **33** in quantitative yield. It was purified by chromatography using methylene chloride as eluent and was crystallized from cyclohexane, mp 172–174 °C; δ 1.45 (s, 9 H, *t*-Bu), 2.77 (ddd, J = 2.8, 3.1, 13.4, 1 H, H_{6e}), 3.05 (ddd, J = 3.4, 12.3, 13.4, 1 H, H_{6a}), 3.38 (ddd, J = 2.8, 12.3, 14.1, 1 H, H_{5a}), 4.47 (ddd, J = 3.1, 3.4, 14.1, 1 H, H_{5e}), 4.61 (d, J = 4.1, 1 H, H_2), 5.76 (d, J = 4.1, 1 H, H_3), 7.06–7.56 (m, 10 H, aromatic). Anal. Calcd for $C_{21}H_{25}NO_2S$: C, 70.95; H, 7.09; N, 3.94. Found: C, 70.89; H, 6.68; N, 3.86.

***N*-(*tert*-Butoxycarbonyl)-*trans*-2,3-diphenyl-1,4-thiazane (61)** was obtained from **49** in quantitative yield. It was purified by chromatography using methylene chloride as eluent, mp 82–84 °C: δ 1.30 (s, 9 H, *t*-Bu), 2.71 (ddd, J = 2.1, 3.9, 12.3, 1 H, H_{6e}), 3.06 (ddd, J = 5.2, 12.3, 12.4, 1 H, H_{6a}), 3.37 (ddd, J = 3.9, 12.4, 14.2, 1 H, H_{5a}), 4.39 (d, J = 6.8, 1 H, H_2), 4.44 (ddd, J = 2.1, 5.2, 14.2, 1 H, H_{5e}), 5.60 (d, J = 6.8, 1 H, H_3), 6.97–7.27 (m, 10 H, aromatic).

(f) General Method of Oxidation of Thioethers to Sulfoxides. (i) With Sodium Metaperiodate. To a solution of 5 mmol of the thioether in 20 mL of ethanol cooled at 0 °C was added 5 mmol of sodium metaperiodate, and the reaction mixture was stirred at 0 °C for 1 h. The cooling bath was removed, and stirring was continued overnight. The reaction mixture was diluted with 20 mL of water, extracted with methylene chloride, dried, and concentrated. **(ii) With *m*-Chloroperoxybenzoic Acid (*m*-CPBA).** To a solution of 0.05 mol of the thioether in 20 mL of methylene chloride was added 0.05 mol of *m*-CPBA acid in 20 mL of methylene chloride, and the mixture was stirred until completion (TLC or ^{1}H-NMR) at room temperature. The reaction mixture was washed three times with an aqueous saturated solution of sodium bicarbonate and once with water. The organic layer was dried and the solvent evaporated. **(iii) With Peroxytrifluoroacetic acid (PTFA).** To a solution of 5 mmol of thioether in 40 mL of TFA cooled with an ice/salt bath was added dropwise 5 mmol of peroxytrifluoroacetic acid dissolved in TFA, and the mixture was stirred for 1 h below 0 °C. When the peracid was consumed (iodide paper indicator), the TFA was evaporated under reduced pressure with benzene in order to remove most of the solvent. The crude product was dissolved in methylene chloride and washed several times with saturated sodium bicarbonate solution and water, dried, and concentrated.

2-Phenyl-1,4-thiazane 1-Oxides (2 and 3). Oxidation of amino–borane complex **66** with $NaIO_4$ afforded a mixture of two amino–borane complexes **82** and **83** epimeric at sulfur. Separation was carried out by chromatography using ethyl acetate as eluent yielding pure **82** (25%) and pure **83** (75%). Both isomers were independently hydrolyzed following the general method to afford free amino sulfoxides **2** and **3**, respectively. Compound **2**: mp 100–102 °C; HRMS calcd for $C_{10}H_{13}NOS$ 195.0717, found 195.0729; δ 2.00 (bs, 1 H, NH), 2.71–2.86 (m, 1 H), 2.96–3.10 (m, 3 H), 3.60–3.76 (m, 2 H), 3.92 (m, 1 H), 7.00–7.20 (m, 5 H, aromatic). Compound **3**: mp 120–122 °C; HRMS calcd for $C_{10}H_{13}NOS$ 195.0717, found 195.0722; δ 1.80 (bs, 1 H, NH), 2.73–3.16 (m, 3 H), 3.35–3.50 (m, 3 H), 3.64–3.71 (m, 1 H), 7.00–7.20 (m, 5 H, aromatic).

