with the compound prepared from 2-bromo-3-methylbenzothiophene 1,1-dioxide. Concentration of the mother liquors afforded an additional 0.1 g., m.p. 170–178°, to raise the yield to 49%.

In a subsequent experiment carried out in absolute ethanol as solvent an aliquot was withdrawn, diluted to the appropriate volume and the absorbance at 325 mμ was observed in a Beckman DU spectrophotometer using in the reference cell an ethanolic piperidine solution of comparable piperidine concentration. The observed absorbance corresponded to a yield of 81% of 2-piperidine-3-methylbenzothiophene 1,1-dioxide (IVa).

(b) **Morpholine.**—A solution of 2.15 g. (0.01 mole) of 3-chloromethylbenzothiophene 1,1-dioxide and 5 ml. (0.06 mole) of morpholine in 20 ml. of benzene was heated under reflux for one hour. Evaporation of the solvent followed by washing the residue with water gave a green gum which on crystallization from ethanol gave 0.68 g. (25%) of a product, m.p. 205–220°. Recrystallization from ethanol gave yellow needles, m.p. 222–224°, undepressed on admixture of 2-morpholino-3-methylbenzothiophene 1,1-dioxide prepared from 2-bromo-3-methylbenzothiophene 1,1-dioxide.

(c) **Sodium Thiophenoxide.**—To a solution of 2.15 g. (0.01 mole) of 3-chloromethylbenzothiophene 1,1-dioxide in 10 ml. of benzene was added a fourfold excess of sodium thiophenoxide in absolute ethanol aand the reaction mixture refluxed for 3 hours. The reaction mixture was cooled and poured into cold water to give 2.56 g. (89%) of a light yellow solid, m.p. 163–167°. Recrystallization from ethanol which included a decolorization with Norite A gave white needles, m.p. 165–167°, identical with the product from the reaction of sodium thiophenoxide and 2-bromo-3-methylbenzothiophene 1,1-dioxide.

(d) **Thiourea.**—A solution of 1.0 g. (0.013 mole) of thiourea and 1.0 g. (0.0038 mole) of 3-chloromethylbenzothiophene 1,1-dioxide in 20 ml. of absolute ethanol was refluxed for 2 hours. On cooling, 1.22 g. (90%) of product was obtained, m.p. 215–230°, soften 209°. Recrystallization from a benzene–methanol mixture gave white crystals, m.p. 217–222°, soften 210°.

An ethanolic solution of the product from the reaction of 3-chloromethyl compound and thiourea had an absorbance at 287 mμ corresponding to a yield of 92% of S_N2' product.

Anal. Calcd. for $C_{10}H_{11}S_2O_2N_2Cl$: C, 41.30, H, 3.81. Found: C, 41.08; H, 3.77.

(e) **Attempted Solvolysis.**—It was possible to recover as much as 90% of 3-chloromethylbenzothiophene 1,1-dioxide from solutions of 95% alcohol or glacial acetic acid which had been refluxed for periods up to 5 days in length.

Reactions of 2-Chloromethylbenzothiophene 1,1-Dioxide with Nucleophilic Reagents. (a) Piperidine.—To a solution of 1.08 g. (0.005 mole) of 2-chloromethylbenzothiophene 1,1-dioxide in 10 ml. of benzene there was added 2.52 g. (0.03 mole) of piperidine. An immediate evolution of heat occurred. After 2 hours at room temperature the reaction mixture was filtered to yield 0.60 g. (98%) of piperidine hydrochloride. Evaporation of the filtrate to dryness followed by the addition of methanol gave 0.5 g. (40%) of product, m.p. 116–123°. Recrystallization from methanol gave white needles, m.p. 124–126°.

Anal. Calcd. for $C_{14}H_{17}O_2NS$: C, 63.85; H, 6.51; N, 5.32. Found: C, 64.34; H, 6.49; N, 5.24.

In an attempted **hydrolysis** 0.5 g. (0.002 mole) of this product dissolved in 10 ml. of 2 *N* hydrochloric acid was heated on a steam-bath for 18 hours, cooled, and neutralized with sodium hydroxide solution. This returned 0.49 g. of starting material, m.p. 123–124°, undepressed on admixture of authentic starting material.

(b) **Sodium Thiophenoxide.**—To a solution of 2.15 g. (0.01 mole) of 2-chloromethylbenzothiophene 1,1-dioxide in 10 ml. of dry benzene there was added a twofold excess of sodium thiophenoxide in absolute ethanol and the mixture refluxed for 3 hours. On cooling and adding water, 2.05 g. (71%) of product was obtained in two crops, m.p. 88–94°. Recrystallization from methanol gave white crystals, m.p. 93–95°.

