The Stereochemistry of Free-Radical Eliminations on β-Phenylsulfinyl Radicals

Thomas E. Boothe,[1a] Joseph L. Greene, Jr.,[1a] Philip B. Shevlin,*[1a]
M. Robert Willcott, III,*[1b] Ruth R. Inners,[1b] and André Cornelis[1c]

Contribution from the Departments of Chemistry, Auburn University,
Auburn, Alabama 36830, and University of Houston, Houston, Texas 77004,
and Laboratoire de Chimie Organique Physique, Institute de Chimie,
Université de Liegé Sart-Tilman par 400 Liegé 1, Belgium.
Received November 21, 1977

Abstract: The four diastereomeric 2-bromo-3-phenylsulfinylbutanes (**5a, 5b, 6a, 6b**) have been synthesized and their configurations deduced through the use of lanthanide shift reagents. The reaction of **5a, 5b, 6a,** and **6b** with tributyltin radicals generates β-phenylsulfinyl *sec*-butyl radicals (**3**) which eliminate phenylsulfinyl radicals to form the 2-butenes in a stereoselective manner. This stereoselectivity is the result of rapid loss of phenylsulfinyl radicals before appreciable rotation about the C2-C3 bond in **3** can occur. There are small differences in the rates of reaction of the diastereomers which are consistent with a modest interaction between sulfur and the developing p orbital of the radical. The relative rates are inconsistent with anchimeric assistance via interaction of the sulfoxide oxygen with the radical p orbital.

Reaction of β-phenylthio alkyl bromides with trialkyltin radicals produces β-phenylthio radicals which eliminate thiophenoxy radicals to generate alkenes nonstereospecifically (eq 1).[2] Reaction of either *erythro-* or *threo*-2-bromo-3-
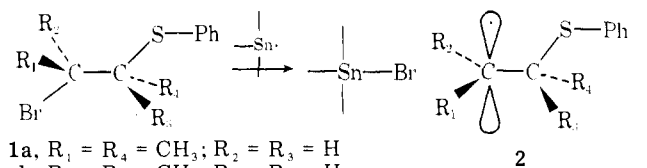

1a, $R_1 = R_4 = CH_3$; $R_2 = R_3 = H$
b, $R_1 = R_3 = CH_3$; $R_2 = R_4 = H$

$$\longrightarrow \text{Ph—S·} + \diagup\!\!=\!\!\diagdown + \diagdown\!\!\diagup\!\!\diagdown \qquad (1)$$

phenylthiobutane (**1a** or **1b**) with tributyltin radicals produces the same mixture of *cis-* and *trans*-2-butene. These results were interpreted to indicate that the barrier to rotation in the intermediate β-phenylthio radical, **2a,** was less than the barrier for elimination of thiophenyoxy radical. Consequently, stabilization of these radicals by sulfur bridging in structures such as **2b** was deemed to be unimportant.

2a   **2b**
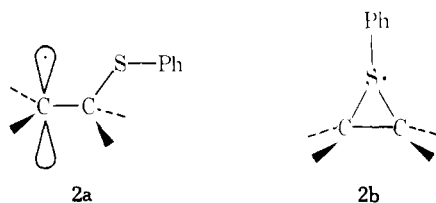
It was thought that an extension of these studies to β-phenylsulfinyl radicals, **3a,** would be important for several reasons. First, there is the question of stabilization of the radical center by the neighboring sulfinyl group. This could occur either by participation of orbitals on sulfur as in **3b** or through orbitals on oxygen as in structure **3c.** Second, a

3a   **3b**   **3c**
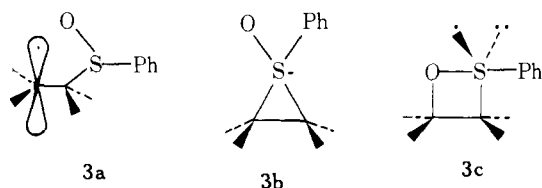
phenylsulfinyl radical, e.g., **4,** is thought to be more stable than a thiophenoxy radical;[3] hence elimination from **3** should be more rapid than from **2.** The effect of the stability of the radical

$$3 \longrightarrow \diagup\!\!=\!\!\diagdown + \cdot\overset{\displaystyle O}{\underset{\displaystyle |}{S}}\text{—Ph}$$

4
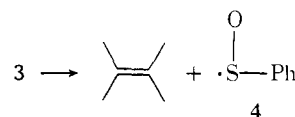
leaving groups on the stereochemistry of elimination warrants investigation.

Elimination of phenylsulfinyl radicals to generate alkenes has been postulated.[4] However, in no case has the stereochemistry of the reaction been studied. We now report the results of a study of the reaction of tribulyltin radicals with the sulfoxides prepared by oxidation of **1a** and **1b.**

Results

Generation and Determination of the Structure of the Four Diastereomeric 2-Bromo-3-phenylsulfinylbutanes. It is obvious that conversion of either **1a** or **1b** to the sulfoxide introduces a stereochemical complication in the form of an additional asymmetric center. Two diastereomers will result from the oxidation of either **1a** or **1b.** Two diastereomers can be separated when either *erythro-* or *threo*-1,2-diphenyl-1-phenylthiopropane is oxidized.[5]

The *m*-chloroperbenzoic acid (MCPA)[6] oxidation of **1a** produced two diastereomers in the ratio of 1.3:1.0, as determined by ^{1}H NMR. These two compounds were separated by column chromatography to give what was shown to be (1*RS*,2*SR*,3*RS*)-3-bromo-2-methyl-1-phenyl-1-thiabutane 1-oxide (**5a**) as the predominant isomer, and

