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4-pentenal, dihydropyran, and possibly 2-pentenal were also observed.7

Conclusions

From this and previous work, 1-18 the reactions of O(³P) atoms with simple cyclic olefins and with the aromatic hydrocarbons can be satisfactorily explained in terms of a general mechanism, such as shown above. The difference in products between the cyclic olefins and aromatic hydrocarbons arises because of the difference in the rate constants for reaction of $O(^{3}P)$ atoms with the reactant and with the reaction products. Thus, the reaction of O(³P) atoms with the aromatic hydrocarbons is slow²³ and produces largely highly reactive unsaturated products (the rate constants for reaction of $O(^{3}P)$ atoms with o-cresol have, however, been shown to be only approximately eight times faster than with toluene at room temperature).²⁷ However, for the simple olefins, the initial reaction is very fast and forms largely saturated, and hence unreactive, products. Thus, the extent of secondary reactions is much smaller in these cases, as observed.

Note Added in Proof. J. J. Havel and K. M. Chan, J. Am. Chem. Soc., 97, 5800 (1975), have recently investigated the products and mechanisms of the reactions of $O(^{3}P)$ atoms with cyclic and bicyclic hydrocarbons, including cyclohexene. The products observed for cyclohexene are analogous to those observed in the present work for 1-methylcyclohexene.

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Chiral Nuclear Magnetic Resonance Solvating Agents. Resolution, Determination of Enantiomeric Purity, and Assignment of Absolute Configuration of Cyclic and Acyclic Sulfinate Esters

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Abstract: Incomplete but stereoselective reaction of (S)-2-methyl-1-butylmagnesium chloride or (S)-2-phenyl-1-butylmagnesium chloride with racemic alkyl p-tolylsulfinates or sultines, namely 3H-2,1-benzoxathiole 1-oxide (11) and 3H-2,1-benzoxathiaine 1-oxide (12), affords, upon recovery of unreacted material, sulfinates or sultines enriched (8-64% ee) in the Senantiomers. In the presence of resolved 1-phenyl-2,2,2-trifluoroethanol, 1-(1-naphthyl)-2,2,2-trifluoroethanol, or 1-phenyl-2,2,3,3,4,4,4-heptafluoro-1-butanol, the enantiomers of a variety of alkyl alkyl- or arylsulfinates have nonidentical ¹H NMR spectra, allowing for direct determination of enantiomeric purity and, on the basis of the relative field positions of the enantiomeric resonances, correlation of absolute configuration. Specific solvation models are proposed to account for the origin and sense of the spectral nonequivalence. Similar ¹H NMR studies of 11 and 12 in the presence of chiral 1-(10-methyl-9anthryl)-2,2,2-trifluoroethanol provide for determination of enantiomeric purity. The solvation model for sulfinates is employed to assign absolute configurations to sultines 11 and 12, based on the relative field positions of the enantiomeric resonances. The validity of the configurational assignment for 11 is established rigorously by stereospecific chemical correlation to (-)-menthyl (-)-(S)-p-tolylsulfinate, while supporting evidence is given for that of 12. CD spectra of 11 and 12 are reported.

The recently reported² ¹H NMR method for assignment of absolute configuration to sulfoxides using chiral 1-aryl-2,2,2-trifluoroethanols (1) is based on a postulated twopoint interaction stabilizing short-lived diastereomeric solvates 2 and 3. The primary interaction is a hydrogen bond from the acidic hydroxyl of 1 to the basic sulfinyl oxygen, while the secondary stabilizing force consists of the dipolar attraction of the electron-poor carbinyl proton to the elec-



tron pair on sulfur. It is proposed that this interaction be termed *carbinyl hydrogen bonding*. The observed spectral nonequivalence arises from differential shielding of enantiomeric protons by the aromatic ring of the fluoro alcohol in solvates 2 and 3.



Sulfinate esters (4), similarly chiral by virtue of asymmetry at sulfur, provide compelling subjects for comparison to sulfoxides, since each sulfinate contains two possible basic sites for the secondary interaction with the carbinyl proton of the fluoro alcohol. This interaction may occur either at the electron pair on sulfur, leading to diastereomeric solvates 5 and 6, or at the electron pairs on the alkoxyl oxygen, leading to diastereomeric solvates 7 and 8. These alterna-



tives are distinguishable, since they lead to opposite predictions for the relative field positions (senses of nonequiva-

lence³) of the resonances of the enantiomers, dependent on which groups fall into the shielding region of the fluoro alcohol's aromatic ring. Although solvates 5 and 6 are essentially those previously advocated for sulfoxides, the analogy is weakened by the fact that the sulfur in sulfinates is expected to be considerably less basic than that in the analogous sulfoxides. Hence, the alternate solvates 7 and 8 are reasonable a priori.

We herein report the results of ¹H NMR studies of optically active sulfinates and sultines in the presence of chiral fluoro alcohols. This technique provides for the direct determination of enantiomeric purity and of absolute configuration via a diastereomeric solvate model proposed for correlation of absolute configuration with observed senses of nonequivalence.

Resolution of Sulfinates and Sultines. Several alkyl methylsulfinates chiral only at sulfur have been available for some time via the stereoselective β -cyclodextrin inclusion method of Mikolajczyk and Drabowicz.⁴ Several examples of the analogous esters of arylsulfinic acids have been obtained in low optical yields by transesterification of diastereomeric sulfinates⁵ or by asymmetric oxidation of sulfinates,^{6a,b} the latter method being applicable also to the analogous preparation of optically active thiolsulfinates.^{6c} Nevertheless, sulfinates were not readily and generally available in significant optical yields until Mikolajczyk and Drabowicz' recently reported asymmetric synthesis.7 This route employs the low-temperature reaction of sulfinyl chlorides with alcohols in the presence of chiral tertiary amines. However, this technique cannot be applied to the resolution of cyclic sulfinates. For that reason, we include here a method of kinetic resolution of sulfinates which, although less convenient than that reported by Mikolajczyk and Drabowicz,⁷ is unique in its applicability to both acyclic and cyclic sulfinates (the latter are hereafter referred to as sultines) as well as, potentially, to a variety of other types of molecules.

