Stereochemistry of Sulfur Compounds. VII. Course of Substitution at Sulfur Attached to Four Different Ligands[1]

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Abstract: Syntheses are reported of diastereomeric compounds (**1**) whose chiral sulfur contains *p*-tolyl, oxygen, chlorine, and *N*-carbomenthoxy groups as ligands. Diastereomer (+)-(*S*)-**1** was purified by recrystallization, and (−)-(*R*)-**1** was prepared pure by a stereochemical reaction cycle from (+)-(*S*)-**1** as follows. Treatment of (+)-(*S*)-**1** with hydrazine produced *N*-carbomenthoxy-*p*-toluenesulfinamide ((+)-(*S*)-**2**) with high inversion of configuration at sulfur. Chlorination of unpurified (+)-(*S*)-**2** in the presence of pyridine gave (−)-(*R*)-**1** of 92% diastereomeric purity, which was recrystallized to diastereomeric purity. This reaction occurred with high retention of configuration at sulfur. By a similar stereochemical reaction cycle, (−)-(*R*)-**1** was converted *via* (−)-(*R*)-**2** to (+)-(*S*)-**1** of 90% diastereomeric purity. In a second stereochemical reaction cycle, (+)-(*S*)-**1** with methylmagnesium bromide gave (−)-(*R*)-**2** with high retention of configuration at sulfur. Chlorination in the presence of pyridine of (−)-(*R*)-**2** without diastereomeric purification gave back (+)-(*S*)-**1** with high retention of configuration at sulfur. The two reactions occurred with overall 95% stereospecificity. Treatment of (+)-(*S*)-**2** (prepared by the hydrazine route from **1**) with methylmagnesium bromide gave (−)-(*S*)-methyl *p*-tolyl sulfoxide ((−)-(*S*)-**3**) of known configuration, the reaction occurring with >68% net inversion at sulfur. Likewise (−)-(*R*)-2 (hydrazine route) gave (+)-(*R*)-**3** with >64% net inversion at sulfur. Treatment of (−)-(*R*)-**2** (prepared from (+)-(*S*)-**1** by the methylmagnesium bromide route) with more methylmagnesium bromide gave (+)-(*R*)-**3** with >82% net inversion at sulfur. With potassium *p*-cresylate, (+)-(*S*)-**1** gave (−)-(*R*)-**4** with 95% net inversion at sulfur. Compound **4** has as ligands at sulfur, oxygen, *p*-tolyl, *p*-cresyl, and *N*-carbomenthoxy. Sulfuric acid hydrolyzed the *N*-carbomenthoxy group of (−)-(*R*)-**4** to produce (+)-(*R*)-**5** with complete retention of configuration, whose chiral sulfur atom possessed the ligands oxygen, imide, *p*-tolyl, and *p*-cresyl. With methylmagnesium bromide, (−)-(*R*)-**4** gave with 88% inversion at sulfur, (−)-(*R*)-**6**, whose sulfur ligands were oxygen, methyl, *p*-tolyl and *N*-carbomenthoxy. Hydrolysis of (−)-(*R*)-**6** with sulfuric acid gave the known (−)-(*R*)-methyl *p*-tolyl sulfoximide ((−)-(*R*)-**7**) with essentially complete retention of configuration. Similar sequences with similar results were carried out with (−)-(*R*)-**1** as starting material. When treated with sodium amide in liquid ammonia, (+)-(*S*)-**1** gave diastereomerically pure (−)-(*R*)-**8** by a reaction that probably occurred with complete inversion of configuration. Compound **8** contains oxygen, amide, *p*-tolyl, and *N*-carbomenthoxy groups as ligands of sulfur. The *N*,*N*-dimethyl derivative of **8**, (−)-(*R*)-**9**, was prepared from (+)-(*S*)-**1** and dimethylamine. The reaction occurred with at least 94% net inversion of configuration at sulfur. When (−)-(*R*)-**9** was hydrolyzed with sulfuric acid, (+)-(*S*)-**10** was obtained mixed with racemic **10**. This reaction occurred with about 75% retention and 25% racemization. Compound **10** has oxygen, imide, dimethylamino, and *p*-tolyl groups as ligands. Similarly (−)-(*R*)-**1** was converted to (−)-(*S*)-**9**, which in turn gave (−)-(*R*)-**10** and racemic **10**. Optically pure (+)-(*S*)-**10** and (−)-(*R*)-**10** were converted with (−)-menthyl chloroformate to diastereomerically pure (−)-(*R*)-**9** and (−)-(*S*)-**9**, respectively, with retention of configuration. All compounds except (*R*)- and (*S*)-**2** were obtained in optically and diastereomerically pure states. The configurations of the compounds and the stereochemical courses of the reactions were assigned with high, but not absolute, confidence on the basis of analogy or direct comparisons with known systems, and on the basis of the symmetry properties of the stereochemical reaction cycles involved. Certain reaction mechanisms are discussed.

The stereochemical course of substitution reactions at chiral sulfur of the tricoordinate-tetravalent state has been extensively studied.[2] An extraordinary variety of reaction mechanisms for nucleophilic, electrophilic, and radical substitutions at sulfur appear available. Although chiral tetracoordinate hexavalent sulfur compounds such as sulfoximides[3] or sulfonimidamides[4] have been known for some years, only recently has the stereochemical course of substitution at sulfur in the "sulfon"[5] oxidation state been examined. Oxygen-isotope-labeled (−)-menthyl phenylmethanesulfonate with *p*-tolylmagnesium bromide gave labeled benzyl *p*-tolyl sulfone with inversion of configuration.[6] In more extensive work, an unstable chiral sulfonimidoyl chloride was prepared from an optically active N-substituted sulfinamide, and the chloride without characterization was converted to optically active sulfonimidamide and sulfonimidate ester.[7] The nucleophilic substitutions were found to go with high inversion of configuration.

We report here the preparation (based on (−)-menthol) of the two optically pure crystalline, diastereomers of *N*-carbomenthoxy-*p*-toluenesulfonimidoyl chloride (**1**), and a study of the stereochemical courses of their reactions. A number of new reactions and compound classes never before prepared in an optically active state are included.

(1) This investigation was supported by the U. S. Public Health Service Research Grant No. GM 12640-09 from the Department of Health, Education, and Welfare.

(2) For reviews, see (a) C. R. Johnson and J. C. Sharp, *Quart. Rep. Sulfur Chem.*, **4**, 1 (1969); (b) A. Nudelman, *Int. J. Sulfur Chem., Part B*, **1**, 1 (1971); (c) D. C. Garwood and D. J. Cram, *J. Amer. Chem. Soc.*, **92**, 4575 (1970); (d) D. J. Cram and J. M. Cram, *Top. Curr. Chem.*, **31**, 1 (1972).

(3) (a) R. Fusco and F. Tenconi, *Chim. Ind. (Milan)*, **47**, 61 (1965); (b) D. R. Rayner, D. M. von Schriltz, J. Day, and D. J. Cram, *J. Amer. Chem. Soc.*, **90**, 2721 (1968); (c) M. A. Sabol, R. W. Davenport, and K. K. Andersen, *Tetrahedron Lett.*, 2159 (1968).

(4) E. S. Levchenko and E. S. Kozlov, *J. Gen. Chem. USSR*, **33**, 3483 (1963).

(5) P. E. Verkade, IUPAC, *Pure Appl. Chem.*, **11**, 1, 155 (1965).

(6) M. A. Sabol and K. K. Andersen, *J. Amer. Chem. Soc.*, **91**, 3603 (1969).

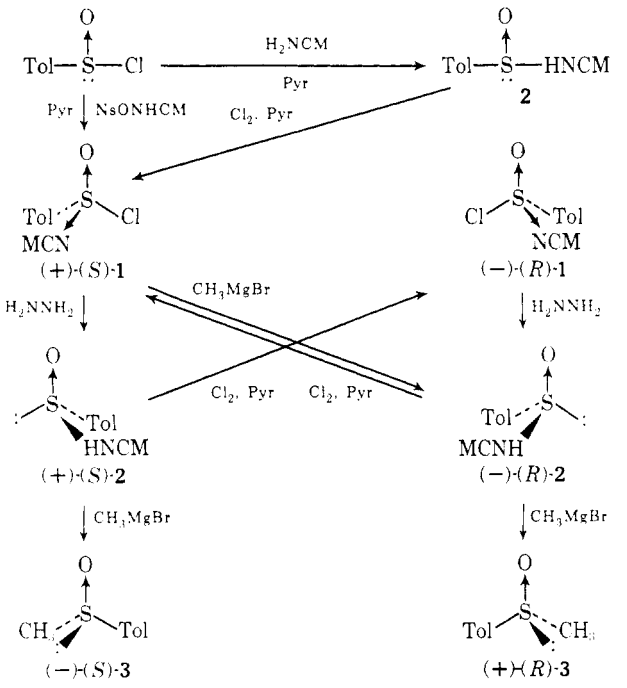
(7) (a) E. U. Jonsson, C. C. Bacon, and C. R. Johnson, *J. Amer. Chem. Soc.*, **93**, 5306 (1971); (b) E. U. Jonsson and C. R. Johnson, *ibid.*, **93**, 5305 (1971).

Results and Discussion

Our study centered on the isolability in a pure, crystalline state of the diastereomeric chlorides, (+)-(*S*)-**1** and (−)-(*R*)-**1**. The first section describes the preparation of these compounds, and the assignment of their configurations and maximum rotations. The second section concerns the conversion of these chlorides to their corresponding esters and amides. The properties of the stereochemical reaction cycles of this work are discussed in the third section.

