Stereochemistry of Sulfur Compounds. II. New Reactions at Chiral Sulfur That Complete the First Monoligostatic Stereochemical Reaction Cycle[1,2]

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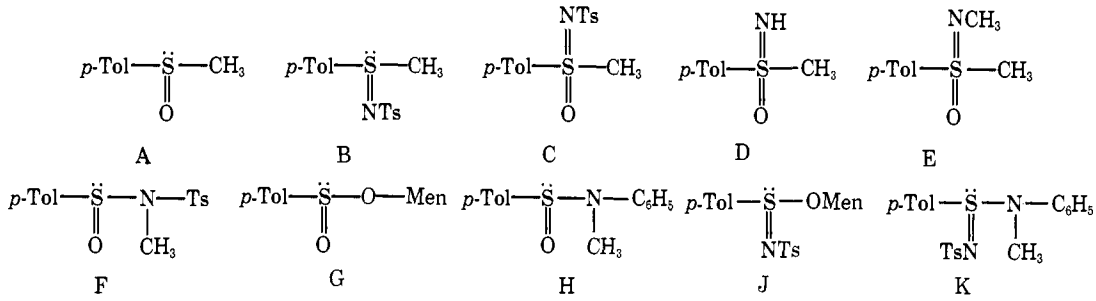
Abstract: This paper describes several new stereospecific reactions at chiral sulfur, and completion of the first known stereochemical reaction cycle in which only a single ligand is common to all compounds of the reaction cycle (monoligostatic). Additional diligostatic and triligostatic stereochemical reaction cycles are described that involve sulfoxides, sulfimides, sulfoximides, sulfinamides, sulfinamidines, sulfinate, and sulfinimidate esters (compounds A–K). The reactions were of 90–100% stereospecificity, and the stereochemical courses of all reactions were assigned. The monoligostatic podal cycle, A → B → C → D → E → F → A (four retentions and two inversions), involved two new reaction types. Reaction D → E went (90%) with formaldehyde–formic acid as reagent. Reaction E → F went (35%) with 94% retention of configuration when E was treated with pyridine and tosyl chloride. The diligostatic podal cycle, A ← D → E → F → A, involved a ligand metathesis and one inversion. A new method for reaction D → A (99% yield, 99% retention) involved nitrous acid as reagent. Cycles A ← G → H → A and B ← J → K → B were completed and are each triligostatic, antipodal and involve three inversions of configuration.



The first paper in this series reported[4] several new stereochemical reaction cycles in which chiral sulfur underwent both electrophilic and nucleophilic substitution reactions. The symmetry properties of some of the reaction cycles did not fit the classical rule that an odd number of inversions necessitated the inclusion of a pair of enantiomers in the reaction cycle. As a result, the general properties of stereochemical reaction cycles were examined, and maps were constructed that described all of the simpler stereochemical reaction cycles that involved simple ligand exchange on chiral tetrahedra.[5] The chemical literature is rich in examples of triligostatic cycles (three ligands common to all chiromers of the cycle), and a few examples of diligostatic cycles can be found, but no examples of either monoligostatic or aligostatic cycles have been reported.

This paper reports completion of the first monoligostatic stereochemical reaction cycle, as well as a new diligostatic and two new triligostatic cycles. It also reports several new stereospecific reactions that involve chiral sulfur, and a new kind of optically active compound chiral at sulfur.

Results and Discussion

Completion of Monoligostatic Cycle. Chart I outlines the reactions used to close this unique stereochemical reaction cycle. The stereochemical courses of the reactions (+)-(*R*)-**1** → (−)-(*S*)-**2** → (−)-(*R*)-**3** → (−)-(*R*)-**4** have been established.[4] The reaction (−)-(*R*)-**4** → (−)-(*R*)-**5** involved a new and convenient method for alkylation of sulfoximides (60–90%). This new method is an adaptation of the Eschweiler–Clarke reductive alkylation of amines with formaldehyde and formic acid. Similar alkylations were performed to give the corresponding *N*-benzyl and *N*-isobutyryl derivatives. We presume the mechanism of this alkylation reaction is similar to that for the alkylation[6] of ordinary amines. This reaction must proceed with retention since no bonds are made or broken to chiral sulfur. Johnson[7] and coworkers have reported the methylation of sulfoximides (70%) with trimethyloxonium fluoroborate.

Conversion of (−)-(*R*)-**5** to (−)-(*R*)-**6** occurred at 25° in pyridine containing 2 equiv of tosyl chloride (30–35%). The reaction occurred with at least 94%

(1) This investigation was supported by the U. S. Public Health Service Research Grant No. GM 12640-07 from the Department of Health, Education, and Welfare.

(2) Preliminary accounts of this work have appeared: (a) A. Nudelman and D. J. Cram, *J. Amer. Chem. Soc.*, **90**, 3869 (1968); (b) T. R. Williams, R. E. Booms, and D. J. Cram, *ibid.*, **93**, 7338 (1971).

(3) This author gratefully acknowledges nonresident tuition grants from Dow Chemical Co. and U. S. Rubber Co.

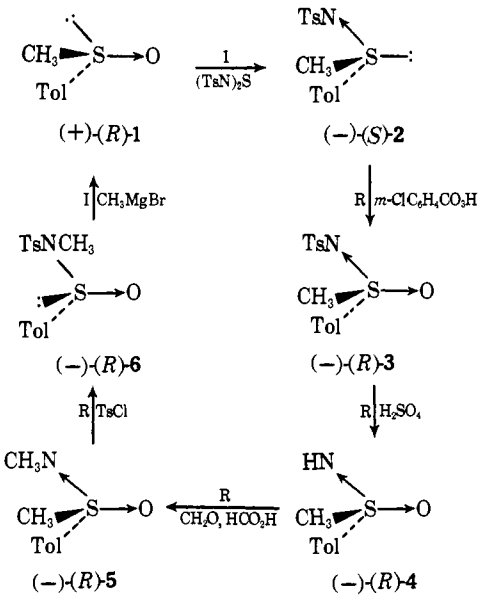
(4) D. J. Cram, J. Day, D. R. Rayner, D. M. von Schriltz, D. J. Duchamp, and D. C. Garwood, *J. Amer. Chem. Soc.*, **92**, 7369 (1970).

(5) (a) D. C. Garwood and D. J. Cram, *ibid.*, **92**, 4575 (1970); (b) D. J. Cram and J. M. Cram, *Top. Current Chem.*, in press.

(6) M. L. Moore, *Org. React.*, **5**, 301 (1949).

(7) C. R. Johnson, M. Haake, and C. W. Schroeck, *J. Amer. Chem. Soc.*, **92**, 6594 (1970).

Chart I. Monoligostatic Cycle

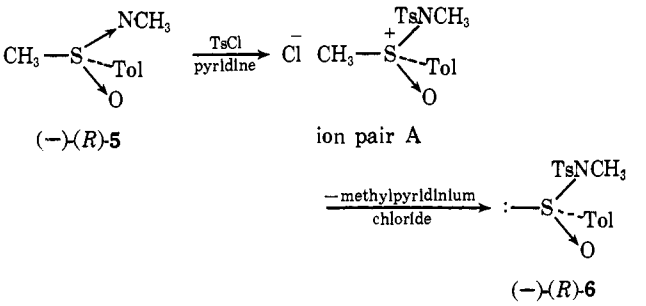


stereospecificity. The stereochemical course and mechanism of this remarkable conversion are discussed below.

The stereochemical reaction cycle was closed by conversion (38%) of (−)-(*R*)-**6** to (+)-(*R*)-**1** with methylmagnesium bromide. The product (+)-(*R*)-**1** was 95% optically pure, one recrystallization of which gave material identical with that reported in the literature.[8] Conversion of **6** to **1** resembles the reaction of *N*,*N*-dialkylsulfinamides with methyllithium to give methyl sulfoxides.[9] Although ordinary sulfinamides are inert to Grignard reagents, **6** possesses the particularly good leaving group *N*-methyl-*p*-toluenesulfonamide. The conversion of **6** to **1** undoubtedly went with inversion of configuration as did the other conversions of sulfinamides to sulfoxides (see next section).

The absolute configurations of all of the chiromers of Chart I are known except that of **6**. The stereochemical courses of the six reactions of Chart I are known with the exception of (−)-**5** → (−)-**6**. These facts allow the absolute configuration of (−)-**6** to be assigned as *R* and the stereochemical course of (−)-**5** → (−)-**6** to be assigned as retention. The reasoning is as follows. Since (−)-**6** gives (+)-(*R*)-**1** with inversion then (−)-**6** must have the *R* configuration. If (−)-(*R*)-**6** is produced from (−)-(*R*)-**5**, this reaction must have gone with retention.