3-Phenyl-1,4-thiazane 1-Oxides (18 and 19). Oxidation of thiazane **17** with $NaIO_4$ afforded a 3:7 mixture of the two possible epimers at sulfur, **18** and **19**. This mixture was purified by chromatography using chloroform/methanol (6:1) as eluent but the isomers were not separated. They were transformed to their corresponding oxalates as follows. To a solution of the mixture **18** and **19** (5 mmol) in the minimum amount of 95% ethanol necessary to effect solution was added 5 mmol of oxalic acid as a concentrated ethanol solution. After a few seconds a precipitate was formed which was collected. Successive crystallizations from ethanol gave the pure epimeric oxalates which were hydrolyzed to the corresponding free amino compounds **18** and **19** by treatment with sodium bicarbonate. Compound **18** (syrup): HRMS calcd for $C_{10}H_{13}NOS$ 195.0717, found 195.0710; δ 2.37 (bs, 1 H, NH), 2.73 (m, 2 H), 2.99 (m, 2 H), 3.35 (m, 2 H), 3.91 (dd, J = 1.6, 11.5, H_3), 7.20–7.40 (m, 5 H, aromatic). Compound **19** (syrup): HRMS calcd for $C_{10}H_{13}NOS$ 195.0717, found 195.0704; δ 2.00 (bs, 1 H, NH), 2.68 (m, 2 H, H_{2a}, H_{6a}), 2.95 (m, 2 H, H_{2e}, H_{6e}), 3.18 (ddd, J = 3.0, 4.0, 13.7, 1 H, H_{5e}), 3.87 (ddd, J = 2.0, 12.7, 12.9, 1 H, H_{5a}), 4.64 (dd, J = 1.6, 11.6, 1 H, H_{3a}), 7.10–7.30 (m, 5 H, aromatic).

***cis*-2,3-Diphenyl-1,4-thiazane 1-Oxide (35).** Oxidation of thiazane **33** with $NaIO_4$, *m*-CPBA, or PTFA (yield >90%) afforded only one sulfoxide, **35**, which was crystallized from cyclohexane, mp 150–151 °C: δ 1.97 (bs, 1 H, NH), 2.63 (dddd, J = 2.0, 2.1, 4.5, 14.4, 1 H, H_{6e}), 3.02 (ddd, J = 4.1, 12.7, 14.4, 1 H, H_{6a}), 3.23 (ddd, J = 4.1, 4.5, 12.6, 1 H, H_{5e}), 3.87 (ddd, J = 2.1, 12.6, 12.7, 1 H, H_{5a}), 3.91 (dd, J = 2.0, 3.2, 1 H, H_2), 5.02 (d, J = 3.2, 1 H, H_3), 6.97–7.73 (m, 10 H, aromatic). Anal. Calcd for $C_{16}H_{17}NOS$: C, 70.81; H, 6.31; N, 5.16. Found: C, 70.33; H, 6.40; N, 4.98.

***trans*-2,3-Diphenyl-1,4-thiazane 1-Oxides (50 and 51).** Oxidation of thiazane **49** afforded a 55:45 ($NaIO_4$) or 35:65 (*m*-CPBA) mixture of the two possible epimers at sulfur, **50** and **51** (yield >90%), which were separated by chromatography using methylene chloride/methanol (15:1) as eluent. Compound **50**: mp 215–216 °C; HRMS calcd for $C_{16}H_{17}NOS$ 271.1030, found 271.1029; δ 2.23 (bs, 1 H, NH), 2.99 (ddd, J = 4.0, 12.6, 13.6, 1 H, H_{6a}), 3.11 (ddd, J = 2.0, 3.0, 13.6, 1 H, H_{6e}), 3.18 (ddd, J = 3.0, 4.0, 13.0, 1 H, H_{5e}), 3.73 (d, J = 10.6, 1 H, H_2), 4.02 (ddd, J = 2.0, 12.6, 13.0, 1 H, H_{5a}), 4.85 (d, J = 10.6, 1 H, H_3), 6.97–7.22 (m, 10 H, aromatic). Compound **51**: mp 250 °C (d); δ 2.10 (bs, 1 H, NH), 3.13 (ddd, J = 3.5, 12.0, 12.7, 1 H, H_{6a}), 3.24 (ddd, J = 1.7, 12.7, 13.9, 1 H, H_{5a}), 3.50 (ddd, J = 3.5, 3.9, 13.9, 1 H, H_{5e}), 3.60 (ddd, J = 1.7, 3.9, 12.0, 1 H, H_{6e}), 3.86 (d, J = 10.4, 1 H, H_2), 4.07 (d, J = 10.4, 1 H, H_3) 7.01–7.14 (m, 10 H, aromatic). Anal. Calcd for $C_{16}H_{17}NOS$: C, 70.81; H, 6.31; N, 5.16. Found: C, 70.37; H, 6.23; N, 5.10.

***N*-Methyl-2-phenyl-1,4-thiazane 1-Oxides (6 and 7).** Oxidation of thiazane **5** with PTFA afforded a 55:45 mixture of these two epimers at sulfur, **6** and **7** (yield 85%). The isomers could not be separated: HRMS calcd for $C_{11}H_{15}NOS$ 209.0874, found 209.0882; δ 2.26 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3), 2.50–3.40 (m, 12 H), 3.65 (dd, J = 3.1, 11.7, 1 H), 3.83 (dd, J = 3.1, 9.4, 1 H), 7.31 (m, 10 H, aromatic).