Preparations, Configurations, and Maximum Rotations of Two Chiral Arylsulfonimidoyl Chlorides. The central compounds of this study, the diastereomeric *N*-carbomenthoxy-*p*-toluenesulfonimidoyl chlorides (**1**), were prepared by two routes (Chart I). The first

Chart I[a]



[a] Tol = *p*-$CH_3C_6H_4$; NCM = NCO_2menthyl-(−); Ns = *p*-$NO_2C_6H_4SO_2$.

formally is a carbomenthoxynitreneation of the unshared electron pair of *p*-toluenesulfinyl chloride. Levchenko utilized a similar procedure to prepare *N*-carboethoxysulfonimidoyl chlorides.[8] The reaction in this case was pyridine catalyzed, and *p*-nitrobenzenesulfonate was the leaving group from nitrogen. The *N*-*p*-nitrobenzenesulfonoxy menthylcarbamate was prepared from optically pure (−)-menthol.[9] The second and superior route to **1** involved reaction of *p*-toluenesulfinyl chloride with (−)-menthylcarbamate to give[10] *N*-carbomenthoxy-*p*-toluenesulfinamide (**2**). Attempts to separate the somewhat unstable diastereomers of **2** were unsuccessful. The mixture was oxidatively chlorinated with chlorine in the presence of pyridine[7a] or with *tert*-butyl hypochlorite[7a] to give **1** as a mixture of two diastereomers. The diastereomers of **1** were isolated by rapid chromatography, and crystallization techniques yielded only (+)-(*S*)-**1**[11] in a pure state (mp 109–110°, $[\alpha]^{25}_{546}$ +229° (*c* 1.08, $CHCl_3$)). Isomer (−)-(*R*)-**1** was produced (90%) by treating (+)-(*S*)-**1** with hydrazine to give (+)-(*S*)-**2**, which without diastereomeric purification was oxidatively chlorinated[7a] to give (−)-(*R*)-**1**[11] of 92% diastereomeric purity. This isomer was purified by crystallization, mp 77.5–79.0°, $[\alpha]^{25}_{546}$ −389° (*c* 1.05, $CHCl_3$). Neither diastereomer changed its rotation or melting point upon repeated recrystallization, and each was stable in the crystalline state in the absence of moisture. Pure (−)-(*R*)-**1** was treated with hydrazine to give (−)-(*R*)-**2**, which without diastereomeric purification was oxidatively chlorinated to give back (+)-(*S*)-**1** of 90% diastereomeric purity.

Grignard reagents reduce arylsulfonyl chlorides to sulfinic acids.[12] When **1** was treated with methylmagnesium bromide, **2** was produced (90%). Accordingly, pure (+)-(*S*)-**1** was treated with methylmagnesium bromide, and without diastereomeric fractionation, the (−)-(*R*)-**2** produced was oxidatively chlorinated to give back (+)-(*S*)-**1** of 95% diastereomeric purity.

Johnson, *et al.*,[7] have demonstrated that oxidative chlorination of sulfinamides to sulfonimidoyl chlorides proceeds with retention of configuration. By analogy, the conversions of sulfinamides **2** to sulfonimidoyl chlorides **1** must have gone with retention of configuration. Thus the reduction of (+)-**1** to (−)-**2** with methylmagnesium bromide must have gone with retention of configuration. In contrast, the reduction of (+)-**1** to (+)-**2** with hydrazine must have occurred with inversion of configuration. Thus the relative, but not the absolute, configurations at sulfur of the isomers of **1** and **2** are established. The absolute configurations were determined as follows.

The configurations of certain sulfinamides have been determined by their conversions with methyllithium to sulfoxides of known configuration.[13] The reaction occurs with inversion of configuration. Methylmagnesium bromide reacted with **2** to give (~30%) methyl *p*-tolyl sulfoxide (**3**). Methyllithium failed to produce the desired product. Accordingly, pure (+)-**1** was reduced with hydrazine to give (+)-**2**, which without diastereomeric purification was converted to (−)-(*S*)-**3** of 68% optical purity of established configuration[14] and maximum rotation.[15] Pure (+)-**1** was reduced with methylmagnesium bromide to (−)-**2**, which after purification was converted with additional methylmagnesium bromide to (+)-**3** of 82% optical purity. Pure (−)-**1** was reduced with hydrazine to (−)-**2**, which similarly was converted to (+)-(*R*)-**3** of 64% optical purity. Since the reactions, (+)-**2** → (−)-**3** and (−)-**2** → (+)-**3** must have gone with inversion of configuration at

(8) E. S. Levchenko, E. S. Kozlov, and A. V. Kirsanov, *Zh. Obshch. Khim.*, **33**, 554 (1963).

(9) W. Lwowski and T. J. Maricich, *J. Amer. Chem. Soc.*, **87**, 3630 (1965).

(10) F. Kurzer, *J. Chem. Soc.*, 549 (1953).

(11) The configurational notations refer to the configuration at sulfur, and not to those of the menthyl residue. Throughout the study, optically pure (−)-menthol was employed.

(12) C. M. Suter, "The Organic Chemistry of Sulfur," Wiley, London, 1944.

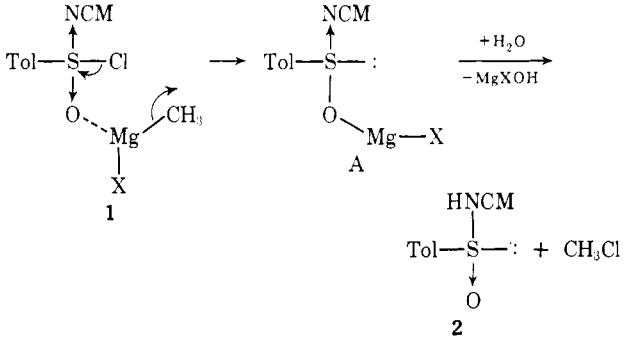
(13) (a) S. Colonna, R. Giovini, and F. Montanari, *Chem. Commun.*, 865 (1968); (b) J. Jacobus and K. Mislow, *ibid.*, 253 (1968).

(14) H. Hope, U. de la Camp, G. D. Horner, A. W. Messing, and L. H. Sommer, *Angew. Chem., Int. Ed. Engl.*, **8**, 612 (1969), and references cited therein.

(15) (a) M. Axelrod, P. Bickart, J. Jacobus, M. M. Green, and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4835 (1968); (b) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., *ibid.*, **87**, 1958 (1965).

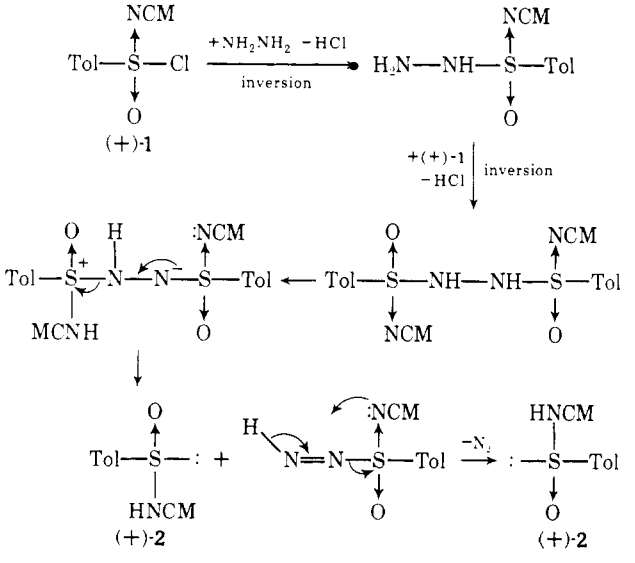
sulfur, the absolute configuration at sulfur of the isomers of **2** and finally of **1** are inferred. Chart I summarizes these conversions and configurational assignments.

The reductions of **1** to **2** proceeded with better than 90% stereospecificity. Those with hydrazine as reagent occurred with inversion, and that with methylmagnesium bromide with retention of configuration. Thus the mechanisms of these reactions are different. The reduction with the Grignard reagent appears to involve nucleophilic attack by methyl on chlorine as formulated. The appearance of a gas during this reaction, probably methyl chloride, is compatible with this hypothesis. In this nucleophilic substitution on chlorine, as in a previously observed nucleophilic substitution at carbon, the stereochemical fate of the leaving group was monitored.[16] Since the bonding electron pair accompanies the leaving group, retention of configuration is both the expected and observed result. The suggested reaction mechanism points to the interesting possibility of preparing optically active sulfinamidate transfer agents such as A for use with electrophiles other than protons.



The observed stereochemical course of the reduction with hydrazine (inversion of configuration) suggests the presence of a nucleophilic substitution (at sulfur) stage in the sequence. A plausible mechanism (Scheme I) is

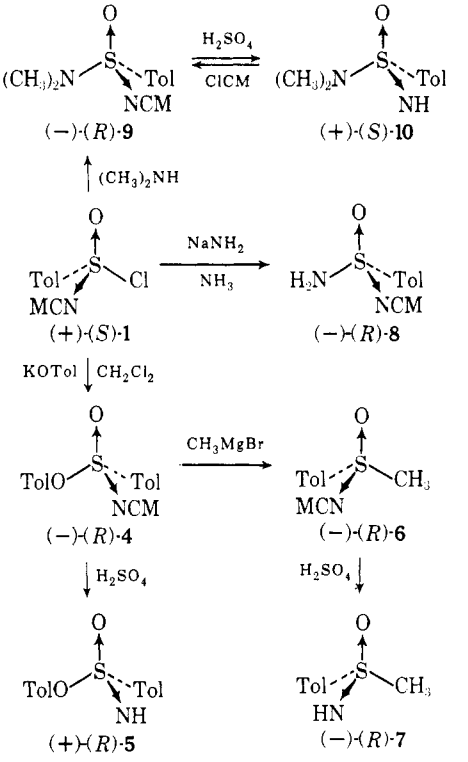
Scheme I



formulated which involves nitrogen formation. Gas evolution was observed in the reaction. The first stage is visualized as going by a pathway that involves the electronegative leaving and entering groups occupying axial positions on a trigonal-bipyramidal transition state or intermediate.[17] Many obvious variants of the mechanism written are equally possible. These involve different orders for the stages after the first, which determined the stereochemical course of the overall reaction.