In the absence of "handles" (i.e., -CO₂H, -NH₂, -OH) for resolution via separation of diastereomeric derivatives, and aside from the possibility that one enantiomer might be preferentially included in β -cyclodextrin,⁴ the only resolution method of sufficient scope appeared to be one in which one enantiomer of the sulfinate or sultine is selectively consumed by a chiral reagent or enzyme system. In view of the known reaction of sulfinates with Grignard reagents to form sulfoxides (Andersen synthesis),⁸ we considered that the low-temperature reaction of a racemic sulfinate or sultine with a limited amount of a chiral Grignard reagent might provide a useful kinetic resolution. Encouraged by our initial experiments with the Grignard reagent derived from (S)-(+)-1-chloro-2-methylbutane (9) we also prepared the Grignard reagent derived from (S)-(+)-1-chloro-2-phenylbutane (10) and were able to obtain sulfinates and sultines in the optical yields shown in Table I via the reaction described in Scheme I. To our knowledge, 3H-2,1-benzoxathiole 1-oxide (11) and 3H,6H-2,1-benzoxathiaine 1oxide (12) are the first examples of optically active sultines. Furthermore, the reaction appears to be stereochemically consistent since, in all cases investigated, the Grignard reagent of S configuration reacts more rapidly with the sulfinate or sultine having the R configuration. Separation of the partially resolved sulfinate or sultine from the more polar sulfoxide product (13 or 14) is readily accomplished by chromatography on silica gel. The resultant products 13 and 14 were characterized by NMR and elemental analysis.

Results of ¹H NMR in Chiral Fluoro Alcohols. The data obtained from ¹H NMR of acyclic sulfinates in the presence of chiral fluoro alcohols **1a**, **lb**, and 1-phenyl-2,2,3,3,4,4,4-heptafluoro-1-butanol (**15**) (Table II), and for

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Table I. Kinetic Resolutions of Sulfinates and Sultines

Resolving agent ^{a, b}		$[\alpha]^{24\pm 1}$ D	% enantiomeric purity		Absolute	67.	% vield of
	Substrate	recovered substrate	By NMR ^c	Calcd	configuration	recovery	13 or 14
9	4d	$-25.4 \pm 0.6^{\circ}$ (c 4.52, EtOH)	12	11.6d	Sd	52.8	42.4
9	4e	$-29.6 \pm 0.1^{\circ}$ (c 5.06, EtOH)	15	14.1d	Sd	56.5	43.2
9	4g	$-44.8 \pm 0.3^{\circ}$ (c 9.19, EtOH)	23	24.1e	Se	48.1	53.0
9	11	$+18.8 \pm 0.3^{\circ}$ (c 7.18, CHCl ₂)	8		S	49.0	36.8
9	12	$+7.3 \pm 0.4^{\circ}$ (c 5.01, CHCl.)	9		S	41.7	32.9
10	4 f	$-104.3 \pm 0.4^{\circ}$ (c 5.01, EtOH)	46	45.5 <i>f</i>	Sf	55.7	45.5
10	4h	$-83.8 \pm 0.5^{\circ}$ (c 5.04, EtOH)	64	63.8e	Se	48.6	46.3
10	11	$+94.0 \pm 0.4^{\circ}$ (c 7.00, CHCl.)	40	38.78	S	43.3	50.3
10	12	$+32.4 \pm 0.4^{\circ}$ (c 5.05, CHCl ₃)	38		S	38.2	48.2

^aGrignard reagent 8 contained 15% of the 3-methyl-1-butyl isomer, for which no correction has been made. ^bGrignard reagent 9 was 92% optically pure; the data connected with 9 have been corrected to 100% optical purity. ^cMeasured directly from enantiomeric peak heights. See Tables II and III. ^dBased on maximum rotations and absolute configurations derived from ref 7. ^eBased on conversion to (R)-(+)-ethyl *p*-tolylsulfoxide. The maximum rotation of $[\alpha]^{25}D + 203.2^{\circ}$ (c 0.6, acetone) has been reported by A. C. Cope and E. A. Caress, J. Am. Chem. Soc., 88, 1711 (1966). ^fBased on conversion to (R)-(+)-methyl *p*-tolysulfoxide. The maximum rotation of $[\alpha] D + 156^{\circ}$ (EtOH) has been reported by K. Mislow, M. Axelrod, D. R. Rayner, H. Gotthardt, L. M. Cogne, and G. S. Hammond, J. Am. Chem. Soc., 87, 4958 (1965). ^gBased on conversion to (R)-(+)-19. Our maximum observed rotation for (S)-(-)-19 is $[\alpha]^{26}D + 113 \pm 1^{\circ}$ (c 2.99, EtOH).

Table II. ¹H NMR Spectral Nonequivalence ($\Delta\delta$) of Sulfinates in Chiral Fluoro Alcohols^a