Anal. Calcd. for $C_{15}H_{12}S_2O_2$: C, 62.48; H, 4.20. Found: C, 62.82; H, 4.35.

(c) **Thiourea.**—A solution of 0.5 g. (0.0025 mole) of 2-chloromethylbenzothiophene 1,1-dioxide and 0.5 g. (0.0065 mole) of thiourea in 5 ml. of benzene and 5 ml. of 95% ethanol was refluxed for 2 hours. On cooling, 0.49 g. (73%) product was obtained, m.p. 200–207° dec. Recrystallization from a methanol–benzene mixture gave white plates, m.p. 203–207° dec.

Anal. Calcd. for $C_{10}H_{11}S_2O_2N_2Cl$: C, 41.30; H, 3.81. Found: C, 41.63; H, 3.85.

Acknowledgment.—We wish to thank the Office of Naval Research and the Standard Oil Company of Indiana for financial assistance. We also wish to thank Dr. Phillip Sokol for checking several of these experiments.

EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF NORTHWESTERN UNIVERSITY]

Effect of the Leaving Group on the Rates of S_N2 and S_N2' Reactions in Allylic Systems

BY F. G. BORDWELL, PHILLIP E. SOKOL AND JAMES D. SPAINHOUR

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The rates of the displacement reaction with thiourea in methanol of the chlorides, bromides and iodides have been measured in the systems: (1) 2-halomethylbenzothiophene 1,1-dioxide (I), (2) 3-halomethylbenzothiophene 1,1-dioxide (II), (3) 3-halo-1-*p*-toluenesulfonyl-1-propene (III), (4) allyl halide and (5) *n*-propyl halide. The halides II undergo S_N2' displacement, whereas the others undergo S_N2 displacement. The RBr/RCl ratios for all of the allylic systems (I, II, III and the allyl halides) are in the range of 28 to 82. The high RBr/RCl ratio (79) for system II shows that this S_N2' reaction, and by analogy other S_N2' reactions, is concerted. The geometry of halides I and II is such that S_N2 displacement can occur only by utilizing a transition state in which the C–X bond is parallel to the orbitals of the π-bond system. The fact that the energies and entropies of activation are remarkably similar for the reactions of I, II, III and the simple allylic halides indicates that allylic systems in general utilize this transition state. Experimental evidence is thereby produced for a transition state for S_N2 and S_N2' reactions, which has been favored by several schools on theoretical grounds.

In the previous paper in this series[1] it was suggested on the basis of product analysis that 2-chloromethylbenzothiophene 1,1-dioxide (Ia) reacts with a number of nucleophilic reagents by an S_N2 mechanism, whereas 3-chloromethylbenzothiophene 1,1-dioxide (IIa) reacts with these same reagents by an S_N2' mechanism. A comparison of the rates of reaction of these chlorides and the corresponding bromides and iodides with thiourea has now been made in order to gain further information concerning the course of these reactions. Extension of the study to the open-chain analog III, and comparison of the rates with those of the corresponding allyl and propyl compounds has

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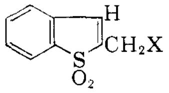
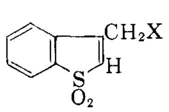
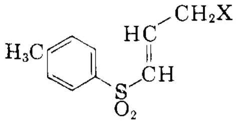
[1] F. G. Bordwell, F. Ross and J. Weinstock, THIS JOURNAL, **82**, 2878 (1960).



Ia, X = Cl
Ib, X = Br
Ic, X = I



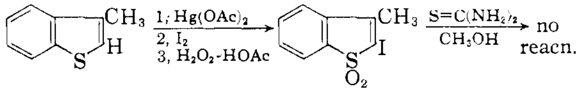
IIa, X = Cl
IIb, X = Br
IIc, X = I



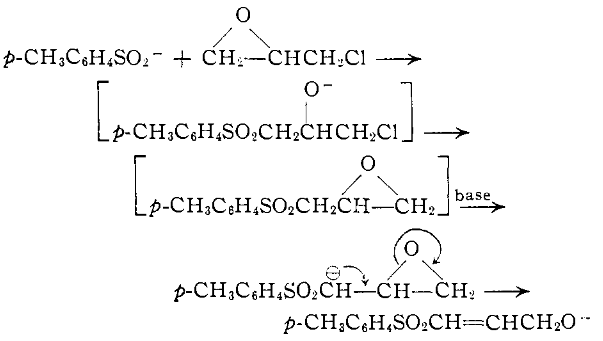
IIIa, X = Cl
IIb, X = Br
IIIc, X = I

revealed some information concerning the reaction mechanism, including a picture of the geometry of the transition state in these reactions.