***N*-Methyl-3-phenyl-1,4-thiazane 1-Oxides (22 and 23).** Oxidation of thiazane **21** with PTFA afforded a 70:30 mixture of the two epimers at sulfur, **22** and **23** (yield 90%), which could not be separated: HRMS calcd for $C_{11}H_{15}NOS$ 209.0874, found 209.0878; δ 2.01 (s, 3 H, CH_3), 2.09 (s, 3 H, CH_3), 2.47–2.61 (m, 1 H), 2.60–2.75 (m, 1 H), 2.85–3.05 (m, 7 H), 3.17–3.45 (m, 4 H), 3.90 (m, 1 H), 7.35 (m, 10 H, aromatic).

***N*-Methyl-*cis*-2,3-diphenyl-1,4-thiazane 1-Oxide (39).** Oxidation of thiazane **37** with PFTA afforded only one sulfoxide, **39**, which was purified by chromatography using methylene chloride/methanol (50:1) as eluent: yield 80%; HRMS calcd for $C_{17}H_{19}NOS$ 285.1187, found 285.1195; δ 2.21 (s, 3 H, CH_3), 2.74 (m, 1 H), 3.12 (m, 1 H), 3.36 (m, 1 H), 3.96 (dd, J = 2.9, 3.2, 1 H, H_2), 4.36 (d, J = 3.2, 1 H, H_3), 6.89–7.64 (m, 10 H, aromatic).

***N*-Methyl-*trans*-2,3-diphenyl-1,4-thiazane 1-Oxides (54 and 55).** Oxidation of thiazane **53** with PTFA afforded a 40:60 mixture of the two epimers at sulfur, **54** and **55** (yield 75%), which could not be separated: HRMS calcd for $C_{17}H_{19}NOS$ 285.1187, found 285.1186. However, sulfoxide **54** was obtained from **39** by overnight reflux in a 10% aqueous/methanolic (1:1) solution of potassium hydroxide. Routine workup of the crude reaction mixture yielded diastereoisomerically pure **54** which was purified by chromatography using methylene chloride–methanol (15:1) as eluent. Compound **54**: HRMS calcd for $C_{17}H_{19}NOS$ 285.1187, found 285.1184; δ 2.10 (s, 3 H, CH_3), 2.93–3.13 (m, 2 H), 3.47–3.61 (m, 2 H), 3.72 (d, J = 10.7, 1 H, H_2), 4.17 (d, J = 10.7, 1 H, H_3), 7.00 (m, 10 H, aromatic). Compound **55** (from the **54** + **55** mixture): δ 2.18 (s, 3 H, CH_3), 2.66–3.70 (m, 4 H), 3.28 (d, J = 10.9, 1 H, H_2), 4.39 (d, J = 10.9, 1 H, H_3), 6.97 (m, 10 H, aromatic).

***N*-(Ethoxycarbonyl)-2-phenyl-1,4-thiazane 1-Oxides (10 and 11).** Oxidation of thiazane **9** with *m*-CPBA afforded a 70:30 mixture of the two epimers at sulfur **10** and **11** (yield 90%): HRMS (mixture **10** + **11**) calcd for $C_{13}H_{17}NO_3S$ 267.0929, found 267.0948. The isomers were separated by chromatography using ethyl acetate as eluent. Compound **10**: mp 121–123 °C; δ 1.27 (t, 3 H, CH_3), 2.67–2.82 (m, 1 H), 2.93–3.03 (m, 1 H), 3.55–3.63 (m, 1 H), 4.10 (q, 2 H, CH_2O), 3.60–4.40 (m, 4 H), 7.20–7.40 (m, 5 H, aromatic). Compound **11**: mp 58–60 °C; δ 1.29 (t, 3 H, CH_3), 2.70–2.82 (m, 1 H), 2.90–3.20 (m, 2 H), 3.47–3.70 (m, 3 H), 4.20 (q, 2 H, CH_2O), 4.20–4.35 (m, 1 H), 7.10–7.30 (m, 5 H, aromatic).

***N*-(Ethoxycarbonyl)-3-phenyl-1,4-thiazane 1-Oxides (26 and 27).** Oxidation of thiazane **25** with *m*-CPBA or PTFA afforded a syrup which was purified by chromatography. The proton NMR spectrum of the obtained compound indicated a <5:>95 mixture of the two possible epimers at sulfur, **26** and **27** (yield 80%) which could not be separated: HRMS (mixture **26** + **27**) calcd for $C_{13}H_{17}NO_3S$ 267.0929, found 267.0926. Compound **27** (from **26** + **27** mixture): δ 1.30 (t, 3 H, CH_3), 2.73 (ddd, J = 3.4, 12.1, 12.8, 1 H, H_{6a}), 3.00 (ddd, J = 1.9, 12.8, 15.0, 1 H, H_{5a}), 3.01 (dd, J = 4.7, 12.9, 1 H, H_{2a}), 3.36 (dddd, J = 1.9, 2.5, 3.6, 12.1, 1 H, H_{6e}), 3.96 (ddd, J = 2.5, 3.7, 12.9, 1 H, H_{2e}), 4.20 (q, 2 H, CH_2O), 4.43 (dddd, J = 1.7, 3.4, 3.6, 15.0, H_{5e}), 6.02 (dd, J = 3.7, 4.7, 1 H, H_{3e}), 7.30–7.50 (m, 5 H, aromatic).

