these values with those for analogous SN2′ reactions will be made in the next paper in this series and the mechanism will be discussed therein.

Experimental Section

Reaction of 2-Bromo-3-methylbenzo[b]thiophene 1,1-Dioxide (1, X = Br) with Piperidine in Absolute Methanol in the Presence of Sodium Methoxide.—To a solution of 259.1 mg (1.00 mmol) of 1 (X = Br) in 10 ml of absolute methanol there was added 341 mg (4.00 mmol) of piperidine and 432 mg (8.00 mmol) of sodium methoxide. The mixture was refluxed 1 hr. Cooling to room temperature and filtering gave 160.6 mg (64.1%) of yellow needles, mp 178.8–181.8°; a mixture melting point with authentic 5[3] was undepressed.

Kinetic Procedures.—Piperidine solutions were prepared from freshly distilled reagent grade piperidine (bp 106°) and standardized by titrating with potassium biphthalate, using a pH meter to determine the end point.

A. Conductometric Determination.—An appropriate weight of halide was placed in one arm of a Y-shaped conductance cell, and dissolved in a known volume of absolute methanol, delivered by volumetric pipet. An appropriate volume of standard piperidine solution was then delivered into the other arm by volumetric pipette. After allowing 20 min for temperature equilibration in a bath controlled to ±0.05° with a thermoregulator, the contents of the two arms were thoroughly mixed and drained into the arm containing the platinized platinum electrodes. The resistance of the solution was then recorded as a function of time.

A plot of log $(R_t/R_t - R_\infty)$ *vs.* time gave straight lines. The slope of the line times 2.303 gave the pseudo-first-order rate constant. The second-order rate constants were then obtained by dividing the pseudo-first-order rate constants by the piperidine concentration. The infinity point was chosen to be between ten and twelve half-lives. For the Guggenheim procedure, the time interval was chosen to be about two to three half-lives. A plot of log $(1/R_{\Delta t} - 1/R_t)$ *vs.* time gave straight lines. Second-order rate constants were then derived from the slope of the line, as described above.

B. Spectrophotometric Determination.—Solutions of twice the desired concentration of halide and piperidine were placed in separate arms of a Y-shaped cell. After allowing 20 min for temperature equilibration in a water bath at 45.0°, the contents of the arms were thoroughly mixed. At appropriate times, 1.00-ml aliquots were withdrawn and diluted to 25.00 ml with absolute methanol. The absorbances of these solutions at 324 mμ were then determined in a Beckman DU spectrophotometer.

Alternatively, 3-ml samples of standard piperidine solutions were equilibrated in the spectrophotometer cuvettes contained in a thermostated cell holder. A 20–50-μl sample of halide solution was then added and the change of absorbance was followed with time.

A plot of log $(D_\infty/D_\infty - D_t)$ *vs.* time gave straight lines. The infinity point was chosen to be between ten and twelve half-lives. The second-order rate constants were then calculated from the slope of the line as described above.

C. Titrimetric Determinations.—Standard solutions of piperidine (100 ml) in 250-ml volumetric flasks with Teflon screw caps were equilibrated 1 hr in a bath controlled to ± 0.02° with a thermoregulator. Halide solutions were prepared by weighing appropriate amounts and dissolving these samples in 25 ml of the desired solvent. Portions (4–10 ml) of the halide solutions were added to the standard piperidine solutions and mixed thoroughly. Aliquots were withdrawn, quenched with 10 ml of 0.25 *M* HNO_3, and titrated with 1.5×10^{-3} *M* silver nitrate solution, using an autotitrator. The volume of titrant was then recorded as a function of time.

A plot of $\log(V_\infty - V_t)$ *vs.* time gave straight lines. The slope of the lines times 2.303 gave the pseudo-first-order rate constant. The second-order rate contants were then obtained by dividing the first-order rate constants by the piperidine concentration. The infinity point was chosen to be at ten or more half-lives.

Registry No.—1 (X = Br), 16934-26-2; 1 (X = Cl), 16934-27-3; 1 (X = I), 16934-28-4; piperidine, 110-89-4; 5, 16934-29-5.

Acknowledgment.—This investigation was supported by the Public Health Service Research Grant No. CA-07351 from the National Cancer Institute.