5a   **5b**
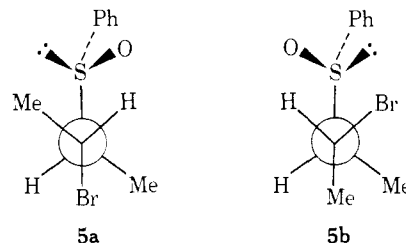
(1*RS*,2*RS*,3*SR*)-3-bromo-2-methyl-1-phenyl-1-thiabutane 1-oxide (**5b**). Oxidation of **1b** with MCPA gave two diastereomers in the ratio of 3.1:1.0 which were inseparable by column chromatography. The predominant isomer was isolated by recrystallization and was shown to be (1*RS*,2*SR*,3*SR*)-3-bromo-2-methyl-1-phenyl-1-thiabutane 1-oxide (**6a**). The partial removal of **6a** from the original reaction mixture left an approximately 1:1 mixture of diastereomers which could not be separated under any conditions investigated. However,

Table I. NMR Chemical Shifts and Coupling Constants for Compounds 5 and 6.[a]

|	5b	5a	6a	6b
δH-2	2.53	2.77	2.94	3.08
δMe-2	1.78	1.93	1.77	1.74
δH-3	4.88	4.19	4.64	4.58
δMe-3	1.03	1.16	1.07	1.14
δPh[b]	7.55	7.57	7.58	7.44
	7.75			7.5
$J_{2,3}$	3.60	6.9	6.35	4.12
$J_{3,Me3}$	6.7	6.9	6.8	
$J_{2,Me2}$	6.86	6.9	6.82	

[a] Chemical shifts are in parts per million from internal Me_4Si; coupling constants are in hertz. [b] Aromatic protons in 5b and 6b show two multiplets while those of 5a and 6a exhibit only one multiplet.

Table II. Normalized Lanthanide Induced Shifts for Compounds 5 and 6[a,b]

	5a	5b	6a	6b
H-2	0.295	0.406	0.308	0.344
Me-2	0.324	0.197	0.308	0.234
H-3	0.228	0.323	0.228	0.295
Me-3	0.153	0.072	0.156	0.127

[a] LIS measured on $CDCl_3$ solution of sulfoxides. The lanthanide-substrate ratios varied from 0 to 0.4 in each case. [b] Normalized data reduction of ApSimon was employed: J. W. ApSimon and H. Beierbeck, *J. Chem. Soc., Chem. Commun.*, 172 (1972).

the reaction of 6a with triethyloxonium tetrafluoroborate[7] and subsequent base hydrolysis produced (1*RS*,2*RS*,3*RS*)-3-bromo-2-methyl-1-phenyl-1-thiabutane 1-oxide (6b) in a 2.0:1.0 ratio with 6a. The Experimental Section gives further details and various means attempted to separate 6a and 6b. In

6a
6b
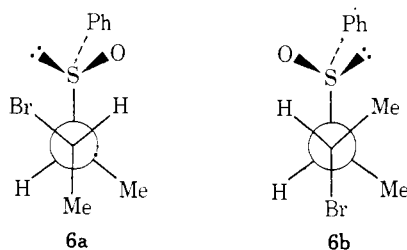
all experiments using 6b, material having this 2.0:1.0 ratio was used except in the competitive reactions, in which a 1.6:1.0 ratio was used.

Assignment of the Relative Stereochemistry of the Newly Created Sulfoxide Group. Four prominent data which can be used to assess the configuration and conformations of compounds 5a, 5b, 6c, and 6b are (1) the mode of synthesis (to fix the configuration at C-2 and C-3, (2) NMR chemical shift patterns, (3) the NMR vicinal coupling between H-2 and H-3 ($J_{2,3}$), and (4) the lanthanide induced chemical shifts (LIS).[8] The pertinent NMR data are found in Tables I and II.

The assignment of configuration to sulfoxides 5a and 5b as well as 6a and 6b is complete when the chirality of the sulfoxide moiety is determined. The strong resemblance of the LIS data for 5a and 6a, the similarity of the chemical shifts of the aliphatic hydrogens, and the nearly identical appearance of the aromatic multiplet all argue that the sulfoxide configuration is identical in these two diastereomers. A similar but less convincing argument applies to 5b and 6b; i.e., the b spectra resemble each other more nearly than they resemble either of the a spectra.

The combination of three acceptable conformations about C_2-C_3, with three acceptable conformations about O-S-C_2, leads to two enantiomeric sets of nine possible conformational
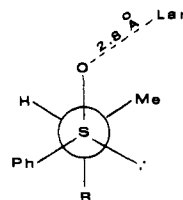
Figure 1.
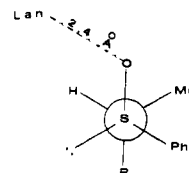
Figure 2.

states for any set of specified configurations. Clearly the entire array of NMR observations is insufficient to rigorously select the correct conformations and configurations for any one of our compounds. Nevertheless we are able to establish a number of important interrelationships which determine the configurations about the sulfoxides, and permit a consistent assignment of conformation.