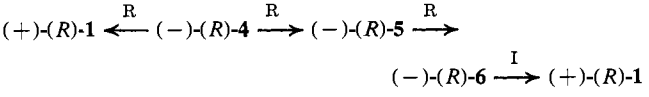
The reaction of (−)-(*R*)-**5** with tosyl chloride in pyridine to give (−)-(*R*)-**6** is interesting mechanistically. Tosylation of nitrogen turns sulfur into a positively charged leaving group for the attached methyl (see ion pair A). In a second stage, pyridine (and possibly chloride ion) attacks methyl displacing sulfur. The electron pair of the methyl–sulfur bond remains with the sulfur atom without perturbing the configuration at sulfur. This reaction represents a nucleophilic substitution at carbon in which the configuration of the leaving group is preserved. This synthesis is the only known source of *N*-tosyl-*N*-alkylsulfinamides. Attempts to produce this new class of compounds by more classical means have failed. Although compound **6**, when crystalline, can be stored for short periods of time at low temperatures, the compound is very labile.



In the cycle of Chart I, the only ligand common to all chiromers of the cycle is the *p*-tolyl group. Replaceable ligands are O, electron pair, NTs, NH, CH_3, NCH_3, and $TsNCH_3$. Thus the cycle is monoligostatic. Of the six chiromers, none are enantiomerically related and therefore the cycle is podal. Two of its six reactions occur with inversion, four with retention, and the cycle contains no ligand metathesis.[5a] The only stereochemical cycle that involves chiral tetrahedra that remains unexemplified is that of the aligostatic variety, in which no ligand is common to all chiromers.

Completion of a Diligostatic Cycle. Earlier[4] we reported the deimidation reaction of (−)-(*R*)-**4** to give (+)-(*R*)-**1** with nitrosyl hexafluorophosphate as reagent. The reaction proceeded with complete retention of configuration, but in yields that varied between 20 and 90%. We here report a superior method. Optically pure (−)-(*R*)-**4**, when treated with aqueous nitrous acid, gave a 99% yield of (+)-(*R*)-**1** of 99% optical purity. This result contrasts with the report[10] that treatment of dimethyl sulfoximide with nitrous acid gave dimethyl sulfone.

This new deimidation reaction, coupled with our other two new reactions, completes the following new stereochemical reaction cycle



All chiromers of this cycle contain *p*-tolyl and oxygen as common ligands, and therefore the cycle is diligostatic. The mobile ligands of the cycle are electron pair, NH, NCH_3, CH_3, and $TsNCH_3$. Like the cycle of Chart I, this cycle is podal, but for a different reason. The presence of a ligand metathesis and one inversion in this cycle becomes the equivalent of the two inversions of Chart I.

Stereochemical Reaction Cycle Involving a Sulfinamide. Chart II outlines the closing of a three-reaction stereochemical cycle again based on nucleophilic substitution reactions at chiral sulfur. This cycle involves an optically active sulfinamide as intermediate. Other investigators,[9] using other compounds, published preliminary reports on cycles similar to that of Chart II while our work was in progress. The reaction of (−)-(*S*)-**7** to give (+)-(*R*)-**1** with inversion of configuration

(8) (a) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., *J. Amer. Chem. Soc.*, 87, 1958 (1965); (b) A. Cerniani and G. Modena, *Gazz. Chim. Ital.*, 89, 843 (1959).

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

(10) J. K. Whitehead and H. R. Bentley, *J. Chem. Soc.*, 1572 (1952).

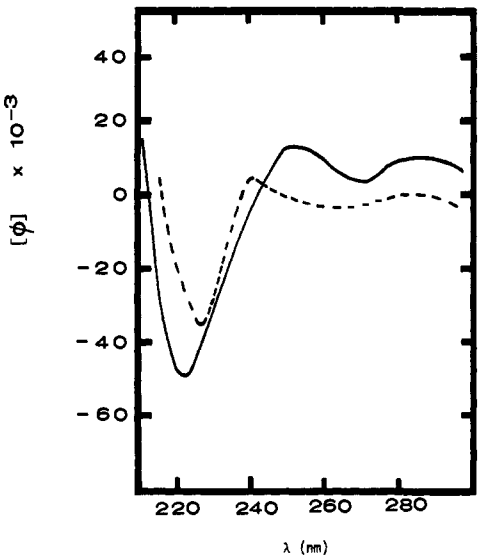
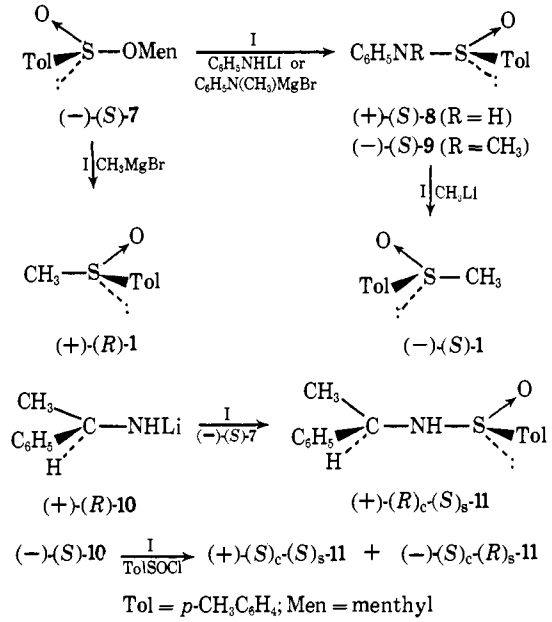


Figure 1. Optical rotatory dispersion curves in absolute methanol at 25° for (+)-(*R*)-benzyl *p*-tolyl sulfoxide (solid line, *c* 0.03) and for (+)-(*S*)-*N*-phenyl-*p*-toluenesulfinamide (broken line, *c* 0.02) taken on a Cary 60 spectrometer.

Chart II. Triligostatic Cycle



has been well documented.[8a,11] Treatment of (−)-(*S*)-**7** (diastereomerically pure) with lithium anilide or lithium *N*-methylanilide gave sulfinamides, (+)-(*S*)-**8** and (−)-(*S*)-**9**, respectively, in essentially optically pure state. These substances had to be handled at low temperature in the absence of light and oxygen to maintain their optical purity. Their racemization by a radical chain reaction is the subject of the next paper[12] in this series. The configuration assigned to (+)-(*S*)-**8** is based on comparison of the optical rotatory dispersion curve of the substance with that of (+)-(*R*)-benzyl *p*-tolyl sulfoxide whose absolute configuration[13] has been established (Figure 1). The close similarity in shapes of these curves, coupled with the similarity in structure of the compounds, provides very substantial, but not unequivocal, evidence that they possess similar configurations. Since the configuration at sulfur of ester (−)-(*S*)-**7** is known,[8a] it can be concluded that amide (+)-(*S*)-**8** was formed with inversion of configuration. Analogous reasoning is applied to formation of (−)-(*S*)-**9** from (−)-(*S*)-**7**. When treated with methyllithium, (−)-(*S*)-**9** produced sulfoxide (−)-(*S*)-**1** of 93% optical purity in 5% yield, and optically inactive bis(*p*-toluenesulfinyl)methane in 4% yield. The relationship between the configurations of (−)-(*S*)-**9** and (−)-(*S*)-**7**[11b] demonstrates that this reaction as well proceeded with inversion of configuration. This reaction completes a three-reaction, triligostatic stereochemical cycle based on **7**, **9**, and **1**, all reactions of which proceeded with a high degree of inversion of configuration, and in which each enantiomer of **1** was produced by a separate pathway (antipodal).

The nmr spectrum (see Experimental Section) of the bis(*p*-toluenesulfinyl)methane indicated a meso configuration for the substance. It probably arose by metallation of (−)-(*S*)-**1**, and the resulting salt reacted with (−)-(*S*)-**9**.[14]

A single diastereomer of sulfinamide (+)-(*R*)$_C$-(*S*)$_S$-**11** was obtained when sulfinate ester (−)-(*S*)-**7** of maximum rotation was treated with the lithium salt of α-phenylethylamine [(+)-(*R*)-**10**] of maximum rotation. Diastereomers of the same sulfinamide were produced [(+)-(*S*)$_C$-(*S*)$_S$-**11** and (−)-(*S*)$_C$-(*R*)$_S$-**11**] when (−)-(*S*)-**10** was treated with racemic *p*-toluenesulfinyl chloride, although the latter diastereomer was not obtained completely free of the former. These reactions are outlined in Chart II and are presumed to go with inversion by analogy with the formation of **8** by a similar reaction. A dramatic solvent effect on the optical rotation of (+)-(*S*)$_C$-(*S*)$_S$-**11** was observed: in chloroform, $[\alpha]^{25}D$ + 41.2, whereas in methanol, $[\alpha]^{25}D$ −64.2°. The other sulfinamides exhibited smaller changes, which are attributed to a difference in the inter- *vs.* intramolecular hydrogen bonding balance in the two media.