Rates of SN2′ and SNi′ Rearrangements in 3-(α-Haloalkyl)benzo[b]thiophene 1,1-Dioxides[1]

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Rate constants have been determined for the reactions of 3-(α-chloroethyl)- and 3-(α-chloro-α-methylethyl)-benzo[b]thiophene 1,1-dioxides (**1a** and **1b**, respectively) with piperidine in benzene. For **1a** the rate of (enamine) product formation (spectrophotometric rate) is slower than the rate of chloride release (titrimetric rate) indicating that the SNi′ type of rearrangement is rate determining. This kinetic analysis predicts formation of an intermediate, and evidence is presented to show that such is formed. For **1b** the rate of (enamine) product formation is equal to the rate of halide release indicating that in this instance the SN2′ step, rather than the SNi′ step, is rate determining.

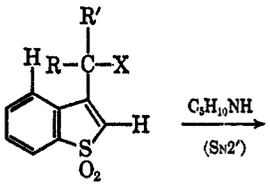
In a previous paper the reaction of secondary and tertiary chlorides **1a** and **1b** with piperidine in benzene was shown to give the enamines **5a** and **5b**, respectively. The suggested pathway involved intermediates **2**, **3**, and **4**.[2] The present paper provides additional experimental evidence for this route and considers the mechanisms of two of the steps in some detail.

The kinetics of the reaction of **1a** and **1b** with excess piperidine in benzene were examined under pseudo-first-order conditions by following the rates of release of chloride ion (titrimetric rates) and the rates of formation of enamines **5a** and **5b** (spectrophotometric rates). The results are summarized in Tables I and II.

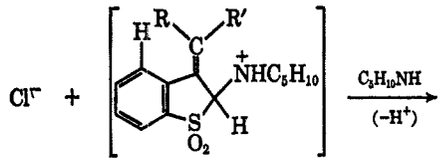
Examination of Tables I and II reveals that for tertiary chloride **1b** the titrimetric and spectrophotometric rates are equal within experimental error. In terms of the suggested reaction scheme this requires that the abnormal allylic displacement (**1b** → **2b**) be rate determining and that the rearrangement steps (**3b** → **4b** → **5b**) be rapid. (Proton removal from **2b** to give **3b** is expected to be fast.) Variation of the piperidine con-

(1) A preliminary account of part of this work has appeared: F. G. Bordwell, R. W. Hemwall, and D. A. Schexnayder, *J. Amer. Chem. Soc.*, **89**, 7144 (1967).

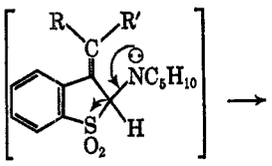
(2) F. G. Bordwell, R. W. Hemwall, and D. A. Schexnayder, *J. Org. Chem.*, **33**, 3233 (1968).



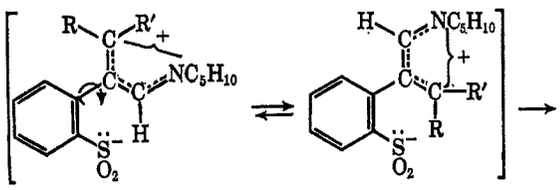
1a, R = H; R′ = Me
b, R = R′ = Me



2a, R = H; R′ = Me
b, R = R′ = Me

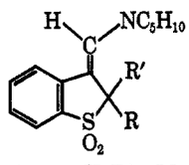


3a, R = H; R′ = Me
b, R = R′ = Me



4a, R = H; R′ = Me
b, R = R′ = Me

4a, R = H; R′ = Me
b, R = R′ = Me



5a, R = H; R′ = Me
b, R = R′ = Me

TABLE I

TITRIMETRIC RATES FOR THE REACTIONS OF 1a AND 1b WITH EXCESS PIPERIDINE IN BENZENE

Chloride[a]	Temp, °C	[Piperidine], M	k_2, M^{-1} sec^{-1} [b]	E_a, kcal/mol	ΔS^*, eu
1a	25.90	0.3017	$5.9 \pm 0.2 \times 10^{-4}$	10	−42
1a	33.80	0.3084	$9.5 \pm 0.5 \times 10^{-4}$		
1a	50.0	0.1195	$2.2 \pm 0.1 \times 10^{-3}$		
1a	50.0	0.2962	$2.0 \pm 0.1 \times 10^{-3}$		
1b	33.82	0.3084	$6.4 \pm 0.2 \times 10^{-5}$	11	−43
1b	50.0	0.2962	$1.7 \pm 0.2 \times 10^{-4}$		
1b	50.0	0.08839	$1.5 \pm 0.2 \times 10^{-4}$		

[a] The halide concentration was of the order of 10^{-3} M. [b] Calculated by dividing the pseudo-first-order rate constants by the piperidine concentration; the values are averages of at least three runs.

centration (Tables I and II) showed that the reaction was first order in piperidine.