Fluoro alcohol	Enriched sulfinate	Sample composition ^b	R'c	$\Delta\delta$, d Hz (sense of nonequivalence)					
				CH ₃ of R group	α	β	γ	δ	
(S)-(+)-1a	(S)-(-)-4a	4.0:1.0:0	-CH ^Q CH ₃ ^β CH ₃ ^γ	4.8 (L)	6.1 (H)	4.6 (H)	0		
(R)-(-)-15	(S) - (-) - 4a	4.4:1.0:0	-CH ^a CH ^β CH ^γ	7.3 (H)	12.3 (L)	5.9 (L)	1.7 (L)		
(R)-(-)-1b	(S) - (-) - 4a	4.2:1.0:3.4	-CH ^a CH ^b CH ^b	10.7 (H)	21.3 (L)	13.8 (L)	5.1 (L)		
(S)-(+)-1a	(R)-(+)-4b	4.0:1.0:0	$-C(CH_{\alpha}^{\alpha})$	6.5 (H)	3.1 (L)				
(<i>S</i>)-(+)-15	(<i>R</i>)-(+)-4b	4.0:1.0:0	$-C(CH^{\alpha})$	11.5 (H)	4.1 (L)				
(S)-(+)-la	(R)-(+)-4c	4.2:1.0:0	-CH ^a CH ^g CH ^y CH ⁵	3.8 (H)	f	f	f	f	
(S)-(+)-1b	(S)-(-)-4d	4.0:1.0:11	$-CH^{\alpha}$	~1.8 (L)	2.9 (H)	5	,	5	
(S)-(+)-1b	(S) - (-) - 4e	4.0:1.0:11	-CH ^A CH ^B	4.0 (L)	f	6.7 (H)			
(S)-(+)-1b	(S)-(-)-4f	4.0:1.0:11	−CH ^ϕ CH ^β CHγ	8.2 (L)	15.7 (H)	8.6 (H)	22.4 (H)		
(S)-(+)-1b	(S) - (-) - 4g	4.0:1.0:11	-CHαH ^β C(CHΥ),	4.1 (L)	4.3 (H)	13.2 (H)	4.2 (H)		
(S)-(+)-1b	(S)-(-)-4h	4.0:1.0:11	$-C(CH_{3}^{\alpha})_{3}$	14.7 (L)s	20.5 (H)s		- <>		

^{*a*} Unless otherwise specified, ¹H NMR spectra were measured at 220 MHz, 28 °C. ^{*b*} Sample composition is given as the mole ratio of fluoro alcohol:sulfinate:carbon tetrachloride. Samples containing no carbon tetrachloride were run neat in thick-walled tubes. ^{*c*} For R' = isopropyl, H^β and H^γ refers to the protons of the lower field and higher field, respectively, of the two isopropyl doublets. For R' = neopentyl, H^α and H^β refer to the lower field and higher field protons, respectively, or the AB quartet. ^{*d*} $\Delta \delta$ is the enantiomeric chemical shift difference. ^{*e*} H and I refer to the high field and low field senses of nonequivalence. ^{*f*} Unresolved multiplets. ^{*g*} Values at 220 MHz, 28°C, calculated from observed spectrum at 100 MHz, 28°C.

Scheme I



sultines 11 and 12 in the presence of fluoro alcohols 1c and 1d (Table III) demonstrate the value of this technique for determination of enantiomeric purity (as shown in Table I) of sulfinates and sultines chiral only at sulfur. The only prior examples of direct determinations of sulfinate enantiomeric purity were those of Mikolajczyk and Drabowicz. These authors employed⁷ a chiral lanthanide shift reagent, tris[3-(trifluoromethylhydroxymethylene)-d-camphorato]europium(III), as the chiral medium for separation of the enantiomeric resonances of sulfinates 4b and 4d, as well as neopentyl methylsulfinate, methyl n-propylsulfinate, and methyl phenylsulfinate. No data regarding magnitudes or senses of nonequivalence were published. Our attempts to determine the enantiomeric purity of sultine 12 using a similar chiral shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-d-camphorato]europium(III), were unsatisfactory. At the ratio of shift reagent:sultine required in order to produce nonequivalence (0.6:1.0 mole ratio), the AB O-methylene protons of the enantiomers were separated 3.6 and 2.4 Hz at 100 MHz and 28°°C. However, the lines were broadened so extensively as to overlap appreciably. By contrast, the enantiomeric resonances of all four methylene protons of 12 are cleanly separated by fluoro alcohols 1c and 1d at 100 Hz and 28 °C.

In our system, the data show a well-defined relationship between absolute configuration and sense of nonequivalence. For all the investigated S-enriched acyclic sulfinates,

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Table III. ¹H NMR Spectral Nonequivalence $(\Delta \delta)$ of Sultines in Chiral Fluoro Alcohols^{*a*}, ^{*b*}



^a Nonequivalence is given for 220 MHz, 28 °C. The data for 12 using fluoro alcohol 1c is calculated from the observed nonequivalence at 100 MHz, 28 °C. Samples were composed of 4.0:1.0: ca. 35 mole ratio of fluoro alcohol:sultine:chloroform-d (in the case of 1c) or carbon tetrachloride (in the case of 1d). ^b The ¹H NMR chemical shifts (ppm in CDCl₃) of the sultine ring protons of 11 are as follows: H^{α} , 5.51; H^{β} , 5.92. For 12: H^{γ} , 3.50; H^{δ} , 4.31; H^{α} , 4.88; H^{β} , 5.23. The assignments are based on the known propensity of protons cis to a sulfinyl oxygen to be deshielded, as described in D. C. Dittmer, R. S. Henion, and N. Takashima, J. Org. Chem., 34, 1310 (1969), and references cited therein. Full ¹H NMR spectral data appear in the Experimental Section. ^cFluoro alcohol 1c, $[\alpha]^{24}$ D -24.0° (c 3.25, CHCl₃), was 82% optically pure. Data are corrected to 100% optical purity. d Fluoro alcohol 1d, [a] 26D +16 $\pm 1^{\circ}$ (c 6.20, CHCl₃), is estimated to be >95% optically pure. No corrections are made on the data using 1d. $e_{\Delta\delta}$ refers to the enantiomeric chemical shift difference. f H and L refer to the high field and low field senses of nonequivalence.

S-(+) fluoro alcohols cause the protons in the sulfinyl R group to have a low field sense of nonequivalence, whereas all protons in the alkoxyl R' group exhibit a high field sense of nonequivalence. These results are consistent with solvate structures 7 and 8 but not 5 and 6. Thus, it may be concluded that the dominant site of the secondary interaction in acyclic sulfinates is the alkoxyl oxygen.

Structures 7 and 8 show the alkoxyl group in a conformation which places R' well away from the R substituent. Such a conformation would appear, as seen from structure 16, to minimize the steric interactions between R and R',



and is in accord with the consistently observed opposite senses of nonequivalence for these groups. The actual extent of population of such a conformation would be expected to vary with R and R'.