Stereochemical Cycle Involving an Arenesulfinamidine.[15] Sulfinimidate esters (−)-(*S*)-**12** and (−)-(*R*)-**12** as a mixture were produced by two procedures. In the first, racemic *N*-*p*-toluenesulfinimidoyl chloride[16] was esterified with menthol and pyridine. In the second (Chart III), lithium menthoxide and racemic *p*-toluenesulfenyl chloride[17] gave menthyl *p*-toluenesulfenate, which without isolation was treated directly with chloramine T to give the desired sulfinimidate ester **12** as a diastereomeric mixture in 50% overall yield. This preparation was patterned after syntheses of other sulfinimidate esters. The two diastereomers were separated by chromatography to give presumably optically pure (−)-(*S*)-**12** and (−)-(*R*)-**12** as viscous oils.

(11) (a) K. K. Andersen, *Tetrahedron Lett.*, 93 (1962); (b) H. Hope, U. de la Camp, G. D. Homer, A. W. Messing, and L. H. Sommer, *Angew. Chem., Int. Ed. Engl.*, 8, 612 (1969).

(12) R. E. Booms and D. J. Cram, *J. Amer. Chem. Soc.*, in press.

(13) C. J. M. Stirling, *J. Chem. Soc.*, 5741 (1963), coupled with the observations of ref 8a and 11.

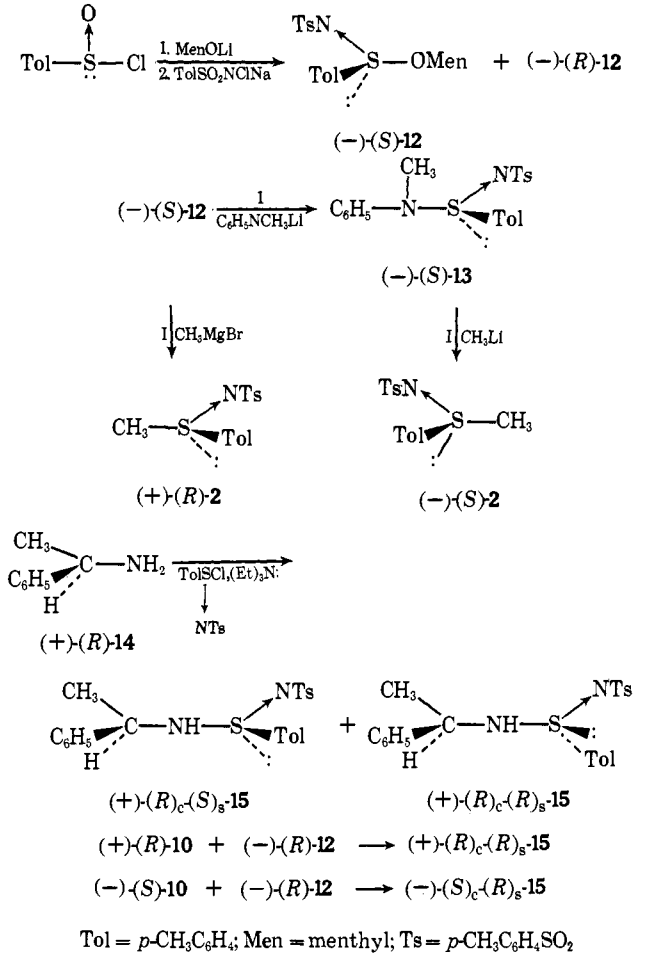
(14) Such a sequence predicts the *dl* rather than the meso configuration, since the salt is expected to react with (−)-(*S*)-**9** with inversion of configuration. Possibly the *dl*-bissulfoxide was initially formed, but either it or its salt was stereochemically labile and epimerized to give a diastereomeric mixture from which meso material crystallized. Both amides (+)-**8** and (−)-**9** are optically labile at 25° in nonpolar solvents (ref 12), and provide a possible analogy.

(15) Names used are IUPAC; see P. Verkade, *Pure Appl. Chem.*, **11**, 155 (1965), except with the most common compounds.

(16) (a) E. S. Levchenko and L. V. Seleznenko, *J. Org. Chem. USSR*, 2, 87 (1966); (b) *ibid.*, 2, 886 (1966).

(17) F. Kurzer and J. R. Powell, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 934.

Chart III. Triligostatic Cycle



Tol = p-$CH_3C_6H_4$; Men = menthyl; Ts = p-$CH_3C_6H_4SO_2$

The absolute configurations of (−)-(*S*)-**12** and (−)-(*R*)-**12** were assigned based on the very close similarity of their structures and optical rotatory dispersion curves (Figure 2) to that of (−)-(*S*)-*p*-toluenesulfinate menthyl ester ((−)-(*S*)-**7**) whose absolute configuration at sulfur is known.[8a] The fact that the curves of (−)-(*S*)-**12** and (−)-(*R*)-**12** are almost mirror images of one another (Figure 2) demonstrates that the chiral centers of the menthyl residue play very little role in determining the curve shape, and can be disregarded in these comparisons. Treatment of (−)-(*S*)-**12** with methylmagnesium bromide produced sulfimide (+)-(*R*)-**2** in 97% optical purity, although in only 5% yield (no attempt was made to maximize yield). Since the configuration of (+)-(*R*)-**2** is known[4] as well as that of the sulfinimidate ester ((−)-(*S*)-**12**), this new substitution reaction occurred with essentially complete inversion of configuration.

The three-reaction stereochemical cycle of Chart III was closed with the following transformations. Treatment of sulfinimidate ester (−)-(*S*)-**12** with lithium *N*-methylanilide gave the sulfinamidine (−)-(*S*)-**13** in 89% optical purity and 47% yield. This kind of compound has been previously prepared, but not in an optically active state.[18] When mixed with methyllithium, sulfinamidine (−)-(*S*)-**13** gave sulfimide (−)-(*S*)-**2** of about 79% optical purity in <0.5% yield. The value given for the stereospecificity of this reaction is minimal, and could not be accurately determined because of the small amount of (−)-(*S*)-**2** produced. The provisional configurational assignments to the stereomers of **12** and **13** depend on several factors: (1) the correlations of ORD curves of Figure 2; (2) analogies between the substrates and reagents of Charts II and III; (3) presumed analogies between the stereochemical courses of the reactions of Charts II and III. Comparison of the optical rotatory dispersion curves of (−)-(*S*)-**12**, (−)-(*S*)-**13**, and (−)-(*S*)-**2** were inconclusive with respect to configurational correlations.

(18) E. S. Levchenko and L. V. Seleznenko, *J. Org. Chem. USSR*, **4**, 144 (1968).

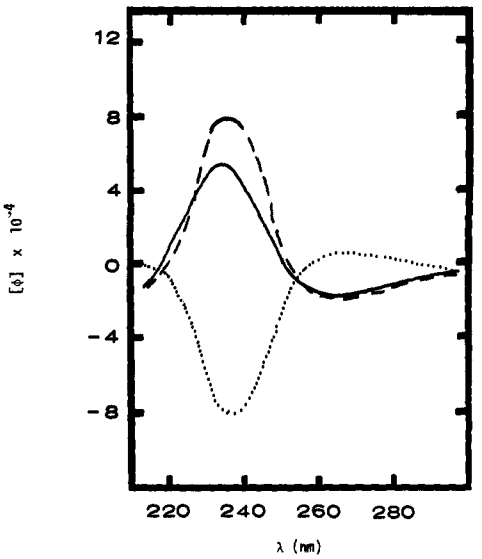


Figure 2. Optical rotatory dispersion curves in absolute methanol at 25° for sulfinamidate esters (−)-(*S*)-**12** (broken line, *c* 0.03) and (−)-(*R*)-**12** (dotted line, *c* 0.03), and for sulfinate ester (−)-(*S*)-**7** (solid line, *c* 0.05) taken on a Cary 60 spectrophotometer.