For secondary chloride **1a** the titrimetric and spectrophotometric rates are not equal; moreover, they are not even of the same kinetic order. Whereas the titrimetric rate shows a first-order dependence on the piperidine concentration, the spectrophotometric rate does not. Instead, the rate actually decreases somewhat with increasing piperidine concentration. We interpret these results to mean that in the reaction sequence **1a** → **2a** → **3a** → **4a** → **5a** the (first order) cleavage of the intermediate **3a** to form dipolar ion **4a** is rate controlling.

The closeness of the activation energy and activation entropy values for the reactions in which halide ion is lost from the secondary chloride **1a** and the tertiary chloride **1b** supports the view that these reactions are proceeding by comparable (SN2′) mechanisms. The 13-fold faster rate for **1a** is the result of a 1 kcal/mol smaller activation energy; the activation entropies are identical within experimental error.

The activation energies and entropies derived from the spectrophotometric constants for the reaction of **1a** are both greatly increased over those derived from the titrimetric rate constants (E_a is increased by 10 kcal/mol and ΔS^* is increased by 24 eu). This is consistent with the suggested difference in rate-determining steps for halide ion loss compared with product formation.

The kinetic data indicate that in the reaction of tertiary chloride **1b** the α-(1-piperidyl) sulfone **3b** was being formed only in steady-state concentrations, but that in the reaction of secondary chloride **1a** the corresponding α-(1-piperidyl) sulfone (**3a**) was being formed as an intermediate. This was confirmed in preparative experiments. When the reaction of **1b** with piperidine was quenched near the (calculated) first half-life the product was shown by nmr analysis to consist of about 50% enamine **5b** and 50% starting chloride **1b**. On the other hand, a similar experiment with **1a** carried out for about four titrimetric half-lives gave a product containing little or no starting chloride (**1a**) or enamine (**5a**). The product of this reaction is believed to be compound **3a** on the basis of its nmr spectrum which consisted of a four-proton multiplet at δ 7.0–7.8 (aromatic protons), a one-proton doublet of doublets at 6.09 (J = 1.3 cps) assigned to the α-methinyl proton (coupled with the allyl proton), a one-proton quartet at 3.85 (J = 1.3 cps, J' = 6.7 cps) assigned to the vinyl proton (coupled with C_α and Me), a three-proton doublet at 1.42 (J = 6.7 cps) assigned to the methyl group, and a complex multiplet centered at 2.81 for the β and γ piperidino protons (the α piperidino protons were partially superimposed with the methyl doublet). This material was rearranged to enamine **5a** by refluxing in benzene for 15 hr. The absorption at δ 6.09 disappeared and a peak at 6.65 appeared (characteristic of **5a**). The rate of enamine production in methanol based on preliminary measurements of the rate of appearance of the 324-mμ band is of the order of 10^{-3} to 10^{-4} sec^{-1}.

Attempts to prepare the tertiary bromide corresponding to **1b** have thus far been unsuccessful, but the secondary bromide (**1a′**) corresponding to **1a** has been prepared;[3] rate data for its reaction with piperidine in methanol and in benzene are given in Table III.

A preparative study of the reaction of the secondary bromide (**1a′**) with piperidine in methanol revealed

(3) P. E. Sokol, Ph.D. Dissertation, Northwestern University, Aug 1959.

TABLE II

SPECTROPHOTOMETRIC RATES FOR THE REACTION OF 1a AND 1b WITH EXCESS PIPERIDINE IN BENZENE

Chloride	Temp, °C	[Piperidine], *M*	*k*	E_a, kcal/mol	ΔS^*, eu
1a	26.0	0.3207	2.7×10^{-6} sec^{-1}		
	26.0	0.3207	2.9×10^{-6} sec^{-1}		
	26.0	0.1069	4.2×10^{-6} sec^{-1}	20	−18
1a	50.0	0.3081	3.5×10^{-5} sec^{-1}		
	50.0	0.3081	3.6×10^{-5} sec^{-1}		
	50.0	0.1849	4.5×10^{-5} sec^{-1}		
1b	50.0	0.3076	1.4×10^{-4} M^{-1} sec^{-1}		
	50.0	0.3076	1.5×10^{-4} M^{-1} sec^{-1}		
	50.0	0.1846	1.4×10^{-4} M^{-1} sec^{-1}		