The coordinates for all nine conformations of any isomer were prepared by computation using standard bond angles and distances. The LIS indexes for the hydrogen and methyl at C-2 were used to find a best lanthanide position. In order to locate the lanthanide we fixed the S-O-Lan angle at 120° [9] and varied the O-Lan distance and the Lan-O-S-C_2 dihedral angle until a fit to the spectral observations was obtained. When this procedure was used for the three conformations about the O-S-C_2 bond, the only conformer which gave a solution with O-Lan distances between 2 and 4 Å was that shown in Figure 1 for 5a and 6a. The corresponding solutions for 5b and 6b are shown in Figure 2. In Figure 1 the Lan-O-S-C_2 dihedral angle is −120° and in Figure 2 it is +120°. Thus, in all cases the Lan-O bond eclipses the orbital containing the electron pair on sulfur.

A qualitative examination of the LIS data in Table II confirms that assignment of sulfoxide configuration. Thus in 5a and 6a the lanthanide is closer to the methyl on C_2 than to H_2 and these methyl hydrogens have the greater LIS. In 5b and 6b the lanthanide is closer to H_2 and it is this hydrogen that feels the greatest LIS.

Reaction of the Diastereomeric 2-Bromo-3-phenylsulfinyl-butanes with Tributyltin Radicals. The four diastereomers were allowed to react with tributyltin radicals, generated from AIBN and tributyltin hydride, in benzene at 80 °C. The resulting 2-butenes were swept from the reaction vessel by a stream of nitrogen, trapped at −196 °C, and analyzed by gas chromatography and infrared spectroscopy. The results are given in Table III. Although no attempt was made to optimize the yields, alkene formation appeared to be the major course of this reaction. Increasing the reaction times and/or the tributyltin hydride concentration resulted in correspondingly higher butene yields (Table III). After 4 h of reaction, NMR analysis showed the presence of unreacted bromo sulfoxide and did not reveal products other than those resulting from the loss of phenylsulfinyl radical from 3. Analysis of the reaction mixture by thin layer chromatography showed no 2-phenyl-sulfinylbutane. It was determined that no isomerization of 5a, 5b, 6a, or 6b occurred under the reaction conditions.

In order to assess the effect of temperature on the stereochemistry of the elimination, tributyltin radicals were generated photolytically and allowed to react with the four diastereomeric bromo sulfoxides at −67 °C in toluene. The results

Table III. Stereochemistry of 2-Butene Formation in the Reaction of 2-Bromo-3-phenylsulfenylbutanes with Tributyltin Radicals

Diastereomer	[Bu$_3$SnH] [bromide]^a	Conditions	2-Butene yield, %	*trans-*/*cis*-2-butene
5a	1.0	1 h, 80 °C	15.8	2.14 ± 0.15
5a	1.0	4 h, 80 °C	55.8	2.02 ± 0.01
5a	5.0	4 h, 80 °C	63.7	2.38 ± 0.14
5a	1.0	$h\nu$, 2 h, −67 °C	13.8	2.43 ± 0.11
5b	1.0	1 h, 80 °C	16.3	0.955 ± 0.005
5b	1.0	4 h, 80 °C	61.7	0.953 ± 0.004
5b	5.0	4 h, 80 °C	71.2	0.891 ± 0.074
5b	1.0	$h\nu$, 2 h, −67 °C	12.7	0.404 ± 0.005
6a	1.0	1 h, 80 °C	25.5	0.426 ± 0.001
6a	1.0	4 h, 80 °C	67.0	0.424 ± 0.042
6a	5.0	4 h, 80 °C	69.1	0.469 ± 0.015
6a	1.0	$h\nu$, 2 h, −67 °C	7.1	0.671 ± 0.019
6b^b	1.0	1 h, 80 °C	17.2	0.208 ± 0.005
6b^b	1.0	4 h, 80 °C	67.2	0.198 ± 0.008
6b^b	1.0	$h\nu$, 2 h, −67 °C	5.8	0.363 ± 0.047

^{a} [Bromide] = 0.13 M, AIBN used as initiator. ^{b} The reaction mixture was 66.9% **6b** and 33.1% **6a**. The reported 2-butene ratios are, however, corrected to 100% **6b**.

of these experiments, shown in Table III, indicate that at both temperatures the 2-butenes are formed stereoselectively. This result is in marked contrast to the nonstereospecific elimination observed from radical **2**.[2] Pure diastereomers were used for each reaction except in the case of **6b**, where a 2:1 mixture of **6b:6a** was used.

We determined that some photochemical isomerization of the sulfoxide group in **5** and **6** did occur under the conditions of the reaction. The photolysis of **5a** for 2 h resulted in 7% isomerization to **5b**; the photolysis of **5b** gave 11% **5a** in 1.5 h, **6a** gave approximately 5% **6b**, and **6b** underwent 13% isomerization to **6a** in 2 h as determined by NMR. No interconversion between **5** and **6** occurred. The photochemical stereomutation of sulfoxides is known[10] so these observations were anticipated.