Sultines 11 and 12 represent a further test for the present model. In 12, by virtue of the constraints of the six-membered ring, the alkoxyl methylene and the sulfinyl methylene bear a nearly cis relationship to each other about the S-O bond, ruling out the conformation represented by 16. Hence, the two methylene groups should not show opposite senses of nonequivalence in any solvate in which the secondary interaction is solely at the alkoxyl oxygen.

With the aid of Dreiding models, the four possible solvates (varying solute absolute configuration and site of secondary interaction) for the interaction of (S)-(+)-1c [or (S)-(+)-1d] with 12 can be illustrated by Figures la-d. Examination of the models reveals that the geometry of the



1a) <u>5,5</u>



<u>5,5</u>

1b)





1d) <u>S</u>,R

Figure 1. Diastereometic solvate models for sultine 12 in fluoro alcohol 1c or 1d. For simplicity, the substituted anthryl group in the fluoro alcohol is represented by a phenyl group. (a) S,S solvate with secondary interaction at alkoxyl oxygen. (b) S,S solvate with secondary interaction at sulfur. (c) S,R solvate with secondary interaction at alkoxyl oxygen. (d) S,R solvate with secondary interaction at sulfur.

six-membered ring⁹ requires a somewhat different pattern of shielding and deshielding than would be predicted from a naive application of the generalization represented by the solvates, 7 and 8, for acyclic sulfinates. For the S,S solvate in which the secondary interaction is at the alkoxyl oxygen (Figure 1a), the aryl group of the alcohol is not expected to shield any groups in sultine 12 appreciably. However, for the S,S solvate in which the secondary interaction is at sulfur (Figure 1b), the S-methylene protons are expected to be substantially shielded. Similarly, for the S,R solvate in which secondary interaction occurs at the alkoxyl oxygen (Figure 1c), the O-methylene protons are expected to be shielded, while, for the S, R solvate in which the secondary interaction is at sulfur (Figure 1d), the O-methylene is expected to be somewhat shielded. Thus, if the secondary interaction were solely at the alkoxyl oxygen, the resonances of the S-methylene protons of both enantiomers of 12 should occur at essentially the same field position, while the



O-methylene resonances of the R enantiomer of 12 should occur at a higher field position than those of (S)-12. Similarly, if the secondary interaction were solely at sulfur, the S-methylene resonances of (S)-12 should occur at higher field than those of (R)-12 while the O-methylene resonances of (R)-12 should occur at higher field than those of (S)-12. Consequently, for sultine 12, the two sites for secondary interaction lead to complementary rather than contradictory predictions with respect to the senses of nonequivalence expected for a given absolute configuration. In fact, the data in Table III for sultine 12 are best explained by an averaged system in which both types of secondary interactions occur.¹⁰ Accordingly, there is no conflict in assigning the S configuration to sultine (+)-12, on the basis of its observed high field sense of S-methylene nonequivalence and low field sense of O-methylene nonequivalence in (S)-(+)-1d [senses are just the opposite, as expected, in (R)-(-)-1c], as shown in Table III.

Solvate models for five-membered sultine 11 are similar to those of its six-membered homologue (12) and it is also assigned the S-(+) configuration on the basis of the ¹H NMR data in Table III.

Independent Assignment of Sultine Absolute Configurations. In order to confirm the assignments of sultine absolute configurations made possible via ¹H NMR through the use of chiral fluoro alcohols, an independent establishment of at least one sultine configuration was desirable. In the case of acyclic sulfinates, absolute configuration is established by conversion, using a Grignard reagent, to a sulfoxide of known configuration.^{4,7} Although not previously reported, the reaction of sultines 11 and 12 with methylmagnesium bromide, and of sultine 11 with p-tolylmagnesium bromide, readily affords the expected optically active sulfoxide alcohols 17, 18, and 19, respectively. By analogy to open-chained sulfinates, this reaction is expected to proceed with inversion at sulfur.¹¹ Sulfoxide alcohols 17, 18, and 19 have not been previously reported, either as racemates or in resolved form. However, it was possible to establish rigorously the configuration of 19, according to the procedure outlined in Scheme I. Sulfoxide alcohol 19 was related by direct stereochemical correlation to menthyl p-tolylsulfinate¹² (20), whose configuration has been established.¹³ Treatment of (-)-menthyl (-)-(S)-p-tolylsulfinate (20) of high diastereomeric purity with the Grignard reagent prepared from 2-bromobenzyl alcohol, protected as its chloromagnesium alkoxide by the method of Balthazor,¹⁴ gave (-)-19. Inversion at sulfur requires that (-)-19 have the S configuration. Opening of (+)-enriched sultine 11 with ptolylmagnesium bromide gives (+)-enriched 19 which then must have the R configuration. Inversion at sulfur¹¹ requires, rigorously, that sultine (+)-11 have the S configuration; this confirms the assignment made using chiral fluoro alcohol 1c.

The absolute configuration of sultine 12 was not rigorously established; however, further experimental evidence supports the S-(+) assignment made above. Thus, the methyl protons of sulfoxide alcohol (-)-18 exhibit the low field sense of nonequivalence in the presence of (R)-(-)-1b, thereby indicating the R configuration according to the method of Pirkle and Beare.^{2,15} A priori, one must be concerned with the possibility that the hydroxyl group of 18 might interfere with this configuration assignment by competitive hydrogen bonding.¹⁶ Although this possibility cannot be ruled out, we merely note that converting the hydroxyl group to the N-methyl carbamate, as in 21, did not significantly alter the magnitude (2.5 Hz for the carbamate vs. 1.6 Hz for the alcohol, employing a 3.0:1.0:33 mole ratio of fluoro alcohol to substrate to chloroform-d, at 100 MHz, 28 °C) or sense of nonequivalence observed in the presence of (R)-(-)-1b. Furthermore, the methyl protons of sulfoxide alcohol (+)-17 similarly show a low field sense of nonequivalence (2.0 Hz under the same conditions) using (R)-(-)-1b, consistent with its rigorously established R configuration.2,15

The use of ORD and CD to relate the absolute configurations of sulfoxides is well established.^{17,18} However, the cases in which it has been applied to sulfinates are so few as to allow no generalizations. The CD spectra of sultines (S)-(+)-11 and (S)-(+)-12 were measured (Figure 2). It was found that the observed bands are similar but of opposite sign. Since ORD of α -methylcycloalkanones has been shown to depend on ring size,¹⁹ this is not a confounding result. Moreover other factors, such as the relationship of the heteroatoms to the aromatic ring and the effect of conformation, must also be taken into account when attempting to compare sultines. Clearly, in cases such as these, the use of chiral fluoro alcohols is the more direct and reliable method for determining absolute configuration.