Stereochemical Course of Nucleophilic Substitution Reactions of Two Chiral Arylsulfonimidoyl Chlorides. Chart II outlines the nucleophilic reactions of pure (+)-

Chart II



(*S*)-**1** and (−)-(*R*)-**1** with potassium *p*-cresylate, which proceeded in about 80% yields after chromatography. The conversion of chloride (+)-(*S*)-**1** to arylsulfonimidate ester (−)-(*R*)-**4** went with 95% stereospecificity. This value is based on a rotation of (−)-(*R*)-**4** obtained when the material was recrystallized to maximum rotation and melting point. Treatment of purified (−)-(*R*)-**4** with concentrated sulfuric acid removed the carbomenthoxy group to produce (60%) the arylsulfonimidate ester, (+)-(*R*)-**5**, in an optically pure state with a sharp melting point. A similar series of reactions with (−)-(*R*)-**1** provided (+)-(*S*)-**4**. After chromatographic purification (the material was an oil) the substance was hydrolyzed to give (−)-(*S*)-**5** of rotation of opposite sign and equal magnitude and of melting point identical with that of (+)-(*R*)-**5**. Since optically pure (−)-(*S*)-**5** and (+)-(*R*)-**5** were produced from different diastereomers, the two diastereomers of **4** appear to have been pure.

Diastereomerically pure (−)-(*R*)-**4** underwent nucleophilic substitution with methylmagnesium bromide to give (40%) sulfoximide (−)-(*R*)-**6** of 88% diastereo-

(16) T. R. Williams, A. Nudelman, R. E. Booms, and D. J. Cram, *J. Amer. Chem. Soc.*, **94**, 4684 1972).

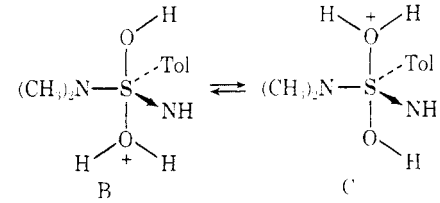
(17) Inversion of configuration can involve an equatorial disposition of both the entering and leaving groups; see ref 2c,d and (a) D. J. Cram, J. Day, D. R. Rayner, D. M. von Schriltz, D. J. Duchamp, and D. C. Garwood, *J. Amer. Chem. Soc.*, **92**, 7369 (1970); (b) D. C. Garwood, M. R. Jones, and D. J. Cram, *ibid.*, **95**, 1925 (1973).

meric purity, which was easily brought to optical purity by recrystallization. Hydrolysis with concentrated sulfuric acid of the sample of (−)-(*R*)-**6** before purification gave 86% optically pure (−)-(*R*)-methyl *p*-tolylsulfoximide ((−)-(*R*)-**7**). The absolute configuration and maximum rotation of (−)-(*R*)-**7** have been determined previously.[17a] Without diastereomeric purification at intermediate stages, pure (−)-(*R*)-**1** served as starting material for the sequence (−)-(*R*)-**1** → (+)-(*S*)-**4** → (+)-(*S*)-**6** → (+)-(*S*)-**7**. The sulfoximide (+)-(*S*)-**7** initially isolated was of 85% optical purity, and therefore the three reactions must have gone with the high stereospecificity observed with the other diastereomeric series. This sample of (+)-(*S*)-**7** was recrystallized to optical purity and converted back to (+)-(*S*)-**6** to establish the maximum rotation of that compound.

The stereochemical courses of these reactions can be assigned with a high, but not complete, degree of confidence. The absolute configurations of the enantiomers of **3** and **7** are very clear. The decarbomenthoxylations of (−)-(*R*)-**4**, (+)-(*S*)-**4**, (−)-(*R*)-**6**, and (+)-(*S*)-**6** as well as the carbomenthoxylation of (+)-(*S*)-**7** do not involve the sulfur chiral center, and must go with retention of configuration. Thus the absolute configurations of (−)-(*R*)-**6** and (+)-(*S*)-**6** are evident. The stereochemical courses assigned to the reactions of Chart I are based on reasoning by analogy with the behavior of similar systems. The assignment of configuration at sulfur of chloride (+)-(*S*)-**1** also depends on analogies. If the configuration of (+)-**1** is assigned properly, the sequences (+)-(*S*)-**1** → (−)-(*R*)-**4** → (−)-(*R*)-**6** and (−)-(*R*)-**1** → (+)-(*S*)-**4** → (+)-(*S*)-**6** must each involve two reactions that follow the same stereochemical courses, either both inversion or both retention. Both reactions are nucleophilic substitutions at saturated sulfur, and have a very high likelihood of having gone with inversion of configuration. Others have reported that phenoxides invert sulfur when substituting for halogen.[7] A body of evidence exists, except in special cases where the nucleophile and leaving group are part of the same ring system,[17] that nucleophilic substitution at sulfur occurs with predominant inversion of configuration.[18]

The reactions of pure (+)-(*S*)-**1** with two other nucleophiles were examined. With sodium amide in liquid ammonia, (+)-(*S*)-**1** gave (37%) sulfonimidamide (−)-(*R*)-**8** with what appeared to be complete stereospecificity. The reaction probably occurred with inversion, and the configuration of **8** is assigned accordingly. Only that tautomer of **8** with both hydrogens on the same nitrogen is formulated in Chart II. The ir spectrum in chloroform of the substance showed a broad N–H stretch region, and only one carbonyl stretch absorption. But spectral data are not conclusive as to which tautomer is the predominant one.

Pure sulfonimidoyl chloride (+)-(*S*)-**1** when mixed with dimethylamine gave (97%) sulfonimidamide (−)-(*R*)-**9** of high diastereomeric purity, recrystallization of which gave pure imidamide. This reaction also probably occurred with inversion, and the configuration of **9** is assigned accordingly. Hydrolysis of diastereomerically pure (−)-(*R*)-**9** with concentrated sulfuric acid gave (80%) hydrolysis product, **10**. Fractional crystallization of this material gave (25%) racemic sulfonimidamide **10** with the same melting point as that prepared previously,[19] as well as the sharp melting enantiomer, (+)-(*S*)-**10**. Since this material was produced without breaking or making bonds to sulfur, the reaction is presumed to have gone predominantly with retention of configuration, but was accompanied by 25% racemization. Conversion of purified (+)-(*S*)-**10** back to (−)-(*R*)-**9** with (−)-methyl chloroformate gave a product of the same melting point and about 6% higher rotation than that produced directly from (+)-(*S*)-**1**. Thus the reaction (+)-(*S*)-**1** → (−)-(*R*)-**9** went with about 94% stereospecificity. The partial racemization that accompanied hydrolysis of (−)-**9** to (+)-**10** probably occurred when the concentrated sulfuric acid reaction mixture was quenched with water. Two equilibrating trigonal-bipyramidal tautomeric intermediates that are enantiomeric (B and C) provide an attractive explanation for that part of the reaction leading to racemic **10**.



B C

As did the prior but different approach of Johnson, *et al.*,[7] these reactions provide a convenient means of preparing in optically pure form, sulfonimidate esters, sulfonimidamides, and sulfoximides. The crystalline character and easy preparation of the arylsulfonimidoyl chlorides (+)-(*S*)-**1** and (−)-(*R*)-**1** should provide a starting point for the preparation of a variety of new optically active compounds chiral at sulfur that carry three different electronegative ligands. The specification of the configurations at sulfur of the diastereomers of **1** offer a textbook example of application of the sequence rule.[20] The ligands of sulfur, Cl, O, N, and C are close to being the four first-row elements of the periodic table to the right of boron.

Stereochemical Reaction Cycles. Chart I contains several unusual triligostatic reaction cycles[2c,d] with oxygen, *N*-carbomenthoxy, and tolyl groups common to the four chiromers, (+)-(*S*)-**1**, (+)-(*S*)-**2**, (−)-(*R*)-**1**, and (−)-(*R*)-**2**. These cycles allow the configurations and ligands at sulfur to be manipulated with considerable choice. Equations 1–3 illustrate podal and antipodal,

$$(+)\text{-}(S)\text{-}\mathbf{1} \xrightarrow{I} (+)\text{-}(S)\text{-}\mathbf{2} \xrightarrow{R} (-)\text{-}(R)\text{-}\mathbf{1} \quad (1)$$

$$(+)\text{-}(S)\text{-}\mathbf{1} \xrightarrow{R} (-)\text{-}(R)\text{-}\mathbf{2} \xrightarrow{R} (+)\text{-}(S)\text{-}\mathbf{1} \quad (2)$$

$$(+)\text{-}(S)\text{-}\mathbf{2} \xleftarrow{I} (+)\text{-}(S)\text{-}\mathbf{1} \xrightarrow{R} (-)\text{-}(R)\text{-}\mathbf{2} \quad (3)$$

two-reaction stereochemical cycles.[2c,d] Inclusion of (−)-(*S*)-**3** and (+)-(*R*)-**3** in the cycles makes them diligostatic, with oxygen and tolyl groups as the ligands common to the chiromers. None of these cycles contain a ligand metathesis.[2c,d] Equation 4 illustrates

(18) T. R. Williams, A. Nudelman, R. E. Booms, and D. J. Cram, *J. Amer. Chem. Soc.*, **94**, 4684 (1972).

(19) E. S. Levchenko, E. S. Kozlov, and A. V. Kirsanov, *J. Gen. Chem. USSR*, **33**, 559 (1962).