The stereoselectivities observed in this free-radical elimination must result from the fact that the rate constant for elimination in **3** (k_e) is greater than that for rotation about the C$_2$–C$_3$ bond (k_r). If this were not true, the same mixture of butenes would be obtained from **5a** and **6a** and from **5b** and **6b**. Thus the results of these studies are in striking contrast to the eliminations from **2**. There are two limiting explanations for this behavior: either k_e from **3** > k_e from **2**, or k_r in **3** < k_r in **2**. A combination of both of these possibilities would also rationalize the results. There is evidence that phenylsulfinyl radicals, **4**, are considerably more stable than phenylthiyl radicals.[3] Thus, homolytic cleavages of S–S bonds which generate phenylsulfinyl radicals are much more rapid than the corresponding fragmentations generating phenythiyl radicals.[11] Facile racemizations of arylbenzyl sulfoxides via homolysis of the S-benzyl bond also provides evidence for the stability of **4**.[12] Since the phenylsulfinyl radical is more stable than the phenylthiyl radical, it is reasonable to expect that k_e from **3** would be greater than k_e from **2**. However, it is also possible that bridging by the sulfinyl group in **3** may result in a lower k_r in **3** than in **2**. If sulfinyl bridging is important in **3**, this effect should manifest itself in the transition state leading to the radical and formation of **3** should be more rapid than formation of **2**. Hence, the relative rate of bromine abstraction from **1**, **5**, and **6** is of interest and has been measured.

Relative Rate of Bromine Abstraction from 1, 5, and 6. The relative rate of bromine abstraction by trialkyltin radicals on the various diastereomers was determined by a series of com-
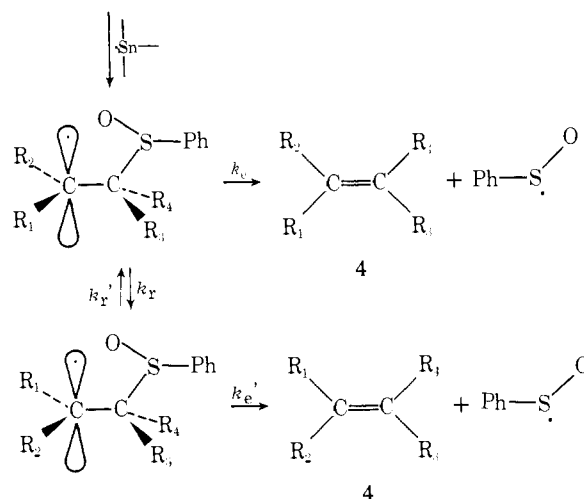
Table IV. Relative Reactivities of **1**, **5**, and **6** toward Tributyltin Radicals

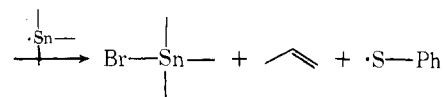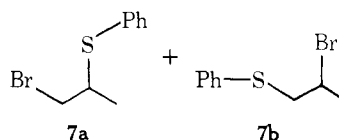| Diastereomer	k_{rel}	Diastereomer	k_{rel}
1a	1.55 ± 0.08	5b	1.45 ± 0.11
1b	1.38 ± 0.09	6a	2.46 ± 0.14
5a	2.19 ± 0.20	6b	1.96 ± 0.16^a

^{a} Corrected to 100% **6b** from the results obtained from a mixture of 61.4% **6b** and 38.6% **6a**.
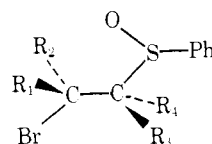
5a and 5b, R$_1$ = R$_4$ = CH$_3$; R$_2$ = R$_3$ = H
6a and 6b, R$_1$ = R$_3$ = CH$_3$; R$_2$ = R$_4$ = H

petition experiments in which the indicated diastereomer of **1**, **5**, or **6** and a mixture of 1-bromo-2-phenylthiobutane (**7a**) and 2-bromo-1-phenylthiobutane (**7b**) compete for tributyltin

radicals. The relative rates of bromine abstraction are then determined by comparison of the ratio of propene to 2-butenes from the various diastereomers and are given in Table IV.

An examination of the relative rates of bromine abstraction in Table IV shows only a slight rate enhancement for the sulfoxides **5a**, **6a**, and **6b** as compared to sulfide **1** in which bridging is unimportant. Sulfoxide **5b** shows no rate enhancement over **1**. Although there appears to be a small anchimeric effect of neighboring sulfinyl group, the stereoselectivity of this radical elimination is probably due to the stability of the phenylsulfinyl radicals which enhances the rate of elimination relative to that of rotation.

Discussion

An examination of the ratios of the 2-butenes in Table III shows that anti elimination of bromine and phenylsulfinyl predominates in the case of **5a**, **6a**, and **6b** while **5b** shows a slight preference for syn elimination. A consideration of the

coupling constants between the vicinal hydrogens on C_2 and C_3 in **5** and **6** (Table I) allows an estimate of the predominant conformer of each diastereomer. This analysis indicates that **5a** and **6b** have their bromine and phenylsulfinyl group anti in the most stable conformer. However, these two groups are predominantly gauche in **5b** and **6a**. Hence, the anti elimination observed in **5a** and **6b** and the syn elimination of **5b** reflect the orientation of the bromine and phenylsulfinyl in starting halide. However, the observed anti elimination of **6a** cannot be rationalized on this basis and must result from some interaction between the phenylsulfinyl group and the developing radical center which causes the anti conformer to react more rapidly than the gauche.

The changes in butene ratios in going from 80 to −67 °C simply reflect the increase in population of the most stable conformer. Thus the concentration of the anti conformer of **5a** and **6b** increases with decreasing temperature and anti elimination becomes increasingly important. Likewise the amount of syn elimination in **5b** and **6a** increases as the concentration of the most stable gauche conformer increases.