In both the conversions, (−)-(*S*)-**12** to (+)-(*R*)-**2** and (−)-(*S*)-**13** to (−)-(*S*)-**2**, sizable quantities of *p*-toluenesulfonamide and methyl *p*-tolyl sulfide were detected along with the desired sulfimide. Apparently **2** was not stable under the reaction conditions, a fact that accounts for the low yields of **2**. Nucleophilic substitution in the sulfinimidoyl series (Chart III) is probably no less favorable than in the sulfinyl series (Chart II). This conclusion is supported by the similarity in yields of the sulfinate ester to sulfinamide and sulfinimidate ester to sulfinamidine conversions.

In the cycle of Chart III, the number of chiromers exceeded the number of reactions by one (4 *vs.* 3), and therefore the cycle is antipodal. Since the cycle is triligostatic (Tol, NTs, and electron pair as common ligands) and cannot contain any ligand metathesis, the cycle must contain an odd number of reactions that went with inversion (one or three).[5] Clearly three inversions must have been involved.

Sulfinamidines (+)-$(R)_C$-$(S)_S$-**15** and (+)-$(R)_C$-$(R)_S$-**15** were produced from racemic *N*-*p*-toluenesulfonyl-*p*-toluenesulfinimidoyl chloride and optically pure α-phenylethylamine ((+)-(*R*)-**14**). The two diastereomers were easily separated by fractional crystallization. Diastereomers (+)-$(R)_C$-$(R)_S$-**15** and (−)-$(S)_C$-$(R)_S$-**15** were also prepared from lithium amides, (+)-(*R*)-**10** and (−)-(*S*)-**10**, respectively, and sulfinimidate ester (−)-(*R*)-**12**. These reactions are presumed by analogy to have occurred with inversion, and the configurations of sulfinamidines **15** are assigned accordingly (see Chart III).

Stereochemical Courses of Substitution at Sulfur. The stereochemical course of the nucleophilic substitution reactions at neutral sulfur appears to be inversion of configuration with three demonstrated exceptions. The first involved ^{18}O exchange of (+)-methyl *p*-tolyl sulfoxide with dimethyl sulfoxide at elevated temperatures.[19a] The second reported exception is the conversion of methionine sulfoxide to methionine sulfimide.[19b] The third involves the reaction of sulfoxide **1** with *N,N*-ditosylsulfodiimide in benzene.[19c,d] Under the appropriate conditions, the following reactions provide product of greater than 90% net inversion of configuration: sulfinic ester to sulfoxide;[8a,11] sulfoxide to sulfimide in pyridine[4] (but see ref 19b for a possible exception); sulfimide to sulfoxide;[4] sulfinate ester to sulfinamide;[2a,9] sulfinamide to sulfoxide[9] (present work); sulfinimidate ester to sulfimide (present work); sulfinimidate ester to sulfinamidine (present work); and sulfinamidine to sulfimide (present work).

At least two general mechanisms can be envisioned for nucleophilic substitution reactions at sulfur that occur with inversion. The first involves a trigonal bipyramid intermediate or transition state in which the incoming and leaving groups occupy the axial positions (aa scheme) and which resembles the geometry envisioned for the SN2 reaction. The second presumes a trigonal bipyramid intermediate or transition state in which the incoming and leaving groups both occupy equatorial positions (ee scheme).[4,20] If the leaving and entering groups are the most electronegative ligands of the trigonal bipyramid,[21] and if the leaving and entering groups are not tied together in a ring system,[4] the aa route is probably of lowest energy.[21] However, in the inversion reactions of Charts II and III the possibility cannot be eliminated that the entering and leaving groups are tied together in a ring system involving a metal atom and that ee routes are followed.

These reactions provide evidence that in nucleophilic substitution reactions at sulfur of the *sulfin* oxidation state, M^+C^- displaces N, O, or X (halogen), M^+N^- displaces O or X, and M^+O^- displaces X. This order resembles that observed in nucleophilic substitutions at carbonyl carbon.

Enough electrophilic substitution and desubstitution reactions at sulfur have now been studied stereochemically to provide the generality that these reactions usually proceed with retention of configuration. Examples are the oxidation of sulfimide to sulfoximide,[4] imidation of sulfoxide to sulfoximide,[4] deimidation of sulfoximide to sulfoxide[4] (present work), and demethylation–tosylation of *N*-methylsulfoximide to give *N*-tosyl-*N*-methylsulfinamide (present work). This generalization is not surprising since the electron pair of the bond involved remains with the chiral center.

Experimental Section

General. Melting points are uncorrected, and all temperatures are in degrees Celsius. Nuclear magnetic resonance spectra were obtained on Varian A-60 or HA-100 instruments on dilute solutions (5–20%) in deuteriochloroform or carbon tetrachloride using tetramethylsilane as internal standard. Infrared spectra were recorded on a Beckman IR-5 spectrophotometer. Optical rotatory dispersion spectra were obtained on a Cary 60 spectrometer in absolute methanol solution. Optical rotations were measured at 25° with a Perkin-Elmer 141 polarimeter and a 1-dm thermostated cell. Mass spectra were obtained with an AEI Model MS-9. Silica gel used for column chromatography was Baker or Merck chromatographic grade. All solvents were reagent grade unless otherwise specified. Solutions were dried with anhydrous sodium or magnesium sulfate. Thin layer chromatograph plates used were Brinkman silica gel G coated on Pyrex plates, or Baker-flex prepared silica gel 1B-F plates. The chromatograms were developed by uv light or by spraying with a 10% solution of phosphomolybdic acid in 2-propanol followed by heating on a hot plate for about 1 min. In the latter case, the tlc plate was carefully observed while being heated since changes in color hue or intensity were often characteristic of a compound. Colors varied from yellow to blue, purple, or brown. The rate of color development was also a characteristic of different compounds.

Methyl Phenyl *N*-Methylsulfoximide. A solution of 10.0 g (64.5 mmol) of methyl phenyl sulfoximide[10,22] in 100 ml of 37% formaldehyde in water and 50 ml of 98% formic acid was heated with stirring under reflux for 25 hr. The solution was cooled, made basic with solid sodium carbonate, diluted with 100 ml of water, and extracted thoroughly with methylene dichloride. The extract was dried, the solvent was evaporated *in vacuo*, and the residual oil was Kugelrohr distilled to yield 10.0 g (92%) of clear colorless oil, bp 120° (0.2 mm). The ir spectrum (neat) gave bands at (cm^{-1}) 2800, 1240, 1150, 1110, 1085, and 980. The nmr spectrum in $CDCl_3$ gave signals at τ 1.9–2.6 (m, 5 H), 6.9 (s, 3 H), 7.4 (s, 3 H). *Anal.* Calcd for $C_8H_{11}NOS$: C, 56.80; H, 6.51. Found: C, 56.67; H, 6.64.

(−)-(*R*)-Methyl *p*-Tolyl *N*-Methylsulfoximide ((−)-(*R*)-5). By the above procedure, from optically pure (−)-(*R*)-methyl *p*-tolyl sulfoximide ((−)-(*R*)-**4**),[4] $[\alpha]^{25}_{436}$ −70.6° (*c* 1.21, acetone), was obtained (90–95%) (−)-(*R*)-**5** as a hygroscopic oil after chromatography (alumina, ether–methanol), or Kugelrohr distillation, bp 135° (0.7 mm), $[\alpha]^{25}_{436}$ −367° (*c* 1.06 acetone). The nmr spectrum of the substance (CCl_4) gave the following signals: τ 2.4 (q, 4 H), 7.0 (s, 3 H), 7.46 (s, 3 H), 7.55 (s, 3 H). *Anal.* Calcd for $C_{15}H_{13}NOS$: C, 59.02; H, 7.15. Found: C, 58.77; H, 7.25.

Similarly, methyl phenyl *N*-benzylsulfoximide was prepared as an oil (70%) from methyl phenyl sulfoximide and benzaldehyde. Its nmr spectrum gave the following signals: τ 1.9–3.0 (m, 10 H), 6.0 (q, 2 H), 6.95 (s, 3 H). *Anal.* Calcd for $C_{14}H_{15}NOS$: C, 68.52; H, 6.17. Found: C, 68.63; H, 6.28.

Similarly methyl phenyl *N*-isobutyrylsulfoximide was prepared as an oil (71%) from the sulfoximide and isobutyraldehyde. Its nmr spectrum ($CDCl_3$) gave the following signals: τ 2.0–2.6 (m, 5 H), 6.90 (s, 3 H), 7.0–7.6 (m, 2 H), 7.8–8.7 (m, 1 H), 9.1 (d, 6 H, J = 7 Hz). *Anal.* Calcd for $C_{11}H_{17}NOS$: C, 62.50; H, 8.12. Found: C, 62.60; H, 8.18.