Experimental Section

Melting points were taken on a Büchi apparatus and are uncorrected. Optical rotations were determined at 589 nm in a Zeiss visual polarimeter, using a 1.0-dm tube. Infrared spectra were recorded on a Perkin-Elmer 237B spectrophotometer. ¹H NMR spectra were obtained with a Varian HR-220, Varian HA-100, or Varian A-60D spectrometer, at 28, 28, or 44 °C, respectively. Mass spectra were obtained using a Varian MAT CH-5 spectrometer. CD measurements were made using a Jasco J-40A spectropolarimeter. Microanalyses were performed by J. Nemeth and his coworkers.

Fluoro Alcohols. Phenyl-2,2,2-trifluoroethanol²⁰ (1a) and 1-(1-naphthyl)-2,2,2-trifluoroethanol²¹ (1b) were prepared, resolved, and purified according to literature methods. The preparation, resolution, purification, and assignment of absolute configuration of fluoro alcohols 1c and 1d is being reported elsewhere.

1-Phenyl-2,2,3,3,4,4,4-heptafluoro-1-butanol (15). The procedure employed, involving the addition of lithium heptafluorobutyrate to phenylmagnesium bromide, was strictly analogous to that reported²¹ for the preparation of 1b. The yield was comparable. Fluoro alcohol 15 was obtained as a colorless liquid: bp 88-90 °C (8.5 mm); ¹H NMR (CDCl₃) δ 2.49 (d, 1, OH), 5.20 (d of d, 1, CH), and 7.45 ppm (s, 5, C₆H₅).

Anal. Calcd for $C_{10}H_7F_7O$: C, 43.49; H, 2.56. Found: C, 43.72; H, 2.81.

(*R*)-(-)-1-Phenyl-2,2,3,3,4,4,4-heptafluoro-1-butanol (15). Resolution was accomplished via chromatographic separation of the diastereomeric carbamates prepared by reaction of 15 with (*R*)-(-)-1-(1-naphthyl)ethyl isocyanate, using a procedure strictly analogous to that described²¹ for 1b. Yields were comparable. The *R*,*R* diastereomer of the carbamate was eluted first, and was recrystallized from hexane: mp 148.0-149.0 °C; $[\alpha]^{25}D - 2.5 \pm 0.8^{\circ}$ (*c* 3.98, CHCl₃).

Anal. Calcd for $C_{23}H_{18}F_7NO_2$: C, 58.36; H, 3.83; N, 2.93. Found: C, 58.56; H, 3.92; N, 2.97.

The S,R carbamate diastereomer was eluted second and was recrystallized from hexane: mp 126.8-128.0 °C; $[\alpha]^{25}D$ +14.9 \pm 0.8° (c 4.07, CHCl₃).

Anal Calcd for $C_{23}H_{18}F_7NO_2$: C, 58.36; H, 3.83; N, 2.93. Found: C, 58.56; H, 3.92; N, 2.97.

Ethanolysis of the first eluted R,R carbamate diastereomer, in ethanolic sodium ethoxide, according to the procedure described previously,²¹ gave (-)-1-phenyl-2,2,3,3,4,4,4-heptafluoro-1-butanol, identical (NMR) with the racemate: $[\alpha]^{26.5}D - 26.7 \pm 0.6^{\circ}$ (c 6.93, EtOH).

The assignment of the R-(-) absolute configuration to 15 was made on the basis of the observed low-field sense of ¹H NMR spectral nonequivalence for the carbinyl hydrogen of a (-)-enriched sample in (R)-(+)-1-(1-naphthyl)ethylamine, according to the method of Beare and Pirkle.²²

Sulfinates. Preparation of 4a-h, all previously reported, was carried out from the corresponding sulfinyl chlorides²³ and alcohols according to the method of Phillips.⁵ Purification was by simple distillation with the exception of 4h, which decomposed before it distilled at 0.05 mm. This compound is obtainable nearly analytically pure after simple removal of the ether following extractive work-up. Partially resolved sulfinates 4a, 4b, and 4c were obtained by stereospecific inclusion in β -cyclodextrin.⁴

Sultines. Preparation of dl-11 and dl-12 was accomplished by the procedure of Durst.²⁴ We report here only the ¹H NMR of these compounds (superscripts refer to structures in Table III).

11: ¹H NMR (CDCl₃) δ 5.51 (d, 1, J = 13.6 Hz, H^{α}), 5.92 (d, 1, J = 13.6 Hz, H^{β}), and 7.20-7.88 ppm (m, 4, C₆H₄).

12: ¹H NMR (CDCl₃) δ 3.50 (d, 1, J = 15.3 Hz, H^{γ}), 4.31 (d, 1, J = 15.3 Hz, H^{δ}), 4.88 (d, 1, J = 13.6 Hz, H^{α}), 5.23 (d, 1, J = 13.6 Hz, H^{β}), and 7.00-7.42 ppm (m, 4, C₆H₄).