***N*-(Ethoxycarbonyl)-*cis*-2,3-diphenyl-1,4-thiazane 1-Oxide (43).** Oxidation of thiazane **41** with $NaIO_4$ or *m*-CPBA afforded only one sulfoxide **43** in 80% yield. It was crystallized from benzene/cyclohexane (1:1), mp 98–100 °C: δ 1.26 (t, 3 H, CH_3), 2.92 (ddd, J = 3.9, 12.5, 13.1, 1 H, H_{6a}), 3.42 (ddd, J = 2.1, 13.1, 15.6, 1 H, H_{5a}), 3.73 (ddd, J = 2.1, 3.8, 12.5, 1 H, H_{6e}), 4.16 (dq, 2 H, CH_2O), 4.29 (d, J = 4.8, 1 H, H_2), 4.45 (dddd, J = 1.3, 3.8, 3.9, 15.6, H_{5e}), 6.00 (dd, J = 1.3, 4.8, 1 H, H_3), 7.08–7.29 (m, 10 H, aromatic). Anal. Calcd for $C_{19}H_{21}NO_3S$: C, 66.45; H, 6.16; N, 4.08. Found: C, 66.15; H, 6.12; N, 3.97.

***N*-(Ethoxycarbonyl)-*trans*-2,3-diphenyl-1,4-thiazane 1-Oxide (58 and 59).** Oxidation of thiazane **57** with $NaIO_4$ (or *m*-CPBA) afforded an equimolar mixture of the two epimers at sulfur, **58** and **59** (yield 90%), which were separated by chromatography using methylene chloride/methanol (10:1) as eluent. Compound **58**: HRMS calcd for $C_{19}H_{21}NO_3S$ 343.1242, found 343.1256; δ 1.13 (t, 3 H, CH_3), 2.66 (ddd, J = 3.0, 3.4, 13.8, 1 H, H_{6e}), 3.26 (ddd, J = 5.4, 11.9, 13.8, 1 H, H_{6a}), 3.94 (ddd, J = 3.4, 11.9, 14.7, 1 H, H_{5a}), 4.01 (q, 2 H, CH_2O), 4.40 (ddd, J = 3.0, 5.4, 14.7, H_{5e}), 4.55 (d, J = 6.0, 1 H, H_2), 5.78 (d, J = 6.0, 1 H, H_3), 6.85–7.18 (m, 10 H, aromatic). Compound **59**: mp 118–119 °C; HRMS calcd for $C_{19}H_{21}NO_3$ 343.1242, found 343.1246; δ 1.09 (t, 3 H, CH_3), 2.98 (ddd, J = 6.4, 11.8, 13.9, 1 H, H_{6a}), 3.10 (ddd, J = 2.4, 4.3, 13.9, 1 H, H_{6e}), 3.53 (ddd, J = 4.3, 11.8, 15.0, 1 H, H_{5a}), 3.99 (q, 2 H, CH_2O), 4.11 (d, J = 8.9, 1 H, H_2), 4.63 (ddd, J = 2.4, 6.4, 15.0, H_{5e}), 5.82 (d, J = 8.9, 1 H, H_3), 6.78–7.14 (m, 10 H, aromatic).

***N*-(*tert*-Butoxycarbonyl)-2-phenyl-1,4-thiazane 1-Oxide (14 and 15).** Oxidation of thiazane **13** with *m*-CPBA afforded a 62:38 inseparable mixture of the two epimers at sulfur **14** and **15**: δ 1.43 (s, 9 H, *t*-Bu), 1.44 (s, 9 H, *t*-Bu), 2.73 (m, 6 H), 3.74 (m, 8 H), 7.14 (m, 10 H).