***N*-Methyl-*N*-tosylbenzenesulfinamide.** To a solution of 1.014 g (6.0 mmol) of methyl phenyl *N*-methylsulfoximide in 5 ml of dry pyridine was added 2.285 g (12.0 mmol) of tosyl chloride. The resulting mixture was stirred at room temperature protected from moisture for 2.5 hr. During this time the color of the reaction mixture went from yellow to orange to brown-black. The reaction was quenched by pouring into 30 ml of ice water and the mixture was extracted with dichloromethane. The extract was dried, and solvent was evaporated below 25° as quickly as possible. However, it was found that storage of the dichloromethane extract at less than 5° overnight had no adverse effect on the yield. The crude reaction mixture was chromatographed on 60 g of Merck silica gel using 250 ml of 10% ether–pentane, and then 20% ether–pentane (100-ml fractions taken). Solvent was removed at <45° *in vacuo*. The sulfinamide was in fractions 11–14. Recrystallization of the material from ether–pentane gave 0.65 g of crystalline sulfinamide (35% yield). An analytical sample melted at 85–86.5°. The substance gave the following ir spectrum in chloroform (cm^{-1}): 1360, 1170, 1120, 1100 (shoulder), and 1070 (shoulder). The nmr spectrum ($CDCl_3$) gave the following signals: τ 2.3 (m, 9 H), 7.41 (s, 3 H), 7.5 (s, 3 H). *Anal.* Calcd for $C_{14}H_{15}NO_3S$: C, 54.48; H, 4.88. Found: C, 54.26; H, 4.83.

(19) (a) S. Oae, M. Yokoyama, M. Kise, and N. Furukawa, *Tetrahedron Lett.*, 4131 (1968); (b) B. W. Christensen and A. Kjaer, *J. Chem. Soc. D*, 934 (1969); (c) B. W. Christensen, *ibid.*, 597 (1971); (d) F. G. Yamagishi, unpublished work.

(20) This possibility was first pointed out by P. C. Haake and F. H. Westheimer, *J. Amer. Chem. Soc.*, 83, 1102 (1961).

(21) E. L. Muetterties and R. A. Schunn, *Quart. Rev., Chem. Soc.*, **20**, 245 (1966).

(22) R. Fusco and F. Tenconi, *Chim. Ind. (Milan)*, **47**, 61 (1965); *Chem. Abstr.*, **62**, 10357*h* (1965).

(−)-(*R*)-*N*-Methyl-*N*-tosyl-*p*-toluenesulfinamide ((−)-(*R*)-6). By the above procedure, 1.00 g (5.34 mmol) of (−)-(*R*)-**5**, $[\alpha]^{25}_{436}$ −367° (*c* 1.02, acetone), was converted to (−)-(*R*)-**6** which was purified by chromatography on 150 g of Merck silica gel with 1.5 l. of 10% ether–pentane and then 2.5 l. of 20% ether–pentane as eluents (100-ml fractions were taken). Some of the end fractions contained small amounts of *N*-methyl-*p*-toluenesulfonamide (tlc analysis). The product-containing fractions (tlc) were combined, the solvent evaporated at low temperature to give 0.59 g (33%) of yellow solid, $[\alpha]^{25}_{436}$ −469° (*c* 1.13, $CHCl_3$). This material was recrystallized from ether–pentane at −20°, filtered, and held in a dry atmosphere. After three such recrystallizations the material gave mp 70.5–73°, $[\alpha]^{25}_{436}$ −533° and $[\alpha]^{25}_{D}$ −225° (*c* 1.14, $CHCl_3$). *Anal.* Calcd for $C_{15}H_{17}NO_3S_2$: C, 55.72; H, 5.30. Found: C, 55.58; H, 5.33.

(+)-(*R*)-Methyl *p*-Tolyl Sulfoxide ((+)-(*R*)-1) from (−)-(*R*)-*N*-Methyl-*N*-tosyl-*p*-toluenesulfinamide ((−)-(*R*)-6). Methylmagnesium bromide (2.58 mmol) as a 3 *M* solution in ether was added to a solution of 0.416 g (1.29 mmol) of (−)-(*R*)-**6** (mp 70.5–73°), $[\alpha]^{25}_{D}$ −225° (*c* 1.14, $CHCl_3$), in 60 ml of anhydrous ether stirred at −78° under an atmosphere of dry nitrogen over a 5 min period. A precipitate formed immediately. After 4 hr stirring at −78° the reaction mixture was quenched with saturated aqueous ammonium chloride at −78°. The mixture was extracted with water, the organic layer was dried, and the solvent was evaporated under reduced pressure. The resulting colorless oil was chromatographed on 40 g of silica gel with ether–pentane mixtures as eluent, 65 75-ml fractions being collected. Fractions 48–61 showed the presence of product by tlc (1:1 pentane–ether as eluent, uv light as developer). These fractions combined to give 76 mg (38%) of white crystalline (+)-(*R*)-**1**, $[\alpha]^{25}_{D}$ +137.7° (*c* 1.46, acetone) (lit.[8a] mp 73.0–74.5°, $[\alpha]^{25}_{D}$ +145.5° (*c* 1.1, acetone)). The nmr and ir spectra of this material were identical with those of authentic **1**. After one recrystallization from ether–pentane, the material had mp 75–76.5°. A mixture melting point with an equal amount of (−)-**1** gave mp 41–43° (lit.[8b] mp 42–43° for racemic **1**).

Deimidation of (−)-(*R*)-Methyl *p*-Tolyl Sulfoximide ((−)-(*R*)-4) to (+)-(*R*)-Methyl *p*-Tolyl Sulfoxide ((+)-(*R*)-1) with Nitrous Acid. Treatment of 0.322 g of (−)-(*R*)-**4**, $[\alpha]^{25}_{546}$ −40.3° (*c* 1.02, acetone), with a twofold excess of sodium nitrite in 25 ml of 2 *M* sulfuric acid with stirring produced a gas, presumably nitrous oxide. The solution was stirred at 25° for 1 hr, and extracted with dichloromethane. The organic layer was dried and evaporated, and the resulting oil crystallized to give 0.299 g of (+)-(*R*)-**1** (99%), $[\alpha]^{25}_{516}$ +178.8° (*c* 1.11, acetone), mp 67.5–76.5°. Recrystallization of this material from hexane gave (+)-(*R*)-**1**, $[\alpha]^{25}_{546}$ +181° (*c* 1.12, acetone), mp 74.7–76.3°, mixture melting point with an equal amount of (−)-(*S*)-**1**, 41.5–44°. An authentic sample[4] of optically pure (+)-(*R*)-**1** gave $[\alpha]^{25}_{546}$ +180.5° (*c* 0.80, acetone), mp 74.7–76.3°. Racemate gave mp 42–43°.[8b]

(+)-(*S*)-*N*-Phenyl-*p*-toluenesulfinamide ((+)-(*S*)-8). To a solution of aniline (1.86 g, 20 mmol) in 50 ml of dry ether, 12.5 ml of a 1.6 *M* solution (20 mmol) of *n*-butyllithium in hexane was added. Once the initial vigorous reaction had subsided, the resulting solution was added under dry nitrogen to a solution in 50 ml of dry ether stirred at 0° of 5.88 g (20 mmol) of menthyl *p*-toluenesulfinate, ((−)-(*S*)-**7**), $[\alpha]^{25}_{D}$ −197.3° (*c* 1.22, acetone), lit.[8a,11] $[\alpha]^{25}_{D}$ −202° (*c* 2, acetone). The reaction mixture was stirred for 1 hr at 0° in a dry nitrogen atmosphere and quenched with saturated aqueous sodium chloride. The organic phase was separated, dried, and evaporated at reduced pressure. The brown-red residue (7.6 g) was chromatographed on 150 g of silica gel with 3:1 pentane–ether solution as eluent. Eight 400-ml fractions were collected. Fractions 6–8 upon evaporation gave the desired amide, (+)-(*S*)-**8**, 1.9 g or 41%, $[\alpha]^{25}_{D}$ +216.9° (*c* 1.02, chloroform), $[\alpha]^{25}_{D}$ +180.5° (*c* 1.27, methanol). After several recrystallizations from cold ether, this amide gave a constant (to further recrystallizations) maximum rotation, $[\alpha]^{25}_{D}$ +224.0° (*c* 2.0, chloroform), $[\alpha]^{25}_{D}$ +184.3° (*c* 1.12, methanol). The melting point of (+)-**8** depends on how it is taken, since decomposition (darkening) occurs before melting. If put in a bath 10° below the melting point, (+)-**8** gives mp 126–127° dec. *Anal.* Calcd for $C_{13}H_{13}NOS$: C, 67.52; H, 5.67. Found: C, 67.69; H, 5.61.