(20) R. S. Cahn and C. K. Ingold, *J. Chem. Soc.*, 612 (1951); R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956).

$$(-)\text{-}(S)\text{-}\mathbf{3} \xleftarrow{I} (+)\text{-}(S)\text{-}\mathbf{2} \xleftarrow{I} (+)\text{-}(S)\text{-}\mathbf{1} \xrightarrow{R} (-)\text{-}(R)\text{-}\mathbf{2} \xrightarrow{I} (+)\text{-}(R)\text{-}\mathbf{3} \quad (4)$$

an antipodal four-reaction cycle with three inversions of configuration.

Combinations of some of the reactions of Charts I and II with the stereospecific (retention) deimidation of (−)-(*R*)-**7** to (+)-(*R*)-**3**[17] (and by implication, (+)-(*S*)-**7** to (−)-(*S*)-**3**) complete a number of new reaction cycles that contain a ligand metathesis. Equations 5 and 6 illustrate six-reaction cycles. That of eq 5 con-

$$\begin{array}{l}(-)\text{-}(R)\text{-}\mathbf{7} \xleftarrow{R} (-)\text{-}(R)\text{-}\mathbf{6} \xleftarrow{I} (-)\text{-}(R)\text{-}\mathbf{4} \xleftarrow{I} (+)\text{-}(S)\text{-}\mathbf{1} \\ \qquad (+)\text{-}(S)\text{-}\mathbf{7} \xrightarrow{R} (-)\text{-}(S)\text{-}\mathbf{3} \xleftarrow{I} (+)\text{-}(S)\text{-}\mathbf{2} \xleftarrow{I} \end{array} \quad (5)$$

tains seven chiromers, and an even number (four) of reactions that go with inversion. That of eq 6 contains

$$\begin{array}{l}(-)\text{-}(R)\text{-}\mathbf{7} \xleftarrow{R} (-)\text{-}(R)\text{-}\mathbf{6} \xleftarrow{I} (-)\text{-}(R)\text{-}\mathbf{4} \xleftarrow{I} (+)\text{-}(S)\text{-}\mathbf{1} \\ \qquad \xrightarrow{R} (+)\text{-}(R)\text{-}\mathbf{3} \xleftarrow{I} (-)\text{-}(R)\text{-}\mathbf{2} \xleftarrow{R} \end{array} \quad (6)$$

six chiromers, and an odd number (three) of reactions that go with inversion. In each cycle, the ligand metathesis is the equivalent of an additional inversion.

Experimental Section

General. Melting points are uncorrected. Pmr spectra were recorded on a Varian A-60 with 20% solutions in $CDCl_3$–1% TMS. Ir spectra were recorded on a Beckman IR-5 spectrophotometer. Optical rotations were measured at 25° with a Perkin-Elmer 141 polarimeter and jacketed cells. Solvents were purified or were reagent grade. Column chromatograms were run with silica gel 60 (~300 mesh) as adsorbent. Thin-layer chromatograms for analytical purposes were run either on commercially prepared sheets (Baker-flex 1B-F) or on glass plates (5 cm × 20 cm) coated with a 0.25 mm layer of silica gel G (Merck) with 0.5% fluorescent indicator added. Preparative thin layer chromatograms were run on glass plates (20 cm × 20 cm) coated with a 2 mm layer of silica gel PF-254 (Merck). Ultraviolet indicator was used in most cases, but this was supplemented by the use of phosphomolybdic acid (solution in ethanol) for indication of nonaromatic compounds.

Preparation of (−)-Menthyl *N*-Hydroxycarbamate. Crude (−)-menthyl chloroformate (0.6 mol), prepared by a modification of the procedure used for the preparation of benzyl chloroformate,[21] was dissolved in a minimum amount of 95% ethanol. Hydroxylamine hydrochloride (69.0 g, 1.0 mol) was dissolved in 200 ml of water, and sodium acetate (144.0 g, 2.0 mol) was dissolved in 500 ml of water. The aqueous solutions were thoroughly mixed, the chloroformate in solution was added quickly to the aqueous solution, and the mixture was stirred for 1.5 hr (white precipitate). The mixture was extracted with dichloromethane. The organic layer was dried (Na_2SO_4), and the solvent was evaporated to give 126 g of an off-white solid which was recrystallized from methylene chloride–pentane to give 120 g (80%) of the desired carbamate, mp 136–137°, $[\alpha]^{25}_{546}$ −95.3° (*c* 1.20, chloroform). *Anal.* Calcd for $C_{11}H_{21}NO_3$: C, 61.37; H, 9.83. Found: C, 61.29; H, 9.90.

(−)-Menthyl *N*-*p*-Nitrobenzenesulfonoxycarbamate. To a solution of 53.8 g (0.25 mol) of (−)-menthyl *N*-hydroxycarbamate in 700 ml of dry ether was added 55.4 g (0.25 mol) of *p*-nitrobenzenesulfonyl chloride as a solid with stirring and cooling in an ice bath. A solution of 29.8 ml (21.4 g, 0.21 mol) of triethylamine in 30 ml of dry ether was added with stirring and cooling at such a rate the reaction mixture remained acidic. Addition was complete after 2 hr. After standing 12 hr, the mixture was filtered and the filtrate evaporated to give a yellow oil which crystallized. Recrystallization of the compound from dichloromethane–pentane gave a first crop of 61 g (61%) of white crystals, mp 106–108°. Further recrystallization gave analytically pure material, 1.4 g, mp 109–110.5°, $[\alpha]^{25}_{546}$ −47.5° (*c* 1.22, chloroform). *Anal.* Calcd for $C_{17}H_{24}N_2O_7S$: C, 50.99; H, 6.04. Found: C, 50.95; H, 5.99.

(+)-(*S*)-*N*-Carbo-(−)-menthoxy-*p*-toluenesulfonimidoyl Chloride ((+)-(*S*)-1) by Method A. To 20 ml (0.4 mol) of thionyl chloride was added 17.8 g (0.10 mol) of sodium *p*-toluenesulfinate as a solid over a period of 20 min with stirring and cooling in an ice bath. The mixture was stirred for 45 min and the unreacted thionyl chloride was removed at 25° by azeotropic distillation with dry benzene (three times). To the sulfinyl chloride–sodium chloride slurry produced was added 20.0 g (0.050 mol) of *N*-*p*-nitrobenzenesulfonoxy (−)-menthyl carbamate in 200 ml of dry benzene. At 0°, 10.0 ml (7.2 g, 0.07 mol) of triethylamine in 30 ml of benzene was added with vigorous stirring over a period of 60 min. The mixture was stirred at 25° for 12 hr. After washing with 200 ml of 10% hydrochloric acid, followed by 200 ml of saturated sodium bicarbonate solution and then 200 ml of water, the organic layer was dried and the solvent was evaporated. The residue was dissolved in 100 ml of 3% ether–pentane, and chromatographed on 800 g of silica gel. Elution with 3% ether in pentane (ten 400-ml fractions were cut) gave in fractions 6–9, 4.6 g of a colorless oil which crystallized rapidly. This material was not characterized since the ir spectrum in chloroform showed no absorption due to a carbonyl group. Further elution with 5% ether–pentane (ten 400-ml fractions were cut) gave 11.8 g (60%) in fractions 12–18 of crude **1** as a light green oil which partially crystallized. Recrystallization from hexane of the combined fractions gave 10.5 g of white crystals, mp 98–105°. Four recrystallizations from ether gave 6.3 g (35%) of (+)-(*S*)-**1**, mp 108–109°, $[\alpha]^{25}_{546}$ +229° (*c* 1.04, $CHCl_3$). Further recrystallization of this material from ether did not change the rotation or melting point significantly: nmr two multiplets, one about τ 2.0 (2 H) and the other about 2.6 (2 H), a broad multiplet about 5.4 (1 H), a sharp singlet at 7.5 (3 H), and a complex multiplet 7.9–9.2 (18 H); ir (chloroform) 3.4 (m), 5.9 (s), 6.25 (w, sharp), 7.7 (m), 8.1 (vs), 8.6 (w), 8.8 (w), 9.2 (m), 9.6 (w), 9.9 (w), 10.4 (m), 11.1 (m), and 12.3 μ (m). *Anal.* Calcd for $C_{18}H_{26}ClNO_3S$: C, 58.13; H, 7.05. Found: C, 58.37; H, 6.96.

Although the mother liquors contained a mixture of (+)- and (−)-**1**, they could not be separated further.

***N*-Carbo-(−)-menthoxy-*p*-toluenesulfinamide (2) as Mixtures of Diastereomers.** To *p*-toluenesulfinyl chloride (prepared from 60 ml (0.66 mol) of thionyl chloride and 50 g (0.28 mol) of sodium *p*-toluenesulfinate) was added 40 g (0.20 mol) of optically pure (−)-menthyl carbamate, prepared by a modification of the procedure used for the preparation of benzyl carbamate.[21] The solid carbamate and liquid sulfinyl chloride were mixed intimately, and 100 g of pyridine was added and the mixture stirred. Heat was evolved. After 45 min, the mixture was added to 200 g of ice and 100 ml of hydrochloric acid. The mixture was shaken with dichloromethane, and the aqueous layer was washed with additional dichloromethane. The combined organic layers were dried and evaporated to give 54 g of an orange oil. Most (~95%) of this material dissolved in pentane. The mixture was filtered, and the filtrate was added to a column of 500 g of silica gel packed in pentane. Elution of the column with pentane and with 5% ether in pentane yielded various disproportionation products of *p*-toluenesulfinyl chloride. Elution of the column with 8% ether in pentane yielded 34.0 g (50%) of a light yellow oil (**2**) which partially crystallized. Elution with 10% ether in pentane afforded 5.0 g of unreacted carbamate. The sample of **2** was not pure by tlc, but did show an ir spectrum identical with that of an authentic sample of the described sulfinamide prepared by another route (see below). Recrystallization of a small amount of crude **2** from dichloromethane–pentane gave white needles: mp 90–91°; $[\alpha]^{25}_{546}$ −40.9° (*c* 1.05, $CHCl_3$); ir (chloroform) 3.0 (w, sharp, N–H), 5.8 (s, carbonyl), 9.0 (s, characteristic of sulfinamides), 12.3 μ (m, arylmethyl); pmr τ 2.1 and 2.8 (2 H, aromatic protons), a broad band centered about 3.1 (1 H, N–H proton), a broad band centered about 5.4 (1 H, menthyl methine proton), a sharp singlet at 7.6 (3 H, arylmethyl), and a complex multiplet 7.9–9.5 (18 H, menthyl alkyl protons). *Anal.* Calcd for $C_{18}H_{27}NO_3S$: C, 64.06; H, 8.06. Found: C, 64.01; H, 8.08.