It should be noted that abstraction of bromine from the three diastereomers that undergo predominant anti elimination is more rapid than from **5b** which gives mainly syn elimination. If we assume that the rate enhancement of anti over syn elimination is due to a modest amount of anchimeric assistance of anti abstraction by the neighboring sulfinyl group, we may evaluate the nature of this neighboring group effect as follows.

Anchimeric assistance of bromine abstraction and consequent stabilization of the radical center could operate by interaction of the sulfur with the developing p orbital of the radical to generate a three-membered bridged structure such as **3b**. Alternately, an interaction between a nonbonding oxygen orbital and the radical p orbital could result in stabilization of the developing radical center with the formation of a four-membered cyclic sulfuranyl radical (**3c**). The ESR spectrum of several nonstrained sulfuranyl radicals has been reported.[13] These radicals are postulated to have trigonal bipyramidal structures and **3c** would probably have the geometry depicted earlier. However, more important than the final geometry of **3c** is the fact that for assistance by oxygen orbitals to occur an initial sulfoxide conformation with oxygen directed toward the developing p orbital of the radical is necessary. The conformations required for this assistance in **5a**, **6a**, and **6b** are those depicted in structures **5a′**, **6a′**, and **6b′**.

A consideration of nonbonded interactions in conformers **5a′**, **6a′**, and **6b′** leads to a relative rate prediction of **6b′** > **5a′**

5a′   **6a′**

6b′
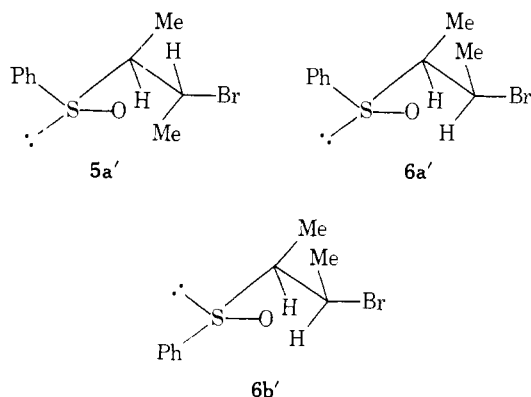
> **6a′**. Conformer **6a′** is relatively unfavorable owing to gauche methyl interactions, a gauche phenyl methyl interaction, and an interaction between the phenyl and the methyl on the developing radical center. Conformer **5a′** has the unfavorable interaction between the phenyl and the methyl on the developing radical. However, conformer **6b′** has only gauche methyl

interactions which are expected to be less severe than a phenyl–methyl interaction. Since the relative rates of reaction of the bromo sulfoxides (**6a** > **5a** > **6b**) are opposite to those predicted for oxygen orbital participation, we conclude that anchimeric assistance to generate **3c** is unimportant.

The situation regarding a three-membered bridged sulfur radical, such as **3b**, is less clear. If this species is formed by initial interaction between the nonbonding sulfur orbital and the developing p orbital, conformers leading to this interaction (**5a″**, **6a″**, and **6b″**) are those which would give the observed

5a″   **6a″**

6b″
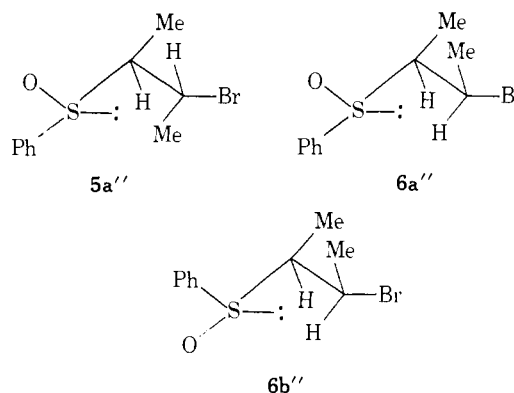
order of reactivities. However, it should be emphasized that the rate differences are small and do not constitute compelling evidence for the intermediacy of structures such as **3b**. The fact that observed rate differences are opposite to those leading to **3c** seems to rule out the intermediacy of these sulfuranyl radicals.

Summary

These experiments indicate that β-phenylsulfinyl radicals, generated by the action of tributyltin radicals on β-bromo sulfoxides, eliminate the phenylsulfinyl radical stereoselectivity. This stereoselectivity results from rapid loss of phenylsulfinyl radical from initial nonequilibrium conformations of the radical. This elimination occurs before rotation about the C–C bond and consequent equilibration of radical conformations can occur. The relative rates of reaction of the diastereomeric bromo sulfoxides are inconsistent with oxygen participation in radical formation and may reflect a small amount of assistance by interaction with the neighboring sulfur.

Experimental Section

Infrared spectra were obtained on a Perkin-Elmer 621 spectrometer; ^{1}H NMR spectra were measured with a Varian A-60, a Varian EM-390, and a Varian XL-100/Nicolet TT-100 spectrometer and are reported in parts per million (δ) downfield from internal Me$_4$Si standard. Carbon-13 magnetic resonance spectra were obtained with a Varian CFT-20 and are reported in parts per million downfield from internal Me$_4$Si.

Gaseous products were identified by infrared spectroscopy and product distributions were determined by gas chromatography on a 20 ft × 0.5 in., 20% dimethylsulfolane on Firebrick column at room temperature using a Carle microdetector. Solution compositions were determined by gas chromatography on a Perkin-Elmer 990 or an Aerograph A-350-B using either a 15 ft or 12 ft × 0.25 in., 20% SE-30 on 60-80 Chromosorb W column.