When the above reaction was carried out at higher temperatures (25 or 35°) or with an excess of lithium anilide, or when the ester was added to the amide, totally racemic product was obtained, mp 137–138° (lit.[23] mp 137–138°).

Racemic *N*-Methyl-*N*-phenyl-*p*-toluenesulfinamide (9). A solution of 12.5 ml (0.02 mol) of *n*-butyllithium 1.6 *M* in hexane was added under nitrogen to a solution of 2.14 g (0.02 mol) of freshly distilled *N*-methylaniline in 25 ml of anhydrous ether. The solution was stirred for several minutes, and was added under pure dry nitrogen with stirring to a solution of 5.88 g (0.02 mol) of menthyl *p*-toluenesulfinate (−)-(*S*)-**7**, $[\alpha]^{25}_{D}$ −197° (*c* 1.3, acetone), or 98% optically pure, dissolved in 50 ml of dry ether held at 0°. The reaction mixture was stirred at 0° for 2 hr and then quenched with a mixture of ice water and dichloromethane. The organic phase was dried and flash evaporated without heat under vacuum to give 7.86 g of a dark yellow oil. Addition of a small amount of pentane caused the oil to crystallize when cooled. This material was chromatographed on 150 g of silica gel and eluted with 3:1 pentane–ether. Ten 200-ml fractions were collected. The solvent from each was removed under vacuum without heat. Fractions 4–6 gave amide **9** as a white solid, 3.5 g (71%), which when recrystallized from ether–pentane gave mp 73–75°; nmr ($CDCl_3$) τ 7.6 (s, 3 H), 7.19 (s, 3 H), 2.71 (s, 5 H), 2.56 (q, 4 H), J_{AB} = 8 cps. This material was completely racemic. *Anal.* Calcd for $C_{14}H_{15}NOS$: C, 68.55; H, 6.16. Found: C, 68.55; H, 6.35.

(−)-(*S*)-*N*-Methyl-*N*-phenyl-*p*-toluenesulfinamide ((−)-(*S*)-9). The above procedure was employed except that methylmagnesium bromide prepared from 0.48 g of magnesium was employed. The product obtained (3.4 g or 70%), mp 83–85°, $[\alpha]^{25}_{578}$ −109.3° (*c* 1.97, chloroform), was stored at −15°, in the dark. *Anal.* Calcd for $C_{14}H_{15}NOS$: C, 68.55; H, 6.16. Found: C, 68.61; H, 6.13.

(−)-(*S*)-Methyl *p*-Tolyl Sulfoxide ((−)-(*S*)-1) from (−)-(*S*)-*N*-Methyl-*N*-phenyl-*p*-toluenesulfinamide ((−)-(*S*)-9). Methyllithium (2.04 mmol) as a 1.79 *M* solution in hexane[24] was added to a solution of 0.500 g (2.04 mmol) of (−)-(*S*)-**9**, $[\alpha]^{25}_{578}$ −108.7° (*c* 1.04, $CHCl_3$), in dry ether stirred at −78° under an atmosphere of dry nitrogen over a 5-min period. After 2 hr stirring at −78° the reaction mixture was quenched with saturated aqueous ammonium chloride, dried and evaporated under reduced pressure, and the resulting yellow oil was chromatographed on 50 g of silica gel with ether–pentane mixtures as eluent. Thirty-five 75-ml fractions were collected. Fractions 22–30 showed the presence of product by tlc (7:3 pentane–ether as eluent, uv light as developer). These fractions were combined and sublimed at room temperature at 20–30 μ pressure. Collected was 16.2 mg (5.2% yield) of white crystalline material, $[\alpha]^{25}_{D}$ −136.1° (*c* 0.36, acetone) (lit.[8a] mp 73.0–74.5°, $[\alpha]^{25}_{D}$ +145.5° (*c* 1.1, acetone)). After one recrystallization from ether–pentane, the material had mp 76.0–76.5° (sealed tube); a mixture melting point with the enantiomeric sulfoxide showed mp 41.5–42.5° (lit.[8b] mp 42–43° for racemic **1**). When the sublimation residue from above was recrystallized from ether–pentane at low temperature, 13 mg (4.3% yield) of bis(*p*-toluenesulfinyl)methane was collected as white needles: mp 121–122°; nmr ($CDCl_2$) τ 7.57 (s, 6 H), 5.89 (q, 2 H), J_{AB} = 12 cps, 2.26–2.75 (m, 8 H). This material had no rotation in $CHCl_3$. *Anal.* Calcd for $C_{15}H_{16}O_2S_2$: C, 61.64; H, 5.52. Found: C, 61.63; H, 5.53.

(+)-(S)$_C$-(S)$_S$-*N*-(1-Phenylethyl)-*p*-toluenesulfinamide ((+)-(S)$_C$-(S)$_S$-11). Method I. By the method used for the preparation of (−)-(*S*)-**9**, amide (+)-(S)$_C$-(S)$_S$-**11** was prepared from 2.42 g (20 mmol) of α-phenylethylamine, $\alpha^{25}D_{obsd}$ −40.1° (neat, *l* = 1 dm), 12.5 ml of a 1.6 *M* solution of *n*-butyllithium (20 mmol) in hexane, and 2.94 g (10 mmol) of menthyl *p*-toluenesulfinate (−)-(*S*)-**7**, $[\alpha]^{25}_{D}$ −200.6° (*c* 1.22, $CHCl_3$). After reaction was complete it was quenched with 10% hydrochloric acid, and dichloromethane was added. The organic phase was dried and evaporated to give 4.8 g of an oily residue which was chromatographed on 120 g of silica gel and eluted with 1:3 ether–pentane solution. After five 200-ml fractions had been collected, 1:1 ether–pentane was used and five additional 200-ml fractions were collected. Fractions 6–10 gave the desired product, 1.8 g (70%), mp 116.5–119.5°, $[\alpha]^{25}_{D}$ +37.2° (*c* 2.85, $CHCl_3$).

Method II. To a solution of 1.21 g (10 mmol) of α-phenylethylamine, $\alpha^{25}D_{obsd}$ −40.1° (neat, *l* = 1 dm), and 1.01 g (10 mmol) of triethylamine in 25 ml of ether was added 1.74 g (10 mmol) of *p*-toluenesulfinyl chloride in 20 ml of ether. The mixture was stirred for 1 hour and quenched with 10% hydrochloric acid and dichloromethane. The organic layer was dried and evaporated under vacuum to give 2.8 g of a viscous gum, which was chromatographed on 120 g of silica gel and eluted with 8:1 pentane–ether. Two initial fractions of 250 ml each were collected, and the next 60

(23) D. Klamann, C. Sass, and M. Zelenka, *Chem. Ber.*, **92**, 1910 (1959).

(24) Standardized by the procedure of A. F. Clifford and R. R. Olsen, *Anal. Chem.*, **32**, 544 (1960).

fractions were 75 ml each. The diastereomeric amides were contained in the 40–60th fractions. Fraction 42, when evaporated, gave a residue, $[\alpha]^{25}D$ −40.5° (*c* 1.72, $CHCl_3$). The rotations of material from subsequent fractions changed from $[\alpha]^{25}D$ −40° to a maximum of +41.2° (*c* 0.85, $CHCl_3$) for fractions 55–58. This material was amide (+)-$(S)_C$-$(S)_S$-**11**, mp 119.5–120° (yield 5%), and its nmr spectrum in $CDCl_3$ demonstrated it to be at least 95% diastereomerically pure: τ 8.42 (d, 3 H), J_{H-H} = 7 cps, 7.70 (s, 3 H), 5.35 (m, 2 H), 2.35–2.90 (m, 9 H). *Anal.* Calcd for $C_{15}H_{17}NOS$: C, 69.48; H, 6.61. Found: C, 69.67; H, 6.56.

By subtracting the nmr spectrum of (+)-$(S)_C$-$(S)_S$-**11** from that of the diastereomeric mixture with $[\alpha]^{25}D$ −40.5°, the spectrum of (−)-$(S)_C$-$(R)_S$-**11** was obtained: ($CDCl_2$) τ 8.58 (d, 3 H), J_{H-H} 7 cps, 7.66 (s, 3 H), 5.51 (m, 2 H), 2.35–2.90 (m, 9 H).