TABLE III

RATES OF REACTION OF SECONDARY BROMIDE (1a′) WITH EXCESS PIPERIDINE IN METHANOL

Temp, °C	[Piperidine], *M*	k_2, M^{-1} sec^{-1} [a]	*k*, sec^{-1} [b]	E_a, kcal/mol	ΔS^*, eu
25.0		$4.3 \pm 0.1 \times 10^{-4}$		15	−26
30.2		$6.5 \pm 0.1 \times 10^{-4}$			
50.0		$3.1 \pm 0.1 \times 10^{-3}$			
50.0	0.3383		3.2×10^{-4}		
50.0	0.1115		2.9×10^{-4}		
50.0		$(3.4 \pm 0.1 \times 10^{-2})$[c]			

[a] Conductometric rates measured by P. E. Sokol.[3] [b] Spectrophotometic rates. [c] Titrimetric rate in benzene.

that about equal amounts of enamine **5a** and SN2 displacement product were formed (by nmr analysis). The rate of halide release in the abnormal allylic displacement reaction with **1a′** is therefore 1.5×10^{-3} M^{-1} sec^{-1} at 50°.[4] Comparison of this value with that obtained in benzene (Table III) shows that this reaction is about 23 times *slower* in methanol than in benzene.[5]

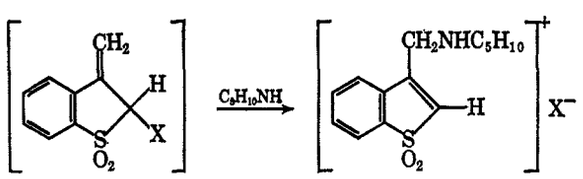
The conductometric rate constants for the reaction of **1a′** with piperidine in methanol were first order in piperidine, whereas the spectrophotometric rate constants were independent of piperidine concentration. This is comparable with the results obtained in benzene. Evidently ring opening is rate determining for secondary bromide **1a′** in methanol, just as it is for secondary chloride **1a** in benzene. The eightfold faster spectrophotometric rate for **1a′** in methanol than for **1a** in benzene indicates that rearrangement of **3a** is faster in methanol by this factor.

Comparison of the rate of halide release for **1a′** in benzene with that of **1a** reveals a Br:Cl leaving group effect of 16:1.

Discussion

SN2′ Displacement Step.—The abnormal allylic displacements for secondary chloride **1a** and **1b** with piperidine in benzene to give **2a** and **2b**, respectively, may be compared with similar (SN2′) reactions of α-methylallyl chloride with diethylamine,[6,7] or dimethylamine[8] under comparable conditions. The rate constant for **1a** with piperidine is, however, two or three powers of ten greater than those for α-methylallyl chloride with secondary amines. The acceleration in rate is due to a sharp drop in activation energy.[9,10]

In the previous paper in this series a comparable SN2′ reaction was observed with secondary halides **6** (X = Cl, Br, or I) with piperidine in methanol to give **7** (not isolated as such).[11] Here the rate constant for halide loss was estimated to be about 2.7×10^{-1} M^{-1} sec^{-1} (X = Br).



6 **7**

It is clear from these results that the sulfonyl group has a strong accelerating effect on the SN2′-type process. This is no doubt associated with its electron-withdrawing property, which reduces the electron density in the π bond and thereby increases the susceptibility of the carbon atom of the C=C bond to nucleophilic attack. The sulfonyl group may also facilitate the SN2′-type process by delocalizing the negative charge developing on the β-carbon atom of the allylic system in the transition state. The relatively small leaving-group effect observed for the reactions of the secondary bromide **1a′** and the secondary chloride **1a** with piperidine in benzene (Br:Cl = 16:1) suggests a dipolar transition state in which there is relatively little C–X bond breaking. The even smaller leaving group effect for the reaction of **6** in methanol (Br:Cl:I = 1.4:1.0:0.25)[11] suggests that in this solvent a (delocalized) dipolar intermediate

(4) For chloride **1** tautomerism to the vinyl chloride has been found to be competitive in methanol (but not in benzene) with the rate of chloride displacement [F. G. Bordwell, R. W. Hemwall, and D. A. Schexnayder, *J. Org. Chem.*, **33**, 3226 (1968)]. This is not true for bromide **1** as shown by the absence of nmr peaks characteristic of the tautomer in a reaction quenched after one half-life.