Other samples of the material were recrystallized from the same solvent mixture to give material pure by tlc, with mp 91–92°, but with $[\alpha]^{25}_{546}$ −20.1° (*c* 1.12, $CHCl_3$). A third sample had mp 90–91°, $[\alpha]^{25}_{546}$ +9.36° (*c* 1.23, $CHCl_3$). Thus the two diastereomers do not depress each other's melting point appreciably, and the melting point cannot be used as a criterion for determining diastereomeric purity. Accordingly no attempt was made to separate the diastereomers of **2**, particularly since crystalline **2** decomposed completely in 24 hr at room temperature.

(+)-(*S*)-*N*-Carbo-(−)-menthoxy-*p*-toluenesulfonimidoyl Chloride ((+)-(*S*)-1) by Method B. Crude sulfinamide **2**, 18.5 g (0.055 mol), was dissolved in 100 ml of dry ether. To this was added 5.0 ml

(21) L. I. Smith, *Org. Syn.*, **23**, 13 (1943).

(5.0 g, 0.062 mol) of dry pyridine. Dry chlorine was bubbled into the vessel with stirring at 0° until the color of the chlorine was no longer discharged. Sufficient water was added to dissolve the precipitated pyridinium salt, and the layers were separated. The organic layer was washed with 10% aqueous hydrochloric acid and with water, dried, and evaporated to give 18.7 g of a yellow oil, which partially crystallized. Addition of pentane induced further crystallization. The crystals were collected to give 12.1 g of a single compound (by tlc). Recrystallization of this material from pentane, from hexane, and then four times from ether gave 7.8 g of diastereomerically pure (+)-(*S*)-**1**, mp 108.5–109.5°, $[\alpha]^{25}_{546}$ +225° (*c* 1.06, $CHCl_3$), undepressed by admixture with a sample of (+)-(*S*)-**1** prepared by method A. Concentration of mother liquors and recrystallization afforded 2.1 g more of pure (+)-(*S*)-**1** to give a total yield of 48%. *Anal.* Calcd for $C_{18}H_{26}ClNO_3S$: C, 58.13; H, 7.05. Found: C, 58.18; H, 6.98.

(+)-(*S*)-*N*-Carbo-(−)-menthoxy-*p*-toluenesulfonimidoyl Chloride ((+)-(*S*)-1) by Method C. Crude sulfinamide **2**, 17.0 g (0.050 mol), was dissolved in 50 ml of dichloromethane. Then 6.0 g (0.055 mol) of *tert*-butyl hypochlorite was added to the solution, and the reaction flask was protected from light. After 30 min the solvent was removed on a rotary evaporator, the flask was evacuated for 12 hr to remove excess hypochlorite and *tert*-butyl alcohol. The crystals that formed were washed with pentane and collected by filtration to give 10 g of crude product. Recrystallization of this material from pentane, from hexane, and then four times from ether afforded 8.2 g of diastereomerically pure (+)-(*S*)-**1**, mp 109–110°, $[\alpha]^{25}_{546}$ +229° (*c* 1.08, $CHCl_3$), mmp (with pure (+)-(*S*)-**1**, method A) 109–110°. Concentration of the mother liquors and cooling afforded 4 g more of crude material which was recrystallized to 2.6 g of pure (+)-(*S*)-**1** to give a 58% yield of product. No crystalline (−)-(*R*)-**1** could be isolated from the reaction mixture, although the remaining material did have a negative rotation and the ir spectrum indicated that a large part of the residue was indeed **1**.

Reduction of (+)-(*S*)-*N*-Carbo-(−)-menthoxy-*p*-toluenesulfonimidoyl Chloride ((+)-(*S*)-1) to (+)-(*S*)-*N*-Carbo-(−)-menthoxy-*p*-toluenesulfinamide ((+)-(*S*)-2) with Hydrazine. To a stirred solution of diastereomerically pure (+)-(*S*)-**1**, 1.80 g (0.49 mmol), in 10 ml of tetrahydrofuran was added 1 ml of 50% aqueous hydrazine solution over 10 min with the temperature maintained at 10°. Vigorous evolution of gas occurred during addition and continued for 5 min after addition was complete. The mixture was stirred for 30 min more, and 50 ml of ethyl ether was added, and the layers were separated. The organic layer was washed three times with 50 ml of saturated aqueous sodium chloride. The ether layer was then dried and evaporated to give 1.65 g (95%) of a viscous oil. The residue was pure by tlc (R_f 0.7, silica gel, 20% ether in pentane, uv indicator) and had $[\alpha]^{25}_{546}$ +24.4° (*c* 1.05, $CHCl_3$). Attempts at crystallization failed. The ir spectrum taken in chloroform had absorption maxima at 3.0 (w, sharp, N–H stretch), 5.8 (s, carbonyl stretch), 9.0 (s, characteristic of sulfinamides), and at 12.3 μ (m, arylmethyl). The spectrum and tlc behavior of this material were identical with those of **2** prepared directly. *Anal.* Calcd for $C_{18}H_{27}NO_3S$: C, 64.06; H, 8.06. Found: C, 64.08; H, 8.10.

Conversion of (+)-(*S*)-*N*-Carbo-(−)-menthoxy-*p*-toluenesulfinamide ((+)-(*S*)-2) to (−)-(*R*)-*N*-Carbo-(−)-menthoxy-*p*-toluenesulfonimidoyl Chloride ((−)-(*R*)-1). Dry chlorine was passed into a 20-ml ether solution of 3.4 g (10.0 mmol) of (+)-(*S*)-**2**, $[\alpha]^{25}_{546}$ +24.4° (*c* 1.18, $CHCl_3$), and 1.0 ml (1.0 g, 12.5 mmol) of pyridine at −70° until the solution became yellow, indicating an excess of chlorine. An additional 50 ml of ether was mixed into the solution and the white precipitate filtered. The filtrate was washed with 10% hydrochloric acid and saturated aqueous sodium chloride, dried, and evaporated to give 4.0 g of a colorless viscous oil. Analysis by tlc (20% ether in pentane, silica gel, uv indicator) showed only one spot corresponding to (+)-(*S*)-**1** and some material at the origin. Quick filtration through silica gel removed the polar material. The eluate was evaporated, and the product that crystallized collected, 3.5 g (95%) of white prisms pure by tlc, mp 73–78°, $[\alpha]^{25}_{546}$ −332° (*c* 1.07, $CHCl_3$). Recrystallization of this material from pentane and then from hexane yielded (−)-(*R*)-**1**, 3.2 g, mp 77.5–79.0°, $[\alpha]^{25}_{546}$ −389° (*c* 1.05, $CHCl_3$). The ir spectrum in chloroform gave as major bands, maxima at 5.9 (s, carbonyl) and at 8.1 μ (vs) and was identical in all respects with that of (+)-(*S*)-**1**. The pmr spectrum showed resonance peaks at τ 2.0 (2 H) and 2.6 (2 H, multiplets, aromatic protons), 5.4 (1 H, broad multiplet, methine proton), 7.5 (3 H, singlet, arylmethyl), and 7.6–9.2 (18 H, multiplet). *Anal.* Calcd for $C_{18}H_{27}ClNO_3S$: C, 58.13; H, 7.05. Found: C, 58.29; H, 6.99.

Reduction of (−)-(*R*)-1 to (−)-(*R*)-2 with Hydrazine. By the same method used for the other diastereomer, 0.37 g (1.0 mmol) of (−)-(*R*)-**1**, $[\alpha]^{25}_{546}$ −381° (*c* 1.20, $CHCl_3$) (diastereomerically pure), was reduced with aqueous hydrazine in tetrahydrofuran to give 0.32 g (95%) of a viscous oil, pure by tlc (silica gel, 20% ether–pentane, uv indicator), $[\alpha]^{25}_{546}$ −112° (*c* 1.08, $CHCl_3$). The ir spectrum in chloroform showed major peaks at 3.0 (w, sharp, N–H), 5.8 (s, carbonyl), 9.0 (s), and 12.3 μ (m, arylmethyl). This spectrum and the tlc behavior of this material were identical with those of **2** prepared directly. *Anal.* Calcd for $C_{18}H_{27}NO_3S$: C, 64.06; H, 8.06. Found: C, 64.12; H, 8.01.

Conversion of (−)-(*R*)-2 to (+)-(*S*)-1. A 0.32-g (0.95 mmol) sample of (−)-(*R*)-**2**, $[\alpha]^{25}_{546}$ −112° (*c* 1.08, $CHCl_3$), from the reaction of pure (−)-(*R*)-**1** with hydrazine, was treated with chlorine in the presence of pyridine in ether solution to give 0.35 g (100%) of a white solid, pure by tlc, mp 95–100°, $[\alpha]^{25}_{546}$ +168° (*c* 1.08, $CHCl_3$). This material was recrystallized three times from ether to give 0.11 g of (+)-(*S*)-**1**, $[\alpha]^{25}_{546}$ +223° (*c* 1.17, $CHCl_3$), mp 108–110°, undepressed by admixture with an equal amount of analytically pure (+)-(*S*)-**1**. The material was identical with pure (+)-(*S*)-**1** by tlc, and the ir spectrum contained the characteristic absorption maxima at 5.9 (s) and 8.1 μ (vs).