The 2-butenes and propene were used as received from the Matheson Co. Tri-*n*-butyltin hydride was prepared by the procedure of Kuivila and Beumel[4] or used as received from Eastman Kodak Co. The benzene and toluene used for reactions were dried and stored over molecular sieves. *m*-Chloroperbenzoic acid (85%) and tri-*n*-butyltin chloride (96%) were obtained from Aldrich. AIBN was used as received from Baker Chemical Co.

(1*RS*,2*SR*,3*RS*)-3-Bromo-2-methyl-1-phenyl-1-thiabutane 1-Oxide (5a) and (1*RS*,2*RS*,3*SR*)-3-Bromo-2-methyl-1-phenyl-1-thiabutane 1-Oxide (5b). 1a[15] (18.7 g, 0.076 mol) was placed in 300 mL of chloroform in a 1000-mL three-necked flask equipped with a low-tem-

perature thermometer, drying tube, and 500-mL addition funnel. In the addition funnel was placed MCPA (15.5 g. 0.076 mol) in 300 mL of chloroform. The flask was cooled to −25 °C with a dry ice-acetone bath. The MCPA solution was added over a 2-h period. The temperature never exceeded −10 °C. The reaction mixture was stored overnight (17 h) at −10 °C. The solution was filtered and washed three times with 100 mL of saturated sodium bicarbonate. The combined aqueous layers were washed with 100 mL of chloroform, the combined organic layers were dried over MgSO₄ and filtered, and the solvent was removed on a rotary evaporator to give 18.1 g (91%) of crude sulfoxides. These were chromatographed on 450 g of silica gel, eluting with hexane with increasing percentages of acetone, collecting 12 mL per fraction. Fractions 161-195 gave 7.49 g (37.6 %) of **5a.** Fractions 205-240 gave a solid which was recrystallized from a 1.7:1.0 ether-hexane mixture to give 4.56 g (22.9%) of **5b,** mp 73.0-74.6 °C. Spectral data for **5a** were as follows: ¹H NMR given in Table I; ¹³C NMR (DCCl₃) δ 8.94, 24.09, 49.26, 68.45, 124.69, 129.29, and 131.23; IR (neat) 3060, 2980, 2938, 1725, 1446, 1385, 1310, 1149, 1088, 1046 (S=O), 840, 751, 702, and 692 cm⁻¹. For **5b:** ¹H NMR given in Table I; ¹³C NMR (DCCl₃) δ 8.68, 23.90, 47.78, 67.98, 125.91, 129.26, and 131.91; IR (CCl₄) 3065, 2982, 2940, 1448, 1385, 1300, 1222, 1190, 1088, 1049 (S=O), 702, and 695 cm⁻¹. The product was stored at −10 °C under N₂.

(1RS,2SR,3SR)-3-Bromo-2-methyl-1-phenyl-1-thiabutane 1-Oxide (6a). 1b¹⁵ (10.0 g, 0.041 mol) was placed in 200 mL of chloroform in a 500-mL three-necked flask equipped with a low-temperature thermometer, drying tube, and an addition funnel. In the addition funnel was placed MCPA (8.32 g, 0.041 mol) in 100 mL of chloroform. The reaction mixture was cooled in a dry ice-CCl₄ bath and the MCPBA solution was added over an 80-min period. The temperature never exceeded −10 °C. The reaction mixture was stored overnight at −10 °C. The solution was filtered and washed three times with 100 mL of saturated sodium bicarbonate. The aqueous layer was washed with 50 mL of chloroform and the combined organic layers were dried over MgSO₄. The solution was filtered and the solvent removed to give a viscous oil which by ¹H NMR was shown to consist of two sulfoxides, in the ratio 3.1:1.0, which were inseparable by column chromatography on silica gel. The residue solidified when placed at −20 °C for 1 month. The solid was recrystallized twice by low-temperature recrystallization using 3:1 ether-hexane mixture to give **6a,** which melted to a clear, colorless liquid before room temperature; 2.74 g (25.6%) was obtained. ¹H NMR given in Table I; ¹³C NMR (DCCl₃) δ 6.23, 22.84, 48.48, 68.05, 124.29, and 131.13; IR (neat) 3060, 2980, 2935, 1478, 1445, 1382, 1086, 1042 (S=O), 749, 700, and 691 cm⁻¹. The product was stored at −10 °C under N₂.

(1RS,2RS,3RS)-3-Bromo-2-methyl-1-phenyl-1-thiabutane 1-Oxide (6b). The general method of Johnson and McCants was used.[7] In a 125-mL Erlenmeyer flask equipped with a drying tube was placed **6a** (1.45 g, 5.56 mmol) in a 1.31 M solution of triethyloxonium tetrafluoroborate. The reaction mixture was stirred at room temperature for 70 min. The solvent was removed on a rotary evaporator, 15 mL of water was added, and the mixture was titrated to phenolphthalein end point with 0.1 N NaOH. Ether (50 mL) was added and the layers were separated. The aqueous layers were washed three times with 25 mL of ether. The ether extracts were dried over MgSO₄ and the ether removed on a rotary evaporator to give 1.25 g (86.5%) of a crude product consisting of 62% **6b** and 38% **6a.** The reaction of triethyloxonium tetrafluoroborate with the 3.1:1.0 mixture of **6a** and **6b** gave a product mixture similar to that obtained from pure **6a.** This reaction mixture was recrystallized several times with 2:1 hexane-ether mixtures to give a substance which melted to a pale yellow liquid below room temperature which consisted of 61.4% **6b** and 38.6% **6a.** Column chromatography on silica gel of a previous reaction mixture gave a small amount of material consisting of 66.9% **6b** and 33.1% **6a:** ¹H NMR of **6b** given in Table I; ¹³C NMR (DCCl₃) δ 8.69, 20.95, 47.22, 67.70, 125.43, 129.29, and 131.83; IR of 2:1 mixture (neat) 3060, 2980, 2940, 1447, 1385, 1310, 1151, 1105, 1088, 1042 (S=O), 951, 821, 752, 702, and 693 cm⁻¹.