***N*-(*tert*-Butoxycarbonyl)-3-phenyl-1,4-thiazane 1-Oxide (30 and 31).** Oxidation of thiazane **29** with *m*-CPBA afforded a syrup formed by a <5:>95 mixture of the two epimers at sulfur **30** and **31**. The major isomer, **31**, was isolated by chromatography using ethyl acetate as eluent: δ 1.48 (s, 9 H, *t*-Bu), 2.71 (ddd, J = 3.8, 12.4, 12.7, 1 H, H_{6a}), 2.93 (dd, J = 4.9, 13.0, 1 H, H_{2a}), 2.95 (ddd, J = 2.1, 12.7, 15.4, 1 H, H_{5a}), 3.35 (dddd, J = 2.1, 2.4, 3.9, 12.4, 1 H, H_{6e}), 3.93 (ddd, J = 2.4, 3.9, 13.0, 1 H, H_{2e}), 4.38 (ddd, J = 3.8, 3.9, 15.4, H_{5e}), 5.94 (dd, J = 3.9, 4.9, 1 H, H_3), 7.40 (m, 5 H, aromatic). The minor isomer, **30**, was obtained diastereoisomerically pure from **19** by reaction with di-*tert*-butyl dicarbonate following the general method of formation of *N*-*tert*-butylcarbamates: δ 1.47 (s, 9 H, *t*-Bu), 2.83 (m, 2 H, $H_{6a}H_{6e}$), 2.95 (dd, J = 6.1, 15.0, 1 H, H_{2a}), 3.65 (ddd, J = 2.1, 3.9, 15.0, 1 H, H_{2e}), 3.77 (ddd, J = 2.6, 12.0, 14.7, 1 H, H_{5a}), 4.22 (ddd, J = 3.8, 3.9, 14.7, 1 H, H_{5e}), 5.69 (dd, J = 3.9, 6.1, H_3), 7.40 (m, 5 H, aromatic).

***N*-(*tert*-Butoxycarbonyl)-*cis*-2,3-diphenyl-1,4-thiazane 1-Oxide (47).** Oxidation of thiazane **45** with $NaIO_4$ (or *m*-CPBA) afforded only one sulfoxide, **47**, in quantitative yield. It was crystallized from benzene/cyclohexane (1:1), mp 196–197 °C: δ 1.47 (s, 9 H, *t*-Bu), 2.93 (ddd, J = 3.9, 12.6, 13.0, 1 H, H_{6a}), 3.40 (ddd, J = 2.1, 13.0, 15.6, 1 H, H_{5a}), 3.73 (ddd, J = 2.1, 3.8, 12.6, 1 H, H_{6e}), 4.27 (d, J = 4.8, 1 H, H_2), 4.41 (ddd, J = 3.8, 3.9, 15.6, H_{5e}), 5.95 (d, J = 4.8, 1 H, H_3), 7.19–7.29 (m, 10 H, aromatic).

***N*-(*tert*-Butoxycarbonyl)-*trans*-2,3-diphenyl-1,4-thiazane 1-Oxide (62 and 63).** Oxidation of thiazane **61** with $NaIO_4$ (or *m*-CPBA) afforded a mixture of the two epimers at sulfur, **62** and **63**, in quantitative yield. The isomers could not be separated. Compound **62** (from **62** + **63** mixture): δ 1.47 (s, 9 H, *t*-Bu), 2.73 (ddd, J = 3.2, 3.4, 13.6, 1 H, H_{6e}), 3.37 (ddd, J = 5.6, 11.9, 13.6, 1 H, H_{6a}), 3.97 (ddd, J = 3.4, 11.9, 14.6, 1 H, H_{5a}), 4.47 (dddd, J = 0.7, 3.2, 5.6, 14.6, H_{5e}), 4.61 (d, J = 6.4, 1 H, H_2), 5.75 (dd, J = 0.7, 6.0, 1 H, H_3), 7.30 (m, 10 H, aromatic). Compound **63** (from **62** + **63** mixture): δ 1.47 (s, 9 H, *t*-Bu), 3.09 (ddd, J = 6.2, 12.1, 13.7, 1 H, H_{6a}), 3.20 (ddd, J = 2.5, 3.9, 13.7, 1 H, H_{6e}), 3.52 (ddd, J = 3.9, 12.1, 15.1, 1 H, H_{5a}), 4.18 (d, J = 8.3, 1 H, H_2), 4.71 (dddd, J = 0.8, 2.5, 6.2, 15.1, H_{5e}), 5.86 (dd, J = 0.8, 8.3, 1 H, H_3), 7.30 (m, 10 H, aromatic).

(g) General Method of Oxidation of Thioethers to Sulfones. (i) With *m*-Chloroperoxybenzoic Acid. To a solution of 5 mmol of the thioether in 20 mL of methylene chloride were added 10 mmol of *m*-CPBA dissolved in 20 mL of methylene chloride and the mixture was stirred at room temperature until reaction was complete (TLC or ^{1}H-NMR). The reaction mixture was washed three times with a saturated solution of sodium bicarbonate and once with water. The organic layer was dried and the solvent distilled at reduced pressure. **(ii) With Hydrogen Peroxide/TFA.** Thioether (1 mmol) was dissolved in a mixture of 6 mL of TFA and 4 mL of hydrogen peroxide. After being stirred at room temperature for 2 h the mixture was treated with 50 mL of water and extracted. The organic solution was cleared with a saturated solution of sodium bicarbonate and then with water, dried, and concentrated.

***N*-(Ethoxycarbonyl)-2-phenyl-1,4-thiazane 1,1-dioxide (12)** was obtained in 80% yield by oxidation of thiazane **9** with *m*-CPBA and was crystallized from diethyl ether, mp 122–123 °C: δ 2.18 (t, 3 H, CH_3), 3.13–3.19 (m, 2 H), 3.30–3.70 (m, 2 H), 4.06–4.25 (m, 3 H, CH_2 and 1 H), 4.30–4.60 (m, 2 H), 7.10–7.30 (m, 5 H, aromatic). Anal. Calcd for $C_{13}H_{17}NO_4S$: C, 55.11; H, 6.05; N, 4.94. Found: C, 54.68; H, 5.75; N, 4.96.