Reaction of (+)-(*S*)-1 with Methylmagnesium Bromide. To a solution of 0.37 g (1.0 mmol) of (+)-(*S*)-**1**, $[\alpha]^{25}_{546}$ +227° (*c* 1.21, $CHCl_3$) (diastereomerically pure), in 10 ml of anhydrous ether was added dropwise over 5 min a twofold excess of methylmagnesium bromide (3 *M* in ether) with stirring and cooling at −80°. The solution became yellow and a yellow precipitate formed. After 10 min the reaction was quenched with a saturated solution of ammonium chloride in water. The mixture was shaken with additional water and ether. The aqueous layer was extracted with two 50-ml portions of ether. The combined ether extracts were dried and evaporated to give 0.35 g of a light yellow oil, whose tlc consisted of two spots. The two compounds were cleanly separated by chromatography over 5 g of silica gel, and eluted with 15% ether in pentane. The first few fractions contained a total of 0.03 g (10%) of methyl *p*-tolyl sulfide, identified by its characteristic odor and by comparison of its tlc with that of an authentic sample. Later fractions contained 0.30 g (90%) of a colorless oil, pure by tlc, $[\alpha]^{25}_{546}$ −117° (*c* 1.06, chloroform). The material was identical by tlc with an analytical sample of (−)-(*R*)-**2**. The ir spectrum in chloroform showed the absorption maxima at 3.0 (w, sharp, N–H stretch), 5.8 (s, carbonyl), and 9.0 μ (s) which appeared in the spectrum of (−)-(*R*)-**2**. All efforts to crystallize this material were unsuccessful. The material decomposed upon standing at room temperature for several days.

Conversion of (−)-(*R*)-2 to (+)-(*S*)-1. A solution of 0.15 g (0.45 mmol) of (−)-(*R*)-**2**, $[\alpha]^{25}_{546}$ −117° (*c* 1.06, $CHCl_3$), from the reduction of (+)-(*S*)-**1** with methylmagnesium bromide was treated with dry chlorine in the presence of pyridine to give 0.15 g (91%) of white crystals, pure by tlc, mp 106.5–108.0°, $[\alpha]^{25}_{546}$ +200° (*c* 1.08, $CHCl_3$) (95% diastereomerically pure). The material was recrystallized twice from ether to give white crystals, mp 108.5–109.0, $[\alpha]^{25}_{546}$ +226° (*c* 1.12, $CHCl_3$). The melting point was not depressed upon admixture of an equal amount of pure (+)-(*S*)-**1**. The substance was identical by tlc with analytically pure (+)-(*S*)-**1** and its ir spectrum showed the absorption peaks at 5.9 (s) and 8.1 μ (vs) characteristic of **1**.

Conversion of (+)-(*S*)-*N*-Carbo-(−)-menthoxy-*p*-toluenesulfinamide ((+)-(*S*)-2) to (−)-(*S*)-Methyl *p*-Tolyl Sulfoxide ((−)-(*S*)-3). A 0.34-g (1.0 mmol) sample of (+)-(*S*)-**2**, $[\alpha]^{25}_{546}$ +24.1° (*c* 1.21, $CHCl_3$) (from the reduction of (+)-(*S*)-**1** with hydrazine), in 5 ml of anhydrous ether was treated with a fivefold excess of methylmagnesium bromide (3 *M* in ether) for 20 min at 25°. The reaction was then quenched with saturated aqueous ammonium chloride. The layers were separated and the aqueous layer was extracted with two 25-ml portions of dichloromethane. The organic layers were combined, dried, and evaporated onto 0.3 g of silica gel. Chromatography of the product on 3 g of silica gel gave, upon elution with 15% ether–pentane, 0.21 g of unidentified material, and with 50% ether–pentane, 0.056 g (37%) of a substance identical by tlc with an authentic sample of **3**.[17a] This substance had mp 58–63°, $[\alpha]^{25}_{546}$ −121° (*c* 1.05, acetone). The isolated product was recrystallized from ether–pentane to give a small amount of crystalline material, mp 73.0–74.0°, $[\alpha]^{25}_{546}$ −171° (*c* 0.651, acetone) (lit.[15a] mp 74.5–75.5°, $[\alpha]^{25}_{546}$ −180.5° (*c* 0.795, acetone) for (−)-(*S*)-**3**). On admixture with an equal amount of optically pure (−)-(*S*)-**3**, the melting point was 73.0–74.5°. The ir spectrum taken in chloroform was identical with that of an analytical sample of **3** most notably in the strong absorption maximum at 9.7 μ, characteristic of sulfoxides. The material was thus identified as (−)-(*S*)-**3**. The

total sample, as isolated by chromatography, was 67% optically pure.

Conversion of (−)-(*R*)-2 to (+)-(*R*)-3. In the same manner as in the previous experiment, 0.50 g (1.48 mmol) of (−)-(*R*)-**2**, $[\alpha]^{25}_{546}$ −110° (*c* 1.11, $CHCl_3$) (from the reduction of diastereomerically pure (−)-(*R*)-**1** with hydrazine), was treated with methylmagnesium bromide. The isolated material, 0.070 g, was a solid, identical with an analytical sample of **3**, by tlc, mp 60–65°, $[\alpha]^{25}_{546}$ +115° (*c* 1.10, acetone). The ir spectrum in chloroform was identical with that of an authentic sample of **3** most notably in the strong absorption maximum at 9.7 μ which is characteristic of sulfoxides. The isolated material was recrystallized from ether–pentane to give 0.03 g (14%) of a crystalline solid, mp 73.5–75.0°, $[\alpha]^{25}_{546}$ +175° (*c* 1.01, acetone) (lit.[17a] mp 74.5–75.5°, $[\alpha]^{25}_{546}$ +180° (*c* 0.795, acetone) for (+)-(*R*)-**3**). The material as isolated by chromatography was 64% optically pure.

Conversion of (−)-(*R*)-2 to (+)-(*R*)-3. A 0.104-g (0.31 mmol) sample of (−)-(*R*)-**2**, $[\alpha]^{25}_{546}$ −118° (*c* 1.17, $CHCl_3$) (produced from the reaction of diastereomerically pure (+)-(*S*)-**1** with methylmagnesium bromide), in anhydrous ether was treated with a fivefold excess of methylmagnesium bromide (3 *M* in ether) with vigorous stirring at room temperature to give 0.024 g (50%) of a white solid, mp 63–66°, $[\alpha]^{25}_{546}$ +147° (*c* 2.27, acetone), which was identical by tlc with an authentic sample of **3**. The ir spectrum showed the strong absorption maximum at 9.7 μ which is characteristic of sulfoxides. Recrystallization of the isolated material from ether–pentane gave material with mp 74.0–75.0°, $[\alpha]^{25}_{546}$ +179° (*c* 1.20, acetone) (lit.[17a] mp 74.5–75.5°, $[\alpha]^{25}_{546}$ +180.5° (*c* 0.795, acetone)). Admixture with an equal amount of optically pure (+)-(*R*)-**3** did not depress the melting point. The material isolated by chromatography was 82% optically pure.

Conversion of (+)-(*S*)-1 to (−)-(*R*)-*p*-Cresyl *N*-Carbo-(−)-menthoxy-*p*-toluenesulfonimidate ((−)-(*R*)-4). To a solution of 0.90 g (2.4 mmol) of pure (+)-(*S*)-**1**, $[\alpha]^{25}_{546}$ +227° (*c* 1.01, $CHCl_3$), in dichloromethane was added 0.70 g (4.7 mmol) of finely divided potassium *p*-cresylate. The mixture was stirred for 10 min and then allowed to stand for 1 hr. Analysis by tlc (silica gel, 20% ether–pentane, uv indicator) showed complete conversion to the desired product and no side products. The reaction mixture was diluted by the addition of 40 ml of dichloromethane and filtered. The filtrate was washed with water, dried, and evaporated to yield 1.05 g of a light yellow oil. Chromatography of this material on 10 g of silica gel, with 5% ether–pentane as eluting agent gave 0.050 g of *p*-cresol in the first few fractions. Elution with 15% ether–pentane gave 0.95 g of a white solid, mp 83–87°, $[\alpha]^{25}_{546}$ −85.3° (*c* 1.23, ethanol). Recrystallization of this material from ether–pentane gave 0.91 g (83%) of white crystals, mp 89.5–91.0°, $[\alpha]^{25}_{546}$ −119° (*c* 1.26, $CHCl_3$), $[\alpha]^{25}_{D}$ −89.8° (*c* 1.33, ethanol). Further recrystallization from ether–pentane produced no change in either the melting point or the rotation. *Anal.* Calcd for $C_{25}H_{33}NO_4S$: C, 67.70; H, 7.50. Found: C, 67.77; H, 7.52.