(+)-$(R)_C$-$(S)_S$-*N*-(**1-Phenylethyl**)-*p*-**toluenesulfinamide** ((+)-$(R)_C(S)_S$-**11**) **from** (−)-(*S*)-**Menthyl** *p*-**Toluenesulfinate** ((−)-(*S*)-**7**). The same procedure described above in method I was employed. The (+)-$(R)_C$-$(S)_S$-**11**, $[\alpha]^{25}D$ +100.9° (*c* 1.36, chloroform), mp 99–100°, was obtained in 73% yield from 10 mmol of α-phenylethylamine, $\alpha^{25}D_{obsd}$ +38.2° (neat, *l* = 1 dm) and 5 mmol of (−)-(*S*)-**7** after stirring for 18 hr at 25°. *Anal.* Calcd for $C_{15}H_{17}NOS$: C, 69.48; H, 6.61. Found: C, 69.42; H, 6.52.

Menthyl *N*-*p*-**Toluenesulfonyl**-*p*-**toluenesulfinimidates** (−)-(*S*)-**12 and** (−)-(*R*)-**12**. *l*-Menthol (5.9 g or 37.8 mmol) was dissolved in 75 ml of dry tetrahydrofuran. To this solution was added 23.6 ml of a 1.6 *M* solution of *n*-butyllithium in hexane (37.8 mmol). The solution was stirred for 5 min and was then added to 6 g of *p*-toluenesulfenyl chloride[17] in 100 ml of dry tetrahydrofuran. To the light yellow solution obtained after 30 min of stirring was added 10.64 g (37.8 mmol) of commercial chloramine T (trihydrate). The mixture was refluxed for 3 hr and filtered, and the filtrate was evaporated under reduced pressure to an oily residue, 17.2 g. This material was chromatographed on 1500 g of silica gel with 9:1 pentane–ether as eluent, and 350 fractions of 150 ml each were collected. The desired product started to appear in the 240th fraction. Material of constant rotation was obtained from fractions 240–275, 2.3 g (13.6%), $[\alpha]^{25}D$ −80.68° (*c* 4.0, $CHCl_3$). The residues from fractions 276–292 (2.8 g or 16.6%) gave $[\alpha]^{25}D$ that decreased from −80 to −40°. Fractions 293–325 contained material (3.6 g or 21.3%) that also gave a constant rotation, $[\alpha]^{25}D$ −40.85° (*c* 2.25, $CHCl_3$). Neither pure diastereomers could be crystallized, and each was analyzed as a viscous oil. *Anal.* Calcd for $C_{24}H_{33}NO_3S_2$: C, 64.41; H, 7.43. Found for first diastereomer: C, 64.15; H, 7.28. Found for second diastereomer: C, 64.39; H, 7.51.

(+)-(*R*)-**Methyl** *p*-**Tolyl** *N*-*p*-**Toluenesulfonylsulfimide** ((+)-(*R*)-**2**) **from** (−)-(*S*)-**Menthyl** *N*-*p*-**Toluenesulfonyl**-*p*-**toluenesulfinimidate** ((−)-(*S*)-**12**). Methylmagnesium bromide (2.08 mmol) prepared from 51 mg of magnesium in dry ether was added to a solution of 0.93 g (2.09 mmol) of (−)-(*S*)-**12**, $[\alpha]^{25}D$ −80.68° (*c* 4.0, $CHCl_3$), in dry ether stirred at −20° under an atmosphere of dry nitrogen. After 2 hr of stirring, the reaction mixture was quenched with saturated aqueous ammonium chloride and was extracted with dichloromethane. The organic phase was dried and evaporated under reduced pressure, and the residue (0.73 g) was chromatographed on 20 g of silica gel with ether as eluent. Twenty 30-ml fractions were collected. Fractions 6–10 showed the presence of product by tlc (9:1 ether–methanol as eluent, phosphomolybdic acid as developer). The crude residue obtained (28.5 mg, 4.5% yield) had mp 123–125°, $[\alpha]^{25}_{546}$ −309.8° (*c* 1.1, acetone) (lit.[25] $[\alpha]^{25}_{546}$ −320.1° (*c* 1.682, acetone), mp 125–125.5°).

(−)-(*S*)-*N*-**Methyl**-*N*-**phenyl**-*N'*-*p*-**toluenesulfonyl**-*p*-**toluenesulfinamidine** ((−)-(*S*)-**13**) **from** (−)-(*S*)-**Menthyl** *N*-*p*-**Toluenesulfonyl**-*p*-**toluenesulfinimidate** ((−)-(*S*)-**12**). A solution of 0.376 g (3.51 mmol) of *N*-methylaniline in 20 ml of dry ether was treated with 2.20 ml (3.51 mmol) of a 1.6 *M* solution of *n*-butyllithium in hexane. The resulting solution was added to a stirred solution of 1.57 g (3.51 mmol) of (−)-(*S*)-**12**, $[\alpha]^{25}D$ −79.8° (*c* 0.62, $CHCl_3$), at −25° under an atmosphere of dry nitrogen over a 30 min period. The mixture was stirred for 2 hr at −25°, quenched with saturated aqueous ammonium chloride, dried, evaporated at reduced pressure, and chromatographed on 200 g of silica gel. The chromatogram was completed as quickly as possible, since the product was observed to decompose on silica gel. Starting material and menthol were first eluted with 4:1 pentane–ether and then the product was removed with 10:90:1 dichloromethane–pentane–ethanol. Seventy-five 100-ml fractions were collected. The desired (−)-(*S*)-**13** was obtained from fractions 72–75 as a yellow oil, 657 mg (47% yield) being collected, $[\alpha]^{25}D$ −128.1° (*c* 1.57, $CHCl_3$). After one recrystallization from absolute ethanol, 517-mg beige plates were obtained, mp 124–126° (decomposition in sealed tube), $[\alpha]^{25}D$ −144.5° (*c* 0.77, $CHCl_3$); nmr ($CDCl_3$) τ 7.68 s (3 H), 7.59 s (3 H), 7.2 s (3 H), and 2.2–3.05 m (13 H). On heating the product to obtain the melting point, it was observed that the sample turned dark brown 10–15° below the observed melting point. *Anal.* Calcd for $C_{21}H_{22}N_2O_2S_2$: C, 63.31; H, 5.57. Found: C, 63.42; H, 5.71.

The maximum rotation of (−)-(*S*)-**13** was determined by preparing (+)-(*R*)-**13** in a similar manner. The product obtained was fractionally recrystallized five times from absolute ethanol to a constant value of $[\alpha]^{25}D$ +143.7° (*c* 0.70, chloroform), mp 122.5–124.5° (decomposition in sealed tube). Therefore, the (−)-(*S*)-**13** obtained, $[\alpha]^{25}D$ −144.5°, approaches maximum rotation.

(−)-(*S*)-**Methyl** *p*-**Tolyl** *N*-*p*-**Toluenesulfonylsulfimide** ((−)-(*S*)-**2**) **from** (−)-(*S*)-*N*-**Methyl**-*N*-**phenyl**-*N'*-*p*-**toluenesulfonyl**-*p*-**toluenesulfinamidine** ((−)-(*S*)-**13**). Methyllithium (1.07 mmol) as a 1.79 *M* solution in hexane[24] was added to a solution of 0.427 g (1.07 mmol) of (−)-(*S*)-**13**, $[\alpha]^{25}D$ −144.5° (*c* 0.77, $CHCl_3$), in 50 ml of freshly distilled tetrahydrofuran stirred at −78° under an atmosphere of dry nitrogen over a 5 min period. The mixture was stirred 2 hr at −78°, quenched with saturated aqueous ammonium chloride and immediately filtered through anhydrous sodium sulfate. The resulting yellow solution was evaporated under reduced pressure and chromatographed on 125 g of silica gel using 90:10:3 pentane–dichloromethane–isopropyl alcohol as eluent. Thirty-five 50-ml fractions were collected. Fractions 26–33 showed the presence of product by tlc (97:3 dichloromethane–isopropyl alcohol as eluent, uv light as developer), as well as another material with a very similar R_f value. Fractions 26–33 were combined and the desired product collected by preparative tlc (1-mm plate eluted twice with 97:3 dichloromethane–isopropyl alcohol and developed with uv light). The resultant product, obtained as an oil, weighed ~0.5 mg (<0.5%), $[\alpha]^{25}_{546}$ −252° (*c* 0.0448, acetone) (lit.[25] $[\alpha]^{25}_{546}$ −320.0° (*c* 1.682, acetone)).