***N*-(Ethoxycarbonyl)-3-phenyl-1,4-thiazane 1,1-dioxide (28)** was obtained in 75% yield by oxidation of thiazane **25** with *m*-CPBA and was crystallized from diethyl ether, mp 80–81 °C: HRMS calcd for $C_{13}C_{17}NO_4S$ 283.0878, found 283.0871; δ 1.26 (t, 3 H, CH_3), 2.99 (dddd, J = 2.7, 2.8, 3.0, 13.9, 1 H, H_{6e}), 3.20 (ddd, J = 4.3, 12.4, 13.9, 1 H, H_{6a}), 3.45 (dd, J = 6.0, 14.9, 1 H, H_{2a}),

3.55 (ddd, J = 2.7, 12.4, 15.0, 1 H, H_{5a}), 2.83 (ddd, J = 2.8, 3.8, 14.9, 1 H, H_{2e}), 4.16 (q, 2 H, CH_2O), 4.51 (ddd, J = 1.9, 4.3, 15.0, H_{5e}), 6.00 (dd, J = 3.8, 6.0, 1 H, H_{3e}), 7.20–7.40 (m, 5 H, aromatic).

***N*-(Ethoxycarbonyl)-*cis*-2,3-diphenyl-1,4-thiazane 1,1-dioxide (44)** was obtained in 90% yield by oxidation of thiazane **41** with *m*-CPBA and was crystallized from benzene/cyclohexane (1:1), mp 179 °C: δ 1.26 (t, 3 H, CH_3), 3.30 (ddd, J = 2.2, 3.5, 14.0, 1 H, H_{6e}), 3.41 (ddd, J = 3.9, 12.9, 14.0, 1 H, H_{6a}), 4.18 (ddd, J = 2.2, 12.9, 15.3, 1 H, H_{5a}), 4.16 (dq, 2 H, CH_2O), 4.66 (d, J = 6.2, 1 H, H_2), 4.71 (dddd, J = 1.6, 3.5, 3.9, 15.3, H_{5e}), 5.97 (dd, J = 1.6, 6.2, 1 H, H_3), 7.14–7.60 (m, 10 H, aromatic). Anal. Calcd for $C_{19}H_{21}NO_4S$: C, 63.49; H, 5.89; N, 3.90. Found: C, 63.15; H, 5.79; N, 3.78.

***N*-(Ethoxycarbonyl)-*trans*-2,3-diphenyl-1,4-thiazane 1,1-dioxide (60)** was obtained in 95% yield by oxidation of thiazane **57** with *m*-CPBA and was crystallized from benzene/cyclohexane, mp 110–112 °C: HRMS calcd for $C_{19}H_{21}NO_4S$ 359.1191, found 359.1199; δ 1.11 (t, 3 H, CH_3), 3.42 (ddd, J = 1.7, 4.6, 13.5, 1 H, H_{6e}), 3.71 (ddd, J = 7.2, 12.0, 13.5, 1 H, H_{6a}), 3.99 (ddd, J = 4.6, 12.0, 15.0, 1 H, H_{5a}), 4.07 (q, 2 H, CH_2O), 4.60 (d, J = 10.2, 1 H, H_2), 4.75 (ddd, J = 1.7, 7.2, 15.0, H_{5e}), 5.80 (d, J = 10.2, 1 H, H_3), 6.93–7.35 (m, 10 H, aromatic).

***N*-(*tert*-Butoxycarbonyl)-2-phenyl-1,4-thiazane 1,1-dioxide (16)** was obtained in 90% yield by oxidation of thiazane **13** with *m*-CPBA: δ 1.47 (s, 9 H, *t*-Bu), 3.12 (m, 2 H, $H_{6e}H_{6a}$), 3.53 (m, 1 H, H_{5a}), 3.69 (dd, J = 11.6, 14.1, 1 H, H_{3a}), 4.06 (dd, J = 3.5, 11.6, 1 H, H_2), 4.54 (m, 2 H, $H_{3e}H_{5e}$), 7.40 (m, 5 H, aromatic).

***N*-(*tert*-Butoxycarbonyl)-3-phenyl-1,4-thiazane 1,1-dioxide (32)** was obtained in 85% yield by oxidation of thiazane **29** with *m*-CPBA, mp 116–117 °C: δ 1.41 (s, 9 H, *t*-Bu), 3.01 (dddd, J = 2.5, 2.8, 3.3, 13.8, 1 H, H_{6e}), 3.21 (ddd, J = 3.7, 11.9, 13.8, 1 H, H_{6a}), 3.43 (dd, J = 5.9, 14.8, 1 H, H_{2a}), 3.55 (ddd, J = 2.8, 11.9, 14.7, 1 H, H_{5a}), 3.78 (ddd, J = 2.5, 4.4, 14.8, 1 H, H_{2e}), 4.49 (dddd, J = 1.8, 3.3, 3.7, 14.7, 1 H, H_{5e}), 5.88 (ddd, J = 1.8, 4.4, 5.9, H_3), 7.35 (m, 5 H, aromatic). Anal. Calcd for $C_{15}H_{21}NO_4S$: C, 57.86; H, 6.80; N, 4.50. Found: C, 57.62; H, 6.49; N, 4.31.