Conversion of (−)-(*R*)-*p*-Cresyl *N*-Carbo-(−)-menthoxy *p*-Toluenesulfonimidate ((−)-(*R*)-4) to (−)-(*R*)-*N*-Carbo-(−)-menthoxy Methyl *p*-Tolylsulfoximide ((−)-)*R*(-6). To a solution of 0.70 g (1.6 mmol) of pure (−)-(*R*)-**4** in 5 ml of anhydrous ether was added a fivefold excess of methylmagnesium bromide in ether over 10 min at 25°. After 30 min the reaction was quenched with saturated aqueous ammonium chloride. Sufficient water was added to dissolve all salts and more ether was added. The layers were separated and the aqueous layer was extracted with two 50-ml portions of ether. The combined organic extracts were dried and evaporated to give 0.53 g of an oil. This was dissolved in dichloromethane and evaporated onto 0.5 g of silica gel. This was added to a column of 10 g of silica gel packed in 10% ether in pentane. Elution of the column with 10% ether–pentane gave 0.088 g of *p*-cresol and 0.103 g of unreacted ester. Elution with 60% ether in pentane gave 0.192 g (40% based on consumed starting material) of a colorless oil which soon crystallized, mp 81–83°, $[\alpha]^{25}_{546}$ −105° (*c* 1.22, $CHCl_3$). Recrystallization from dichloromethane–pentane gave 0.18 g of white needles of (−)-(*R*)-**6**, mp 85–86°, $[\alpha]^{25}_{546}$ −123° (*c* 0.75, $CHCl_3$). The ir spectrum had, among other things, a strong sulfonimidoyl absorption band at 8.08 μ, moderate bands at 9.15 and at 9.70 μ, and a moderate arylmethyl band at 12.34 μ. The nmr spectrum showed an S-CH_3 singlet at τ 7.4. *Anal.* Calcd for $C_{19}H_{29}NO_3S$: C, 64.92; H, 8.32. Found: C, 65.34; H, 8.45.

Hydrolysis of (−)-(*R*)-*N*-Carbo-(−)-menthoxy Methyl *p*-Tolylsulfoximide ((−)-(*R*)-6) to (−)-(*R*)-Methyl *p*-Tolylsulfoximide ((−)-(*R*)-7). A mixture of 0.19 g (0.54 mmol) of (−)-(*R*)-**6**, $[\alpha]^{25}_{546}$ −105° (*c* 1.22, $CHCl_3$), 87% diastereomerically pure, and 1 ml of concentrated H_2SO_4 was stirred for several minutes until gas evolution diminished. The mixture was occasionally stirred over 4 hr and then allowed to stand for 12 hr. About 1 g of ice was added, and enough sodium carbonate to give a pH of 8. The mixture was extracted with two 50-ml portions of ether. The combined ether layers were dried and evaporated to give 0.084 g of residue (apparently a great deal of unextracted product remained in the aqueous layer). The semisolid residue was dissolved in a minimum amount of dichloromethane and spotted on a 5 × 20 cm preparative layer chromatographic (plc) plate (silica gel PF-254, 2 mm thick) and developed four times with 40% ether in pentane. The band with lowest R_f (uv indicator) was scraped off and extracted with chloroform which was evaporated to give 0.051 g of material showing two spots by tlc (silica gel, Baker-flex IBF, uv indicator, ether). This material was dissolved in a minimum amount of dichloromethane and spotted onto another plc plate. Development with ether gave two well-separated bands. The band with the lower R_f values was scraped off and extracted with chloroform. The solution was evaporated to give a colorless viscous liquid. After a stream of dry nitrogen had been passed into the flask for 30 min, the substance crystallized to give 0.025 g (27%) of a white solid, mp 55–58°, $[\alpha]^{25}_{546}$ −34.0° (*c* 0.830, acetone). The material was identical by tlc with an authentic sample of (−)-(*R*)-**7** prepared by the imidation of methyl *p*-tolyl sulfoxide,[17a] and was 86% optically pure. The ir spectrum had major absorption bands at 2.99 (w, sharp, N–H stretch), 8.18 (vs, O=S=N), and 11.7 μ (s, arylmethyl), and was identical with the spectrum of an authentic sample of (−)-(*R*)-**7**. The isolated material was recrystallized from acetone–ether to give a small amount of material with mp 59–60°, $[\alpha]^{25}_{546}$ −39.1° (*c* 2.02, acetone) (lit.[17a] mp 59–61°, $[\alpha]^{25}_{546}$ −39.9° (*c* 2.28, acetone) for (−)-(*R*)-**7**).

Conversion of (−)-(*R*)-1 to (−)-(*S*)-4. A 0.19-g (0.5 mmol) sample of pure (−)-(*R*)-**1**, $[\alpha]^{25}_{546}$ −385° (*c* 1.37, $CHCl_3$), was converted to the corresponding ester, (+)-(*S*)-**4**, an oil after chromatography, 0.18 g (85%), $[\alpha]^{25}_{D}$ +2.40° (*c* 1.04, ethanol). The ir spectrum showed major absorption maxima at 5.93 (s, carbonyl), 7.90 (vs, sulfonimidoyl function), and 12.25 μ (m, arylmethyl). *Anal.* Calcd for $C_{25}H_{33}NO_4S$: C, 67.70; H, 7.50. Found: C, 67.75; H, 7.58.

Conversion of (+)-(*S*)-4 to (+)-(*S*)-6. A 1.00-g (2.26 mmol) sample of ester (+)-(*S*)-**4**, $[\alpha]^{25}_{D}$ +2.4° (*c* 1.04, ethanol), diastereomerically pure, was treated with methylmagnesium bromide in anhydrous ether at 25° for 30 min. Isolation steps were the same as those used in the case of the other diastereomer. Purification by chromatography afforded 0.20 g of unreacted ester **4**, and 0.50 g (78%, based on consumed **4**) of (−)-(*R*)-**6** as a colorless oil, pure by tlc, $[\alpha]^{25}_{546}$ +16.4° (*c* 1.15, $CHCl_3$). The isolated material gave an ir spectrum identical with that of the previously analyzed (−)-(*R*)-**6** including bands at 6.00 (s), 8.08 (vs), 9.15 (m), 9.70 (m), and 12.34 μ (m). The nmr spectrum showed an *S*-methyl singlet at τ 7.4. *Anal.* Calcd for $C_{19}H_{29}NO_3S$: C, 64.92; H, 8.32. Found: C, 65.11; H, 8.37.

Hydrolysis of (+)-(*S*)-6 to (+)-(*S*)-7. Treatment of 0.50 g (1.5 mmol) of the above sample of (+)-(*S*)-**6** with 2 ml of concentrated sulfuric acid and isolation work-up by neutralization with sodium carbonate gave, upon purification by silica gel chromatography, 0.15 g of a white solid, mp 62–65°, $[\alpha]^{25}_{546}$ +33.8° (*c* 2.34, acetone). The material was identical by ir and by tlc with an authentic sample of **7**, and was 85% optically pure. The ir spectrum in chloroform contained the following major absorption maxima: 2.99 (w, sharp, N–H), 8.18 (vs), 8.90 (m), 9.10 (m), 9.50 (m), 9.70 (m), and 11.71 μ (m, arylmethyl). Recrystallization of the product from dichloromethane–pentane gave a small amount of material, mp 68–69°, $[\alpha]^{25}_{546}$ +38.5° (*c* 0.710, acetone) (lit.[17a] mp 68–69°, $[\alpha]^{25}_{546}$ +39.9° (*c* 2.28, acetone) for (+)-(*S*)-**7**).

Conversion of (+)-(*S*)-7 to (+)-(*S*)-6. A mixture of 0.085 g (0.5 mmol) of optically pure (+)-(*S*)-**7**, $[\alpha]^{25}_{546}$ +39.8° (*c* 1.22, acetone), and 0.20 g (1.0 mmol) of (−)-menthyl chloroformate was treated with 1 ml of pyridine. This mixture was swirled for 5 min, during which a voluminous white precipitate formed. The mixture was poured into ice and concentrated hydrochloric acid. The mixture was extracted with two 25-ml portions of dichloromethane; the combined organic layers were dried and evaporated to give 0.3 g of a yellow oil. This was dissolved in a minimum amount of dichloromethane and spotted on a 5 × 20 cm plc plate. The plate was developed twice in 1:1 ether–pentane. Collection of the band with the lower R_f value and extraction with chloroform afforded 0.02 g (16%) of a colorless oil, identical by tlc and ir with the previously prepared (+)-(*S*)-**6**. This material had $[\alpha]^{25}_{546}$ +36.0° (*c* 1.56, acetone). The ir spectrum had major absorption bands at 3.40 (m), 6.00 (s), 8.08 (vs), 9.15 (m, broad), and 12.34 μ (m).

Hydrolysis of (−)-(*R*)-*p*-Cresyl *N*-Carbo-(−)-menthoxy *p*-Toluenesulfonimidate ((−)-(*R*)-4) to (+)-(*R*)-*p*-Cresyl *p*-Toluenesulfonimidate ((+)-(*R*)-5). To a 0.44-g (1.0 mmol) sample of pure (−)-(*R*)-**4**, $[\alpha]^{25}D$ −89.0° (*c* 1.01, ethanol), was added 1 ml of concentrated sulfuric acid. The mixture was swirled until gas evolution had diminished and then allowed to stand for 2 hr. Ice (2 g) was added and the mixture neutralized with sodium carbonate. The neutral solution was diluted with sufficient water to dissolve the inorganic salts, and then extracted with three 50-ml portions of dichloromethane. The combined organic layers were dried and evaporated onto 0.5 g of silica gel. This was added to a column packed in 10% ether–pentane. Elution with 40% ether in pentane gave 0.19 g (79%) of (+)-(*R*)-**5** as a white solid, mp 68.5–69.5°, $[\alpha]^{25}_{546}$ +22.2° (*c* 1.29, $CHCl_3$). Recrystallization of the compound from dichloromethane–pentane produced no change in melting point or in rotation. Slow evaporation from ether–pentane gave material with only one crystal shape. This material gave an ir spectrum in chloroform with the following major absorption peaks: 2.98 (w, sharp, N–H stretch), 6.62 (m, sharp), 7.76 (s), 8.40 (m), 8.69 (s), 9.20 (m), 10.4 (w, broad), 11.72 (m), 12.02 (m), and 12.25 μ (w, arylmethyl). *Anal.* Calcd for $C_{14}H_{15}NO_2S$: C, 64.34; H, 5.78. Found: C, 64.26; H, 5.80.