Reaction of 6a and 6b with Mercuric Chloride. In an attempt to separate the two sulfoxides obtained from the reaction of MCPA with **1b,** the sulfoxide mixture was reacted with mercuric chloride.[7] A hot solution of mercuric chloride (8.0 g, 29.5 mmol) in 45 mL of 60% aqueous ethanol was added to a solution of **6a** and **6b,** from the oxidation of **1b** (2.0 g, 7.35 mmol) in 15 mL of 95% ethanol. After heating on a steam bath for 5 min, the solution was cooled to 0 °C in an ice-water bath. The solid which precipitated was filtered. The filtrate was

extracted four times with dichloromethane, dried over MgSO₄, and removed on a rotary evaporator to give a solid. Fractional crystallization was not successful. Column chromatography on silica gel and eluting with benzene did not effect separation. The mercuric chloride complex can be converted to the sulfoxides by dissolving in 100 mL of 60% aqueous ethanol and refluxing for 2 h with 100 mL of 1% KCN in 50% ethanol. The reaction mixture was washed five times with 100 mL of dichloromethane, and the organic layers were dried over MgSO₄ and removed on a rotary evaporator. No separation of diastereomers could be obtained by this method.

Thermally Initiated Reactions of 5 and 6 with Tributyltin Hydride. In a typical run, the appropriate diastereomeric bromo sulfoxide (100 mg, 0.383 mmol) and AIBN (62.9 mg, 0.383 mmol) in benzene (2.0 mL) were placed in a Pyrex tube and flushed with a stream of nitrogen. Tributyltin hydride (111.5 mg, 0.383 mmol) in benzene (1.0 mL) was added and the mixture was heated at 80 °C. The gaseous products were continuously swept from the reactor through a water-cooled spiral condenser into a trap at −196 °C by a stream of nitrogen. The contents of the trap were distilled under vacuum from −78 to −196 °C. The distillate was analyzed by IR spectroscopy and gas chromatography. Thin layer chromatographic analysis of the benzene solution showed no detectable 2-phenylsulfinylbutane. Heating the four sulfoxides under these reaction conditions did not result in interconversion of the diastereomers as determined by ¹H NMR.

Photolytically Initiated Reaction of 5 and 6 with Tributyltin Hydride. In a typical run, the appropriate diastereomer (100 mg, 0.383 mmol) and AIBN (62.9 mg, 0.383 mmol) were placed in a 1.2 × 20 cm Pyrex tube with toluene (2.0 mL). Tri-*n*-butyltin hydride (111.5 mg, 0.383 mmol) in 1.0 mL of toluene was added. The sample was photolyzed for 120 min at −67 °C in an ethanol-dry ice bath (the reaction temperature was determined with an iron-constantan thermocouple) with a Hanovia 654A36 medium-pressure Hg lamp placed adjacent to the reaction tube. The gaseous products were continuously removed under vacuum (0.2 mm) and trapped at −196 °C. Subsequent treatment was the same as in thermal reactions. The photolysis of **5a** under the reaction conditions for 2 h gave 7% isomerization to **5b;** the photolysis of **5b** gave 11% isomerization in 1.5 h. **6a** gave about 5% **6b,** and **6b** underwent 13% isomerization to **6a** in 2 h, as determined by ¹H NMR.

2-Phenylsulfinylbutane. The oxidation of 2-phenylthiobutane with 1 equiv of MCPA was accomplished according to the procedure given for **5** and **6,** bp 111.2-114.7 °C (0.45 mm) [lit.¹⁶ bp 114-115 °C (0.002 mm)]. Examination by thin layer chromatography showed two diastereomers: ¹H NMR (CCl₄) δ 1.05 (complex m, 6 H), 1.61 (m, 1 H), 1.89 (m, 1 H), 2.48 (m, 1 H), 7.55 (m, 5 H); ¹³C NMR (DCCl₃) δ 13.80, 14.53, 15.06, 15.86, 25.82, 27.77, 65.02, 128.44, 129.05, 132.50, 134.19, and 134.60.

Preparation of a Mixture of 1-Bromo-2-phenylthiopropane (7a) and 2-Bromo-1-phenylthiopropane (7b). In a 1000-mL three-necked flask fitted with a mechanical stirrer, thermometer, and funnel with a drying tube attached was placed PBr₃ (45 g). Dry pyridine (9 g) was added over a 39-min period, followed by 45 mL of benzene. The mixture cooled to −5 °C with a ice-salt bath. A mixture of 2-phenylthio-1-propanol¹⁷ (81.0 g, 0.48 M) and pyridine (3 g) was added slowly from the funnel over a 2-h period. The reaction mixture was stirred for an additional 48 h. Benzene (500 mL) was added, the solution filtered, and the benzene removed on a rotary evaporator. The residue was distilled to give 59.5 g (54.0%) of a clear liquid, bp 110-112 °C (0.9-1.2 mm). A ¹H NMR analysis revealed that the clear liquid contained a 75:25 mixture of **7b** and **7a.** A similar mixture has been reported in the reaction of 2-methylsulfonyloxy-1-phenylthiopropane with lithium bromide,¹⁸ bp 76 °C (0.01 mm). Spectra of product obtained in this work were identical with that reported: ¹H NMR (CCl₄) δ 1.43 (d, 0.8 H), 1.77 (d, 2.2 H), 3.33 (m, 2.2 H), 4.05 (m, 0.8 H), 7.21 (m, 5 H).