***N*-(*tert*-Butoxycarbonyl)-*cis*-2,3-diphenyl-1,4-thiazane 1,1-dioxide (48)** was obtained in 90% yield by oxidation of thiazane **45** with *m*-CPBA and was crystallized from cyclohexane, mp 173–174 °C: δ 1.43 (s, 9 H, *t*-Bu), 3.28 (ddd, J = 2.3, 3.3, 13.9, 1 H, H_{6e}), 3.38 (ddd, J = 4.0, 12.8, 13.9, 1 H, H_{6a}), 4.12 (ddd, J = 2.3, 12.8, 15.2, 1 H, H_{5a}), 4.65 (d, J = 6.3, 1 H, H_2), 4.66 (dddd, J = 1.6, 3.3, 4.0, 15.2, H_{5e}), 5.90 (dd, J = 1.6, 6.3, 1 H, H_3), 7.06–7.46 (m, 10 H, aromatic).

***N*-(*tert*-Butoxycarbonyl)-*trans*-2,3-diphenyl-1,4-thiazane 1,1-dioxide (64)** was obtained in 95% yield by oxidation of thiazane **61** with *m*-CPBA and was crystallized from benzene/cyclohexane, mp 196 °C: δ 1.34 (s, 9 H, *t*-Bu), 3.40 (ddd, J = 1.6, 4.5, 13.3, 1 H, H_{6e}), 3.70 (ddd, J = 7.1, 12.1, 13.3, 1 H, H_{6a}), 3.93 (ddd, J = 4.5, 12.1, 15.0, 1 H, H_{5a}), 4.56 (d, J = 10.2, 1 H, H_2), 4.76 (ddd, J = 1.6, 7.1, 15.0, H_{5e}), 5.73 (d, J = 10.2, 1 H, H_3), 6.83–7.29 (m, 10 H, aromatic). Anal. Calcd for $C_{21}H_{25}NO_4S$: C, 65.09; H, 6.50; N, 3.62. Found: C, 65.27; H, 6.36; N, 3.52.

(h) General Method of Hydrolysis of Carbamates. Ethyl Carbamates. To a solution of 1 g of the *N*-ethoxycarbonyl derivative in 25 mL of methanol was added 25 mL of a 10% ethanolic solution of potassium hydroxide. The mixture was refluxed for 6 h, neutralized (pH 7) with 10% hydrochloric acid, and diluted with 25 mL of water. Routine workup afforded the crude product. ***tert*-Butyl Carbamates.** To a 25-mL mixture of 3 N hydrochloric acid and ethyl acetate was added 1 g of the appropriate *N*-*tert*-butoxycarbonyl derivative. The mixture was stirred at room temperature for 1 h, and the solvent was distilled at reduced pressure. The residue was dissolved in 50 mL of 50% aqueous methanol and neutralized with sodium bicarbonate. Routine workup afforded the crude product.

2-Phenyl-1,4-thiazane 1,1-dioxide (4) was obtained in 85% yield by basic hydrolysis of sulfone **12** and was crystallized from diethyl ether/methylene chloride, mp 125–127 °C: δ 1.90 (bs, 1 H, NH), 3.05 (m, 2 H), 3.33 (m, 3 H), 3.49 (dd, J = 11.6, 13.4, H_{3a}), 4.05 (dd, J = 3.4, 11.6, H_{2a}), 7.30–7.50 (m, 5 H, aromatic). Anal. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.20; N, 6.63. Found: C, 56.68; H, 6.23; N, 6.48.

3-Phenyl-1,4-thiazane 1,1-dioxide (20) was obtained in 73% yield by basic hydrolysis of sulfone **28** and was crystallized from diethyl ether/methylene chloride, mp 120 °C (d): δ 1.90 (bs, 1 H, NH), 2.90–3.05 (m, 3 H), 3.10–3.50 (m, 3 H), 4.00–4.15 (m, 1 H), 7.10–7.30 (m, 5 H, aromatic). Anal. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.20; N, 6.63. Found: C, 56.57; H, 6.13; N, 6.46.

***cis*-2,3-Diphenyl-1,4-thiazane 1,1-dioxide (36)** was obtained by acid hydrolysis of sulfone **48** or by direct oxidation of thiazane **33** with H_2O_2/TFA (80% yield in each case). It was crystallized from carbon tetrachloride/cyclohexane, mp 174–175 °C: HRMS calcd for $C_{16}H_{17}NO_2S$ 287.0980, found 287.0982; δ 1.89 (bs, 1 H, NH), 3.00 (m, 1 H), 3.59 (m, 3 H), 4.12 (dd, J = 3.1, 3.3, H_2), 4.93 (d, J = 3.3, H_3), 6.85–7.43 (m, 10 H, aromatic).