(S)-(+)-1-Chloro-2-methylbutane. The method of Brown and Groot²⁵ was employed, starting with 2-methyl-1-butanol (K and K laboratories) containing 15% (¹H NMR integration) 3-methyl-1-butanol and having a rotation $[\alpha]^{24}D - 4.95 \pm 0.04^{\circ}$ (neat, l = 1, $d_4^{24} 0.8189$) [lit.²⁶ $[\alpha]^{27.5}D - 5.86^{\circ}$ (neat, l = 1, $d_4^{27.5} 0.813$)], corresponding to >99% optical purity when corrected for the inactive isomer. The product 1-chloro-2-methylbutane was assumed to contain 15% 1-chloro-3-methylbutane, since work-up involved no careful fractionation. Its observed rotation, $\alpha^{23.6}D + 1.19 \pm 0.03^{\circ}$ (neat, l = 1) [lit.²⁷ $\alpha^{25}D + 1.44^{\circ}$ (neat, l = 1)], corresponds to an optical purity of >97% when corrected for the inactive isomer.

(S)-2-Methyl-1-butylmagnesium Chloride (9). The method of Mosher²⁸ was employed, starting with 1-chloro-2-methylbutane



Figure 2. CD spectra of 11 and 12. Measurements were made using partially resolved samples and are corrected to 100% enantiomeric purity. Bands below 250 nm were obscured by solvent absorptions.

(23.0 g, 0.217 mol) and magnesium turnings (7.15 g, 0.30 g-atom)in 230 ml of anhydrous ether under a nitrogen atmosphere. Analysis by acid titration established its base strength as 0.85 M; however, use in subsequent reactions indicated an effective activity of 0.74 M.

(S)-(+)-1-Chloro-2-phenylbutane. Material having an observed rotation $\alpha^{24.5}D$ +5.47 ± 0.04° (neat, l = 1) [lit.²⁹ $\alpha^{25}D$ +5.95° (neat, l = 1)], corresponding to an optical purity of 92%, was prepared by the procedure of Mosher and co-workers.²⁹

(S)-2-Phenyl-1-butylmagnesium Chloride (10). The Grignard reagent was prepared, by the method of Mosher and co-workers,²⁹ from (S)-(+)-1-chloro-2-phenylbutane (22.0 g, 0.131 mol) and magnesium turnings (3.41 g, 0.14 g-atom) in 130 ml of anhydrous ether under a nitrogen atmosphere. Analysis by acid titration gave a base strength of 0.86 M. In subsequent reactions it showed an effective activity of 0.74 M.

Kinetic Resolutions. A typical reaction is described. In a threenecked flask equipped with a pressure-vented nitrogen inlet, a mechanical stirrer, and a serum stopper, the sulfinate (25 mmol) was dissolved in 60 ml of anhydrous ether and cooled to -70° in a dry ice-2-propanol bath (in the cases of sultine 11 and 12 amounts of ether were increased to 625 and 150 ml, respectively, because of their insolubility at -70 °C). To the stirred mixture was added, at -70 °C, over a 50-min period via syringe (Hamilton, gas tight), a solution of the Grignard reagent (12.5 mmol) in ether. Formation of a precipitate and the tendency toward rapid rise in temperature during addition indicated that reaction was occurring. The mixture was stirred for 40 min at -70 °C, allowed to warm to 0 °C, and worked up by addition of 2.5 ml of saturated aqueous ammonium chloride. Upon stirring, a dry solid appeared, which was separated by filtration and rinsed with ether. The filtrate was dried (MgSO₄) and the solvent removed at reduced pressure to give a mixture of the partially resolved sulfinate or sultine and the corresponding sulfoxide 13 or sulfoxide alcohol 14. This mixture was chromatographed on silica gel. The partially resolved sulfinate or sultine was eluted with methylene chloride. Careful removal of the solvent at reduced pressure (the last traces were removed at 0.05 mm) gave material showing no extraneous peaks in the ¹H NMR. Elution with ethyl acetate yielded the analogous 13 or 14. Similar removal of the solvent gave material exhibiting an elemental analysis and a ¹H NMR spectrum consistent with the assigned structure. Products 13 and 14 derived from isomerically contaminated Grignard reagent 9 were presumed to contain a similar fraction of the 3methyl-1-butyl isomer

(-)-Menthyl (S)-(-)-p-Tolylsulfinate (20). Preparation was carried out by the method of Phillips,⁵ starting with (-)-menthol. Three recrystallizations of the product from hexane gave 20, $[\alpha]^{23}D - 199 \pm 2^{\circ}$ (c 2.01, acetone) [lit.³⁰ $[\alpha]^{25}D - 199.19^{\circ}$ (c 2, acetone)].

(S)-(-)-2-(Hydroxymethyl)phenyl 4-Methylphenyl Sulfoxide (19). A 200-ml three-necked flask was fitted with pressure-vented nitrogen inlet, condenser, mechanical stirrer, and 125-ml serum-stoppered, pressure-equalizing dropping funnel. In the funnel, the protected halide was prepared as follows.¹⁴ To a solution of 2-bromobenzyl alcohol (2.81 g, 15.5 mmol) in 35 ml of anhydrous tetrahydrofuran was slowly added, via syringe, with magnetic stirring, ethylmagnesium chloride (3.1 M in ether, 5.08 ml, 15.7 mmol). After this mixture had stood for 30 min, a small amount was added to the main flask, which contained magnesium (0.38 g, 15.6 mgatoms) in 5 ml of anhydrous tetrahydrofuran. After reaction had been initiated with 1,2-dibromoethane, the contents of the funnel were added to the flask over a 1-h period, during the last 15 min of which external heat was supplied to cause reflux. After an additional 1 h of reflux, the solution was allowed to cool to room temperature. A solution of freshly prepared (S)-(-)-20 (3.54 g, 12.02 mmol) was then rapidly added. After 30 min of stirring, 80 ml of saturated aqueous ammonium chloride was added. After separation of the layers, the aqueous layer was extracted with three 100ml portions of ether. The combined organic layers were dried (MgSO₄) and the solvent removed. The residue was chromatographed on silica gel, using methylene chloride to remove impurities, followed by ethyl acetate. The crude product, 19 (1.69 g, 6.88 mmol, 56.3%), eluted with the ethyl acetate solvent front, was recrystallized from ether-hexane: mp 92.0-93.0 °C; $[\alpha]^{26}D - 113 \pm$ 1° (c 2.99, EtOH); ¹H NMR (CDCl₃) δ 2.34 (s, 3, CH₃), 3.75 (s, 1, OH), 4.62 (AB, 2, CH₂), and 7.08-7.88 ppm (m, 8, both C₆H₄). Anal. Calcd for C₁₄H₁₄SO₂: C, 68.26; H, 5.73; S, 13.02. Found:

C, 68.10; H, 5.52; S, 12.90. (*R*)-(+)-2-(Hydroxymethyl)phenyl 4-Methylphenyl Sulfoxide (19).