(5) The rate of reaction of tertiary chloride **1b** also is slower in methanol than in benzene. This unusual solvent effect is discussed further in the next paper in this series: F. G. Bordwell and D. A. Schexnayder, *J. Org. Chem.*, **33**, 3240 (1968).

(6) W. G. Young, J. D. Webb, and H. L. Goering, *J. Amer. Chem. Soc.*, **73**, 1076 (1951).

(7) D. C. Dittmer and A. F. Marcantonio, *ibid.*, **86**, 5621 (1964).

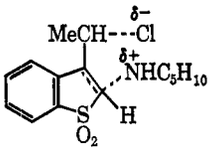
(8) W. G. Young and I. J. Wilk, *ibid.*, **79**, 4793 (1957).

(9) For diethylamine in benzene, $k = 5.8 \times 10^{-6}$ M^{-1} sec^{-1} at 60°; E_a = 15 kcal/mol; $\Delta S^* = -39$ eu.[7] For dimethylamine, $k = 1.5 \times 10^{-6}$ M^{-1} sec^{-1} at 49.6°; E_a = 18 kcal/mol; $\Delta S^* = -26$ eu.[8]

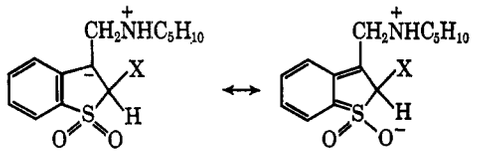
(10) The activation energies and entropies are also low for SN2 reactions in benzene solution. Thus, for the reaction of aniline with phenacyl bromide, E_a = 8.1 ($\Delta S^* = -56$) compared with E_a = 12.4 ($\Delta S^* = -33$) in methanol; see H. E. Cox, *J. Chem. Soc.*, **119**, 142 (1921).

(11) Compound **6** is formed *in situ* from the 2-halo-3-methylbenzo[*b*]thiophene 1,1-dioxide by tautomerism; **7** loses a proton and is then tautomerized to an enamine.[3]

may actually be formed. If a dipolar intermediate is formed irreversibly (*i.e.*, rate of halide loss ≫ rate of reversal of piperidine addition) the addition step would be rate determining and the leaving-group effect would be negligible.



transition state for
1a + piperidine

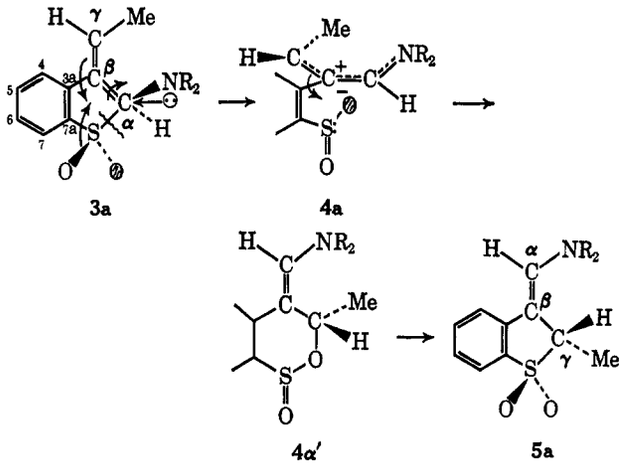


intermediate from **6** + piperidine

SNi′ Rearrangement Step.—The rearrangement of intermediates **3a** and **3b** to **5a** and **5b**, respectively, *via* dipolar ions **4a** and **4b** is related to SNi′-type rearrangements.[12] Intermediates **3a** and **3b** are α-amino sulfones. Few members of this functional class appear to have been prepared to date, which suggests that they may be labile.[13] In any event the lability of α-hydroxy sulfones[14] provides ample precedent for the strong driving force attributed herein to the 1-piperidyl group in the solvolysis of **3a** and **3b**.[15,16]