***trans*-2,3-Diphenyl-1,4-thiazane 1,1-dioxide (52)** was obtained by acid hydrolysis of sulfone **64** (90% yield) or by basic hydrolysis of sulfone **60** (70% yield). It was crystallized from carbon tetrachloride/cyclohexane, mp 184–185 °C: δ 2.23 (bs, 1 H, NH), 3.25 (ddd, J = 2.4, 2.9, 13.6, 1 H, H_{6e}), 3.38 (ddd, J = 4.2, 12.5, 13.6, 1 H, H_{6a}), 3.51 (ddd, J = 2.9, 4.2, 13.0, 1 H, H_{5e}), 3.61 (ddd, J = 2.4, 12.5, 13.0, 1 H, H_{5a}), 4.22 (d, J = 10.6, H_2), 4.41 (d, J = 10.6, 1 H, H_3), 7.89–7.14 (m, 10 H, aromatic). Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 66.63; H, 5.90; N, 4.51.

***N*-Methyl-2-phenyl-1,4-thiazane 1,1-dioxide (8)** was obtained in 80% yield by oxidation of thiazane **5** with H_2O_2/TFA: HRMS calcd for $C_{11}H_{15}NO_2S$ 225.0823, found 225.0818; δ 2.44 (s, 3 H, CH_3), 2.89–3.38 (m, 6 H), 4.26 (dd, J = 5.1, 9.6, 1 H), 7.40 (m, 5 H, aromatic).

***N*-Methyl-3-phenyl-1,4-thiazane 1,1-dioxide (24)** was obtained in 85% yield by oxidation of thiazane **21** with H_2O_2/TFA: HRMS calcd for $C_{11}H_{15}NO_2S$ 225.0823, found 225.0816; δ 2.08 (s, 3 H, CH_3), 2.92–3.44 (m, 6 H), 3.69 (dd, J = 2.7, 11.5, 1 H), 7.30 (m, 5 H, aromatic).

***N*-Methyl-*cis*-2,3-diphenyl-1,4-thiazane 1,1-dioxide (40)** was obtained in 80% yield by oxidation of thiazane **37** with H_2O_2/TFA and was purified by chromatography using methylene chloride/methanol (15:1) as eluent, mp 178–179 °C: HRMS calcd for $C_{17}H_{19}NO_2S$ 301.1136, found 301.1122; δ 2.14 (s, 3 H, CH_3), 2.98 (dddd, J = 2.8, 3.3, 3.4, 14.5, 1 H, H_{6e}), 3.10 (ddd, J = 2.8, 12.9, 13.1, 1 H, H_{5a}), 3.47 (ddd, J = 3.3, 4.1, 12.9, 1 H, H_{5e}), 3.79 (ddd, J = 4.1, 13.1, 14.5, 1 H, H_{6a}), 3.93 (dd, J = 3.3, 3.4, 1 H, H_2), 4.27 (d, J = 3.3, 1 H, H_3), 6.89–7.56 (m, 10 H, aromatic).

***N*-Methyl-*trans*-2,3-diphenyl-1,4-thiazane 1,1-dioxide (56)** was obtained in 75% yield by oxidation of thiazane **53** with H_2O_2/TFA and was purified by chromatography using methylene chloride/methanol (50:1) as eluent, mp 218–219 °C: HRMS calcd for $C_{17}H_{19}NO_2S$ 301.1136, found 301.1140; δ 2.06 (s, 3 H, CH_3), 3.23 (ddd, J = 2.2, 12.8, 13.2, 1 H, H_{5a}), 3.24 (ddd, J = 2.2, 3.8, 13.9, 1 H, H_{6e}), 3.34 (ddd, J = 3.7, 3.8, 13.2, 1 H, H_{5e}), 3.52 (ddd, J = 3.8, 12.8, 13.9, 1 H, H_{6a}), 3.89 (d, J = 10.7, 1 H, H_2), 4.23 (d, J = 10.7, 1 H, H_3), 6.93–7.31 (m, 10 H, aromatic).

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Supplementary Material Available: Mass and infrared spectral data of 1,4-thiazanes, 1,4-thiazane *S*-oxides, 1,4-thiazane *S*,*S*-dioxides, and intermediates, proton NMR spectra of **2**, **41**, **6/7** mixture, ^{13}C NMR spectra of **1**, **3–5**, **8–13**, **16–21**, **24**, **25**, **28**, **29**, **32**, **33**, **35–37**, **39**, **40**, **43–45**, **47–54**, **56–61**, **64**, and the mixtures of **14/15**, **22/23**, **26/27**, **30/31**, and **62/63**, and atomic coordinates, anisotropic thermal parameters, bond lengths, bond angles, and torsion angles of *cis*-2,3-diphenyl-1,4-thiazane (65 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.