To a stirred solution of sultine 11 (0.528 g, 3.42 mmol), having $[\alpha]^{24}D + 86.5 \pm 0.4^{\circ}$ (c 7.00, CHCl₃), in 25 ml of anhydrous ether was added, over a 5-min period at 0 °C, *p*-tolylmagnesium bromide (0.93 M in tetrahydrofuran, 9.2 ml, 8.6 mmol). After 1 h of stirring, 20 ml of saturated aqueous ammonium chloride was added. After separation of the layers, the aqueous layer was extracted with three 75-ml portions of ether. The organic layers were combined and dried (MgSO₄) and the solvent was removed at reduced pressure. Chromatography of the residue on silica gel, eluting with ether, gave analytically pure, crystalline 19 (0.631 g, 2.56 mmol, 74.9%): mp 93.1-103.5 °C; $[\alpha]^{23}D + 40.2 \pm 0.9^{\circ}$ (c 3.01, EtOH); ¹H NMR (CDCl₃) δ 2.32 (s, 3, CH₃), 3.78 (s, 1, OH), 4.62 (AB, 2, CH₂), and 7.05-7.88 ppm (m, 8, both C₆H₇).

Anal. Calcd for C₁₄H₁₄SO₂: C, 68.26; H, 5.73; S, 13.02. Found: C, 68.04; H, 5.95; S, 12.77.

(*R*)-(+)-2-(Hydroxymethyl)phenyl Methyl Sulfoxide (17). Sultine 11 (0.50 g, 3.25 mmol) having $[\alpha]^{25}D + 18.8 \pm 0.3^{\circ}$, was converted by the action of methylmagnesium bromide (2.5 M in ether, 3.0 ml, 7.5 mmol), in a procedure similar to that described for preparation of 19, to sulfoxide alcohol 17. Crystalline 17 (0.350 g, 2.05 mmol, 63.3%) was isolated by chromatography on silica gel, using ethyl acetate: mp 58.9-60.9 °C; $[\alpha]^{24}D + 12.2 \pm 0.8^{\circ}$ (c 4.02, acetone); NMR (CDCl₃) δ 2.72 (s, 3, CH₃), 4.28 (s, 1, OH), 4.68 (AB, 2, CH₂), and 7.29-7.95 ppm (m, 4, C₆H₄).

Anal. Calcd for $C_8H_{10}SO_2$: C, 56.45; H, 5.92. Found: C, 56.29; H, 5.98.

(R)-(-)-2-(Hydroxymethyl)benzyl Methyl Sulfoxide (18). Sultine 12 (0.741 g, 4.40 mmol) having $[\alpha]^{25}D + 7.3 \pm 0.4^{\circ}$ (c 5.01, CHCl₃) was converted, using methylmagnesium bromide (2.5 M in ether, 4.5 ml, 11 mmol), by the procedure described above for preparation of 19, to sulfoxide alcohol 18. Pure 18 (0.577 g, 3.12 mmol, 70.9%) was obtained as an oil by chromatography on silica gel, eluting with ethyl acetate: $[\alpha]^{25}D - 10.5 \pm 0.4^{\circ}$ (c 4.01, acetone); ¹H NMR (CDCl₃) δ 2.37 (s, 3, CH₃), 3.97 (AB, 2, SCH₂), 4.42 (m, 3, OCH₂ and OH), and 7.06-7.34 ppm (m, 4, C₆H₄).

Anal. Calcd for C₉H₁₂SO₂: C, 58.67; H, 6.56. Found: C, 58.29; H, 6.70.

(R)-(-)-2-(Methylsulfinylmethyl)benzyl N-Methylcarbamate

(21). A solution of R-(-)-18 (0.452 g, 2.51 mmol) having $[\alpha]^{25}D$ $-10.5 \pm 0.4^{\circ}$ (c 4.01, acetone), freshly distilled methyl isocyanate (0.464 g, 8.14 mmol), and N.N-dimethyl-2-aminoethanol (ca. 10 μ l, catalytic amount) in 25 ml of methylene chloride was allowed to react at room temperature for 3 days. The residue obtained by evaporation of the volatile materials under a stream of nitrogen was chromatographed on a 1×3 in. column of silica gel, eluting with ethyl acetate. Sulfoxide carbamate 21 (0.328 g, 1.36 mmol, 54.2%) was obtained as a colorless, intractable oil: $[\alpha]^{26}D = 8.5 \pm$ 0.7° (c 4.00, acetone); ir (neat liquid) 3300 (NH), 1710 (C=O), 1530, 1260, 1130, 1060 (SO), and 770 cm⁻¹; ¹H NMR (CDCl₃) δ 2.52 (s, 3, SCH₃), 2.75 (d, 3, NCH₃), 4.11 (s, 2, SCH₂), 5.08 (broad m, 1, NH), 5.17 (s, 2, OCH₂), and 7.20-7.45 ppm (m, 4, C₆H₄); mass spectrum (10 eV) m/e (rel intensity) 241 (0.6, M⁺), 179 (12), 178 (93), 134 (41), 122 (10), 121 (100), 120 (15), 105 (35), 93 (38), 91 (9).