Competitive Reactions of 5 and 6 with 7a and 7b. The appropriate diastereomeric bromo sulfoxide (100 mg, 0.383 mmol), a 3:1 mixture of **7b** and **7a** (88.5 mg, 0.383 mmol), AIBN (6.3 mg, 0.0383 mmol), and tributyltin hydride (11.2 mg, 0.0383 mmol) was treated as previously described for the thermally initiated reactions. The relative reactivity was determined by comparing the amounts of 2-butenes and propene produced using gas chromatography.

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Phase Transition Autocatalysis of the Hydrolysis of Some Esters of Azo Dyes

Richard L. Reeves,* Shelley A. Harkaway, and Richard T. Klingbiel

Contribution from the Research Laboratories, Eastman Kodak Company, Rochester, New York 14650. Received October 20, 1977

Abstract: Acetate and chloroacetate esters of some water-soluble azonaphthol and azophenol dyes form supersaturated solutions at concentrations as low as 10^{-5} M when aqueous solutions are mixed with buffers to give final ionic strengths as low as 0.01. Nucleation occurs slowly in the presence of atmospheric dust to give dilute colloidal dispersions of particles having Stokes radii of 0.3–0.4 μm. In the absence of dust, nucleation does not occur for periods up to 2 weeks. At neutral pH values, where hydrolysis of the acetates in homogeneous solution is very slow, formation of the colloidal particles is accompanied by accelerations by factors of 80–100. When nucleation takes place before appreciable hydrolysis has occurred in the supersaturated solution, the result is autocatalysis. Under conditions of higher pH or with more reactive chloroacetate esters, all the hydrolysis occurs in the homogeneous solution before nucleation can take place and autocatalysis is not observed. Ultrafiltration, seeding, and light-scattering experiments are described which establish that the autocatalysis results from formation of the colloidal phase.

A number of studies have shown that many amphiphilic azo dyes form association colloids in aqueous solution.[1-6] Those that form such colloids most readily are usually complex molecules such as Congo red or benzopurpurin with molecular weights of around 700 or greater. The presence of electrolytes facilitates colloid formation. On the other hand, many studies of simpler dyes with molecular weights around 400, such as the sulfonated phenylazonaphthols, have shown that in the absence of high electrolyte concentrations, the degree of aggregation is quite low.[1,2,6-10] Many properties of the solutions of the low molecular weight dyes have been interpreted in terms of a monomer–dimer equilibrium to relatively high dye concentrations.[7-10] What has apparently gone unnoticed, however, is the fact that a number of the simpler dyes readily form metastable solutions in water or dilute buffers and yield colloidal aggregates on aging. Light scattering results from these laboratories have shown that a number of simple dyes form colloidal dispersions from supersaturated solutions at surprisingly low concentrations.[11] Nucleation to particle sizes of less than 1 μm may occur quite slowly and is promoted by the presence of atmospheric dust or some other suitable surface. The simplest dyes such as methyl orange or orange II may nucleate to colloidal dispersions in the vicinity of a roughened Wilhelmy plate at concentrations where the dyes have been thought to be soluble.[12]

We now wish to report that these phase transitions occur in buffered aqueous solutions of esters of simple dyes. The formation of the colloids can accelerate by factors of 80–100 hydrolysis reactions that are quite slow in homogeneous solution. Since the phase transition involves the reactant and occurs during the hydrolysis, the result is an autocatalysis of the hydrolysis. To our knowledge, there have been no previous reports of either nucleation from supersaturated ester solutions or of autocatalysis of ester hydrolysis by any mechanism. We report kinetic results for the hydrolysis of esters I–III which are re-

I

II, R = —COCH₃
III, R = —COCH₂Cl
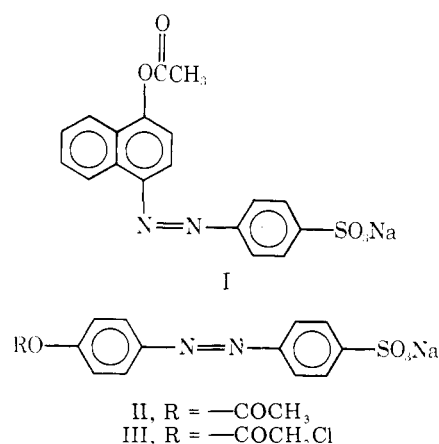
spectively the acetates or chloroacetates of the dyes orange I (IV) and 4′-hydroxyphenylazobenzene-4-sulfonic acid (V).

Experimental Section

Orange I acetate was material used in an earlier study.[13] Dye V was esterified in N,N-dimethylformamide solution by treatment with an excess of the appropriate acid anhydride, using triethylamine as catalyst. The dye was purified beforehand by recrystallization of the sodium salt until a single band was obtained by a high-resolution chromatographic method.[14]