A similar experiment using a larger amount of racemic **13** yielded product that analyzed correctly by ir and nmr.

N-(α-**Phenylethyl**)-*N'*-*p*-**toluenesulfonyl**-*p*-**toluenesulfinamidine** ((+)-$(R)_C$-$(S)_S$-**15 and** (+)-$(R)_C$-$(R)_S$-**15**). A solution of 4.84 g (40 mmol) of α-phenylethylamine, $\alpha^{25}D_{obsd}$ +38.2° (neat, *l* = 1 dm), and 5 g of triethylamine in 20 ml of dichloromethane was added to 13.1 g (40 mmol) of *N*-*p*-toluenesulfonyl-*p*-toluenesulfinimidoyl chloride dissolved in 50 ml of dichloromethane. A very exothermic reaction ensued, and the mixture turned dark gray-brown in color. After 1 hr of stirring the mixture was quenched with 10% hydrochloric acid. The organic phase was separated, dried, and evaporated. The dark viscous residue (16 g) was crystallized from methanol. After two recrystallizations, a white fluffy solid (2.78 g or 35%) was obtained, mp 204–206°, $[\alpha]^{25}D$ +22.53° (*c* 0.75, tetrahydrofuran). *Anal.* Calcd for $C_{22}H_{24}N_2O_2S_2$: C, 64.06; H, 5.87. Found: C, 63.78; H, 5.94.

From the mother liquor, after three recrystallizations from ether, was obtained the other diastereomer as 1.62 g (20%) of a white fluffy solid, mp 166.5–167.2°, $[\alpha]^{25}D$ +126.4° (*c* 1.91, tetrahydrofuran). *Anal.* Calcd for $C_{22}H_{24}N_2O_2S_2$: C, 64.06; H, 5.87. Found: C, 64.10; H, 5.86.

N-(α-**Phenylethyl**)-*N'*-*p*-**toluenesulfonyl**-*p*-**toluenesulfinamidine** ((+)-$(R)_C$-$(R)_S$-**15 and** (−)-$(S)_C$-$(R)_S$-**15**) **from** (−)-(*R*)-**Menthyl** *N*-*p*-**Toluenesulfonyl**-*p*-**toluenesulfinimidate** ((−)-(*R*)-**12**). A solution of 0.35 g (2.9 mmol) of α-phenylethylamine, $\alpha^{25}D_{obsd}$ +38.2° (neat, *l* = 1 dm), in 25 ml of dry tetrahydrofuran was treated with 1.81 ml of a 1.6 *M* solution (2.9 mmol) of *n*-butyllithium in hexane. The resulting solution was added to a stirred solution of 0.13 g (0.29 mmol) of (−)-(*R*)-menthyl *N*-*p*-toluenesulfonyl-*p*-toluenesulfinimidate, $[\alpha]^{25}D$ −40.85° (*c* 2.25, $CHCl_3$). The mixture was heated for 1 hr at 40–50°, the solvent was evaporated, and the residue was chromatographed on 75 g of silica gel with 5% ether–dichloromethane as developer. Ten 100-ml fractions were collected. The desired (+)-$(R)_C$-$(R)_S$-**15** was produced upon evaporation of fractions 6–8, yield 66.3 mg (56%), $[\alpha]^{25}D$ +133.1° (*c* 0.54, tetrahydrofuran). The ir and ORD spectra of this material were identical with those of the previously obtained (+)-$(R)_C$-$(R)_S$-**15** (see above).

The same procedure was applied to the preparation of the diastereomeric amide, (−)-$(S)_C$-$(R)_S$-**15**, except that α-phenylethylamine, $\alpha^{25}D_{obsd}$ −40.5° (neat, *l* = 1 dm), was employed. The product (50%), mp 201–202°, $[\alpha]^{25}D$ −22.15° (*c* 0.65, tetrahydro-

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furan), had an ORD spectrum enantiomeric to that of the previously prepared sample, (+)-(*R*)c-(*S*)s-**15**, $[\alpha]^{25}D$ +22.53° (*c* 0.75, tetrahydrofuran) (see above). *Anal.* Calcd for $C_{22}H_{24}N_2O_2S_2$: C, 64.06; H, 5.87. Found: C, 63.92; H, 5.74.

N-*p*-**Toluenesulfonyl**-*p*-**toluenesulfinimidoyl Chloride.** This compound was obtained (90%),[16] mp 141.5–142.5°, from dichloromethane–ether. *Anal.* Calcd for $C_{14}H_{14}ClNO_2S_2$: C, 51.29; H, 4.30. Found: C, 51.21; H, 4.25.

Stereoselective Synthesis of Hydroazulenes from Cyclodecadienols

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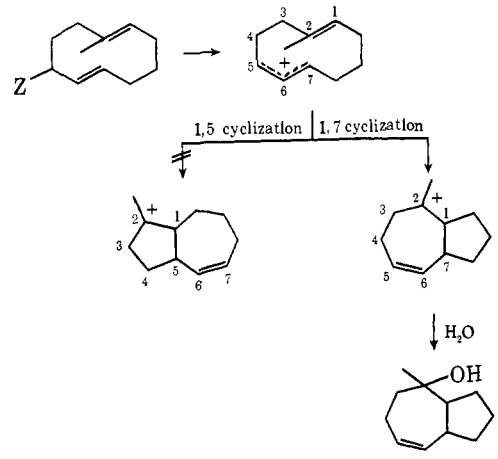
Abstract: The feasibility of a new synthetic route to hydroazulenes *via* transannular cyclization of cyclodecadienol derivatives was demonstrated with four systems. In each case an incipient allylic cation was generated through solvolysis of the *p*-nitrobenzoate derivative or the alcohol itself. The first system, 8-methyl-*trans,trans*-2,7-cyclodecadien-1-yl *p*-nitrobenzoate (**3a**), afforded 2-*anti*-methyl-*trans*-bicyclo[5.3.0]dec-5-en-2-ol (**4a**) in 80% yield upon solvolysis in buffered aqueous dioxane. The 4-methyl homolog of the aforementioned *p*-nitrobenzoate yielded 2-*anti*,8-*anti*-dimethyl-*trans*-bicyclo[5.3.0]dec-5-en-2-ol (**4b**) in nearly 60% yield upon similar treatment. An allylic isomer of cyclodecadienyl *p*-nitrobenzoate **3a**, namely 6-methyl-*cis,trans*-2,6-cyclodecadien-1-yl *p*-nitrobenzoate (**16**), gave rise to the previously obtained hydroazulenol **4a** in over 40% yield. Finally, the tertiary alcohol 1,6-dimethyl-*cis,trans*-2,6-cyclodecadien-1-ol, a homolog of alcohol **15**, afforded 2,7-*anti*-dimethyl-*trans*-bicyclo[5.3.0]dec-5-en-2-yl acetate (**19**) in over 70% yield upon acetolysis at room temperature. The structures of the hydroazulenols were deduced from spectral data and by comparison with authentic samples of the dihydro derivatives.

In the 35 years since Pfau and Plattner's brilliant work on the structure of azulene[2] a considerable number of natural products with the parent hydroazulene ring system have been identified as constituents of diverse plant extracts.[3] Progress in stereoselective synthetic approaches to this rapidly growing family of sesquiterpenes has by no means kept pace with the structure work. Thus, but a small handful of even the simpler hydroazulenes have been synthesized to date.[4,5] In this report we describe initial work on a new stereoselective route to substituted hydroazulenols which should find applications in natural product synthesis.[6]

Cyclodecenyl cations have been implicated in hydroazulene biosynthesis[7] and this concept of synthesis has been applied *in vitro* with cyclodecadienes[8] and related epoxides.[9] Our plan for cyclodecadiene cyclization envisioned the selective electrophilic activation of a specific double bond of the appropriate precursor through solvolysis of an allylic alcohol derivative (Scheme I).

Scheme I



A priori, two possible pathways, namely 1,5 and 1,7 cyclization, might be considered for the presumed allyl cation thereby generated. However, as will be shown, an analysis of the controlling geometric factors clearly indicates that 1,7 cyclization should be the favored reaction course.

The starting material for our initial studies was prepared from the unsaturated keto mesylate **1a**[10] as outlined in Chart I. Accordingly, hydroboration followed by base treatment led directly to the *trans,trans*-cyclodecadienol **2a** in 60% yield.[11] The *p*-nitrobenzoate

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