The enaminium cation part of **4a** can be formed by C–S bond rupture accompanied by a slight clockwise twist around C_α–C_β and rehybridization of C_α. If at the same time a slightly clockwise rotation occurs around C_{7a}–S and a comparable counterclockwise rotation occurs around C_{3a}–C_β, an intermediate will be formed in which an oxygen atom (shaded) of the sulfinite ion is held above the plane of the enaminium moiety (**4a**).[17,18] (This geometry is precisely that suggested for the ion pair in the SNi′ rearrangement of allylic chlorides.[12])

One would expect this to lead to the sulfinate ester **4a′**, but sulfinates are known to isomerize to sulfones,[19]



3a **4a** **4a′** **5a**

and this type of isomerism (by C–O bond cleavage and further rotation) should be particularly facile for the allylic transformation **4a′** → **5a**. According to this picture the rearrangement of **4a** to **5a** is somewhat analogous to the SNi′ rearrangement of an allyl carboxylate ester in which scrambling in the (labeled) carboxylate ion of the ion pair occurs by internal return.[20] In the present system both the cation and anion parts of the "ion pair" are ambident. Since the species is a dipolar ion rather than an ion pair, ionization and internal return can occur until the most stable species is obtained.

The limited amount of data available indicate that, as expected, the rearrangement **3a** → **5a** is faster in methanol than in benzene, a solvent of poorer ionizing power.

For the tertiary chloride **1b**, the SN2′ reaction forming **2b** is 13 times slower than that for the secondary chloride **1a** (forming **2a**). This is probably due to the steric effect associated with placing a methyl group (compared with a hydrogen atom) in opposition to the *peri* hydrogen atom (shown) in the transition state. In the rearrangement of **3b** to **5b** this same steric effect provides an accelerating factor, which is no doubt aided by the stabilization of the incipient cation by the extra methyl group. The result is that for the transformation of **1b** to **5b** in benzene the rearrangement **3b** → **5b** is rapid and the SN2′ reaction (**1b** → **2b**) is rate controlling. For the transformation of **1a** to **5a** the SN2′ step is faster and the rearrangement step (**3a** → **5a**) is slower; the latter becomes rate controlling in this series.

Registry No.—**1a**, 16934-30-8; **1b**, 16934-31-9; **1a′**, 16934-32-0.

Acknowledgment.—This investigation was supported by the Public Health Service Research Grant No. CA-07351 from the National Cancer Institute.

(12) See (a) R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 753 (1956); (b) A. Streitwieser, Jr., *ibid.*, 571 (1956); (c) P. B. D. de la Mare, "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, Chapter 2, for reviews of allylic rearrangements.

(13) E. Meyer, R. Nacke, and M. Gmeiner {*J. Prakt. Chem.*, [2] **63**, 167 (1901)} report the preparation of $(p\text{-MeC}_6H_4SO_2CH_2)_2NH$ and $p\text{-MeC}_6H_4SO_2CH_2NHC_6H_5$, which would be expected to be more stable than **3a** or **3b**. They are decomposed by alcoholic alkali. See H. Hellmann and G. Opitz, *Chem. Ber.*, **90**, 8 (1957), for an example of a facile hydrolysis of an α-amino sulfone.

(14) E. P. Kohler and M. Reimer, *Amer. Chem. J.*, **31**, 163 (1904).

(15) Note also that the RO grouping provides about a 10^9 accelerating rate on the solvolysis of alkyl halides ($ROCH_2X$ *vs.* RCH_2X).[16] The R_2N group should produce a considerably larger activating effect.

(16) See H. Böhme and K. Sell, *Chem. Ber.*, **81**, 123 (1948), and ref 12c, p 103.

(17) By analogy with allyl cations the enaminium ion would be expected to maintain its configuration.[18]

(18) W. G. Young, S. H. Sharman, and S. Winstein, *J. Amer. Chem. Soc.*, **82**, 1376 (1960); J. H. Brewster and H. O. Baeyer, *J. Org. Chem.*, **29**, 105 (1964).

(19) J. Kenyon and H. Phillips, *J. Chem. Soc.*, 1676 (1930); C. L. Arens, M. P. Balfe, and J. Kenyon [*ibid.*, 485 (1938)] report that a small amount of optically active sulfone of *retained* configurations is formed in such an isomerizaton.

(20) H. L. Goering, J. P. Blanchard, and E. F. Silversmith, *J. Amer. Chem. Soc.*, **76**, 5409 (1954); H. L. Goering and E. F. Silversmith, *ibid.*, **77**, 1129 (1955).