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- (10) The suggestion, derived from sultines, that there is a facile equilibrium between the secondary interaction at sulfur and at the alkoxyl oxygen accounts for a previously noted trend in the spectra of acyclic sulfinates in chiral fluoro alcohols. One notes that, as the number of substituents on the α carbon of the alkoxyl mojety increases, the magnitude of nonequivalence for the sulfnyl substituent (methyl, p-tolyl) in-creases. Presumably increasing the bulk of the alkoxyl substituent causes certain nonequivalence-engendering conformers to be increasingly effectual. Let us suppose that for simple sulfinates as well as for suitines, diastereometric solvates stemming from both types of secondary interaction occur, with the interaction at the alkoxyl oxygen predominating and determining the sense of nonequivalence. In proceeding from methoxyl to tert-butoxy, the observed increase in nonequivalence suggests increasing dominance of the secondary interaction at the alkoxyl oxygen. Although the level of substitution of the α carbon would be expected to augment the basicity of the oxygen somewhat, thereby increasing its interaction with the acidic carbinyl hydrogen, the magnitude of the nonequivalence increase would suggest an additional factor. As previously noted, the alkoxyl substituent R' should tend to be approximately trans to the sulfinyl substituent R in acyclic sulfinates. Bulky alkoxyl groups would be expected to more heavily populate this trans conformation. In this event, the alkoxyl R' would be expected to hinder interaction of the carbinyl proton with the electron pair on sulfur, and divert the secondary interaction to the alkoxyl oxygen. Although this may seem a troublesome complication it is not; the smallest possible R' group, methoxyl, still shows clear preference for the secondary interaction at the alkoxyl oxygen. Larger alkoxyl substituents give great-er nonequivalence magnitudes of predictable senses.
- (11) The evidence for inversion at sulfur in the reactions of nucleophiles, especially Grignard reagents, is well established. Our analogy (upon which our argument for inversion in the case of sultines is based) is occasioned by the structural similarity of sulfines to acyclic sulfinates and supported by our observation that the reaction of Grignard reagents with sultines (as in the case for sulfinates) is stereospecific, the enantiomeric purity of the sulfoxide alcohol product being identical, allowing for experimental error, to that of the starting sulfine.
- (12) Initial attempts to establish the absolute configuration of 11 involved treatment of a 2.0:1.0 diastereomeric mixture of *R*-enriched menthyl methylsulfinates with a twofold excess of the Grignard reagent from 2-bromobenzyl alcohoi (protected as its chloromagnesium alkoxide) and "activated" magnesium [see R. D. Rieke and S. C. Bales, *J. Am. Chem. Soc.*, 96, 1775 (1974)]. A 2.5:1.0 mixture of (+)-17:(-)-17 [[α]²²D 65.7 ± 0.7° (c 4.02, acetone)] was obtained in 32.1% isolated yield. This yield does not mathematically preclude the possibility that

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Aromatic Substitution. XXXVII.¹ Stannic and Aluminum Chloride Catalyzed Friedel-Crafts Alkylation of Naphthalene with Alkyl Halides. Differentiation of Kinetically and Thermodynamically Controlled Product Compositions, and the Isomerization of Alkylnaphthalenes

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Abstract: The AlCl3- and SnCl4-catalyzed Friedel-Crafts alkylation (methylation, ethylation, isopropylation, and tert-butylation) of naphthalene with alkyl halides was studied in nitromethane, carbon disulfide, and benzene solution. Alkylations in nitromethane show the least isomerization giving 75-100% α and 25-0% β substitution. Ready isomerization of α -alkylnaphthalenes under usual Friedel-Crafts conditions leads to substantially increased β -alkylnaphthalene formation. To ascertain the effect of acid-catalyzed isomerization, the AlCl₃-catalyzed isomerization of α - and β -alkyl-(methyl-, ethyl-, isopropyl-, tert-butyl-)naphthalenes was studied, including determination of equilibrium composition of the α/β isomeric pairs.

Compared to the extensively studied Friedel-Crafts alkylation of benzene and its derivatives,² the alkylation of naphthalene received relatively little attention. Whitmore and James reported the formation of β -tert-butylnaphthalene (and higher alkylation products) in the aluminum chloride catalyzed alkylation of naphthalene with isobutylene.³ Other reports of the alkylation of naphthalene with olefins, alcohols, or alkyl halides also showed preferential formation of the β isomer.^{4,5}

The preferential formation of the β isomer has been argued on steric grounds in the case of bulky reagent-catalyst complexes and on the basis of rearrangement of the kinetically favored α isomer.

In more recent studies using H₃PO₄-BF₃ catalyst propylene, 1-butene, cis-2-butene, and trans-2-butene were found to give 70-74% α - and 26-30% β -alkylnaphthalenes. Isobutylene, and diisobutylene, however, gave exclusively β -tertbutylnaphthalene.⁶ Alkylations were considered to be carried out under kinetically controlled conditions. The formation of no detectable amount of α -tert-butylnaphthalene in the reaction of isobutylene was explained on the basis that in this case, for steric reasons, the β isomer becomes the exclusive kinetic product.

In the H_2SO_4 -catalyzed alkylation of naphthalene with 2-butene the α/β isomer ratio was found to be dependent on the temperature and varied from 1.5 to 4.7

The Friedel-Crafts alkylation of naphthalene thus seems to be still controversial, and no clear understanding of directive effects and selectivities was yet obtained.

Besides possible steric effects the varying isomer ratios giving generally preference of β isomer observed in the Friedel-Crafts alkylations of naphthalene could have been effected by secondary isomerization processes of the alkylnaphthalenes initially formed in the reactions. Whereas the Friedel-Crafts isomerization of alkylbenzenes was extensively investigated,⁸ apparently no such study of the isomerization of alkylnaphthalenes was yet reported.

In continued study of Friedel-Crafts alkylation and isomerization reactions it was, therefore, felt of substantial interest to carry out a study of the alkylation of naphtha-