Hydrolysis of (+)-(*S*)-4 to (−)-(*S*)-5. A 0.22-g (0.50 mmol) sample of pure (+)-(*S*)-**4** was converted to (−)-(*S*)-**5**, by treatment with concentrated sulfuric acid. The isolated product was a solid, 0.078 g (60%), mp 68.5–69.5°, $[\alpha]^{25}_{546}$ −22.0° (*c* 1.16, $CHCl_3$). Recrystallization of the product from dichloromethane–pentane produced no change in either melting point or rotation. The ir spectrum in chloroform had the following features: 2.98 (w, sharp), 6.62 (m, sharp), 7.76 (s), 8.40 (m), 8.69 (s), 9.20 (m), 10.4 (w, broad), 11.72 (m), 12.02 (m), and 12.25 μ (w, arylmethyl). *Anal.* Calcd for $C_{14}H_{15}NO_2S$: C, 64.34; H, 5.78. Found: C, 64.31; H, 5.71.

Conversion of (+)-(*S*)-1 to (−)-(*R*)-*N*-Carbo-(−)-menthoxy-*p*-toluenesulfonimid-*N*′,*N*′-dimethylamide ((−)-(*R*)-9). To a stirred solution of 1.0 g (2.7 mmol) of diastereomerically pure (+)-(*S*)-**1**, $[\alpha]^{25}_{546}$ +223° (*c* 1.21, $CHCl_3$), in 10 ml of ether was added an excess of anhydrous dimethylamine through a Dry Ice condenser. After addition was completed, the mixture was stirred for 15 min, then filtered. The filtrate was diluted with 50 ml of ether and then washed with 10 ml of water. The ether layer was dried and evaporated. Treatment of the partially crystalline residue with 1 ml of pentane induced complete crystallization. Evaporation of the pentane left 0.96 g (97%) of a white solid pure by tlc (R_f 0.8, silica gel, 20% ether–pentane, uv indicator), mp 67–70°, $[\alpha]^{25}_{546}$ −20.8° (*c* 1.05, $CHCl_3$). Recrystallization from hexane gave analytically pure (−)-(*R*)-**9**, mp 70–71°, $[\alpha]^{25}_{546}$ −19.2° (*c* 1.25, $CHCl_3$). The ir spectrum in chloroform showed, among other things, a strong carbonyl absorption band at 5.98 μ, a very strong sulfonimidoyl absorption band at 8.05 μ, a strong absorption peak at 10.50 μ, a strong band at 11.05 μ, and a weak arylmethyl band at 12.26 μ. The nmr spectrum showed a singlet (6 H) at τ 7.2 (*N*-methyl protons). *Anal.* Calcd for $C_{20}H_{32}N_2O_3S$: C, 63.12; H, 8.48. Found: C, 63.10; H, 8.42.

Hydrolysis of (−)-(*R*)-9 to (+)-(*S*)-*p*-Toluenesulfonimid-*N*,*N*-dimethylamide ((+)-(*S*)-10). A mixture of 0.95 g (2.5 mmol) of pure (−)-(*R*)-**9**, $[\alpha]^{25}_{546}$ −19.2° (*c* 1.25, $CHCl_3$), and 1 ml of concentrated sulfuric acid was swirled until vigorous gas evolution had ceased. The resulting solution was allowed to stand for 1 hr, after which 1 g of ice was added and the mixture neutralized by the addition of solid sodium carbonate. Sufficient water was added to dissolve all inorganic salts and the mixture was extracted with two 50-ml portions of dichloromethane. The combined organic layers were dried and evaporated onto 1 g of silica gel. This was added to a column of 10 g of silica gel packed in 15% ether in pentane. Elution of the column with 15% ether–pentane gave, in the first fractions, 0.35 g of an unidentified aliphatic compound. Elution with 20% ether–pentane gave 0.21 g of unreacted starting material; and elution with 30% ether–pentane gave 0.32 g (80%) of a colorless oil which crystallized upon standing, mp 80–115° (most material melted 80–85°, remainder at 110–115°), $[\alpha]^{25}_{546}$ +8.0° (*c* 1.10, $CHCl_3$). Slow evaporation of this material from 1:1 ether–pentane gave two different types of crystals. Recrystallization of the entire 0.32 g from chloroform–pentane gave a first crop of 0.075 g (25%) of white crystals, $[\alpha]^{25}_{546}$ 0.00° (*c* 1.21, $CHCl_3$), mp 116–117° (lit.[19] mp (for (±)-**10**) 118–119°). The remaining mixture upon evaporation and recrystallization from dichloromethane–pentane gave 0.23 g, mp 86.5–88.0°, $[\alpha]^{25}_{546}$ +42.0° (*c* 1.06, $CHCl_3$). Repeated recrystallization of the sample from chloroform–pentane did not change either the melting point or the rotation, and the material was considered to be optically pure. The racemate and the optically pure material had identical tlc R_f values (0.5 with 25% ether–pentane as developer), and did not separate when spotted together. Likewise the ir spectra in chloroform were identical, showing the following absorption maxima: 3.05 (m, sharp, N–H stretch), 3.40 (m), 6.25 (m), 6.85 (m), 7.98 (vs), 8.80 (s), 10.10 (m, broad), 10.70 (s), and 12.25 μ (m, arylmethyl). The nmr spectrum showed a broad band at τ 5.2 (1 H, N–H) and a singlet at 7.2 (6 H, *N*-methyl protons). *Anal.* Calcd for $C_9H_{14}N_2OS$: C, 54.54; H, 7.12. Found: C, 54.19; H, 6.91.

The material isolated from the chromatogram was 25% racemic **10**. The seemingly anomalous low rotation of +8.0° for the chromatographically pure material was probably due to nonrepresentative selection of the sample for polarimetric analysis. The sample was taken from a slowly evaporated fraction in which racemate and optically pure material crystallized separately, and the mixture was not homogenized before a sample was removed.

Conversion of (+)-(*S*)-10 to (−)-(*R*)-*N*-Carbo-(−)-menthoxy-*p*-toluenesulfonimid-*N*′,*N*′-dimethylamide ((−)-(*R*)-9). To a mixture of 0.070 g (0.41 mmol) of (+)-(*S*)-**10**, $[\alpha]^{25}_{546}$ +42.0° (*c* 1.06, $CHCl_3$), optically pure, and 0.20 g (0.91 mmol) of (−)-menthyl chloroformate was added 0.50 ml (0.50 g, 6 mmol) of pyridine. The solution was swirled for a few seconds whereupon a voluminous white precipitate formed. After 10 min this was poured into a mixture of 1 ml of concentrated hydrochloric acid and 1 g of ice. The mixture was extracted with two 25-ml portions of dichloromethane. The combined extracts were dried and evaporated to give 0.23 g of oil. This mixture was separated into its components by preparative layer chromatography (silica gel PF-254, 2 mm thick, 10% ether–pentane, uv indicator). Removal of the band corresponding to the expected product and extraction with chloroform yielded 0.050 g (32%) of a single (by tlc) compound which soon crystallized, mp 70–71°, $[\alpha]^{25}_{546}$ −17.6° (*c* 1.11, $CHCl_3$). This material was identical by tlc (R_f 0.8, silica gel, 20% ether–pentane) with the sample of (−)-(*R*)-**9** prepared previously. The ir spectrum in chloroform showed the following major peaks: 5.98 (s), 8.05 (vs), 10.50 (s), 11.05 (s), and 12.26 μ (w). The nmr spectrum showed a singlet (6 H) at τ 7.2 (*N*-methyl protons).

***N*-Carbo-(−)-menthoxy-*p*-toluenesulfonimidamide ((−)-(*R*)-8).** To a mixture of 0.37 g (1.0 mmol) of pure (+)-(*S*)-**1**, $[\alpha]^{25}_{546}$ +227° (*c* 1.23, $CHCl_3$), and 0.08 g (2 mmol) of sodium amide was added 30 ml of liquid ammonia *via* a Dry Ice condenser while the mixture was stirred with cooling in a Dry Ice–acetone bath. The solution was allowed to reflux for 4 hr, and the ammonia was allowed to evaporate leaving a solid residue. This was washed with water and extracted with three 25-ml portions of dichloromethane. The organic layers were combined, dried, and evaporated onto 4 g of silica gel. This was added dry to a column of 16 g of silica gel packed in pentane. Elution of the column with 25% ether–pentane gave 0.03 g (9%) of (−)-menthyl carbamate, mp 158–160°. Elution with 1:1 ether–pentane gave in five fractions 0.13 g (37%) of a white solid pure by tlc (1:1 ether–pentane, silica gel, uv indicator), mp 168.5–169.0°, $[\alpha]^{25}_{546}$ −63° (*c* 0.46, $CHCl_3$). The ir spectrum of this compound differed from that of starting material only in that a broad N–H stretch band appeared at 3.0 μ, that the carbonyl absorption appeared at 6.0 μ (a shift of 0.25 μ from that of **1**), and that the large sulfonyl absorption band appeared at 7.8 μ (instead of 8.0 μ as in **1**). The nmr spectrum in deuteriochloroform showed multiplets at τ 2.1 (2 H), and 2.7 (2 H), and a broad band at 5.5 (1 H) overlapping a broad band at 5.9 (2 H), a sharp singlet at 7.6 (3 H), and a complex multiplet 7.8–9.4 (18 H). *Anal.* Calcd for $C_{18}H_{28}N_2O_3S$: C, 61.33; H, 8.01. Found: C, 61.44; H, 7.93.