The structures of Ia and IIa follow from their modes of preparation.[1] The corresponding bromides (Ib and IIb) and iodides (Ic and IIc) were obtained from the chlorides (Ia and IIa) by the reaction of sodium bromide or sodium iodide in acetone. These SN2 displacements are normal for Ia, but are the only nucleophilic displacements which we have thus far encountered where IIa reacts by an SN2 rather than an SN2′ mechanism. The assigned structures of Ib and IIb are secure from their modes of preparation, since the most reasonable alternatives, 3-bromo-2-methylbenzothiophene 1,1-dioxide (for Ib) and 2-bromo-3-methylbenzothiophene 1,1-dioxide (for IIb) are known,[1,2] and these compounds fail to react with thiourea under the conditions of the reaction herein described. The alternative structure for IIc, 2-iodo-3-methylbenzothiophene 1,1-dioxide, was excluded by synthesis of this compound. It, too, failed to react with thiourea in methanol solution.



Compound IIIa has been prepared previously from the corresponding alcohol.[3] The corresponding bromide IIIb was prepared from the alcohol and phosphorous tribromide, and the iodide IIIc was obtained from IIIa and sodium iodide. All three halides had a strong band at 10.4 μ (*trans*-CH=CH—), which is consistent with the assigned structures.

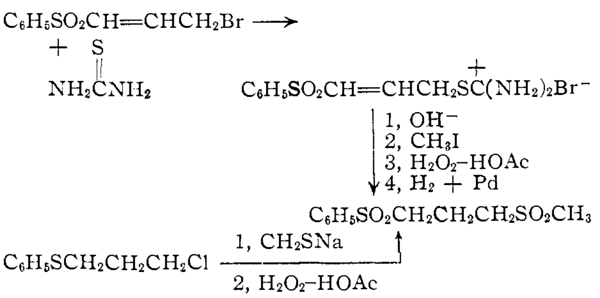


$$p\text{-}CH_3C_6H_4SO_2^- + \overset{\overset{O}{/\ \backslash}}{CH_2—CHCH_2Cl} \longrightarrow \left[p\text{-}CH_3C_6H_4SO_2CH_2\overset{O^-}{\overset{|}{C}}HCH_2Cl\right] \longrightarrow \left[p\text{-}CH_3C_6H_4SO_2CH_2\overset{\overset{O}{/\ \backslash}}{CH—CH_2}\right] \xrightarrow{base}$$

$$p\text{-}CH_3C_6H_4SO_2\overset{\ominus}{C}H—\overset{\overset{O}{/\ \backslash}}{CH—CH_2} \longrightarrow p\text{-}CH_3C_6H_4SO_2CH{=}CHCH_2O^-$$

Eight halides (Ia-Ic, IIa-IIc, IIIa-IIIb) reacted with thiourea to give high yields of sharp-melting thiuronium salts. The thiuronium salt of IIIc decomposed on attempted purification. It is believed that the products from Ia-Ic and IIIa-IIIc represent clean SN2 reactions, whereas those from IIa-IIc arise from clean SN2′ reactions. Since the halides themselves are inert to methanolysis, it is highly unlikely that these products are the result of rearrangements subsequent to the displacements. The structures of the thiuronium salts formed from Ib-Ic and from IIb-IIc are secure since their ultraviolet spectra in each instance corresponded with those from Ia or IIa, respectively.[1] The structure of the thiuronium salt from IIa was established further by hydrolysis to 2-keto-3-methyl-2,3-dihydrobenzothiophene 1,1-dioxide (isolated as its 2,4-dinitrophenylhydrazone derivative[1]), showing that the group was indeed attached to the 2-position. When the hydrolysis was carried out in the presence of methyl iodide, 2-methylmercapto-3-methylbenzothiophene 1,1-dioxide was isolated, which was found to be identical with the SN2′ product formed from IIa and the sodium salt of methanethiol. This established the presence of the C_2–S bond in the thiuronium salt.

It remained to establish the structures of the thiuronium salts from IIIa-IIIb. The thiuronium salts from IIIa and IIIb each had an absorption maximum at 10.4 μ (*trans* CH=CH) corresponding to similar bands in the halides, strongly suggesting that they were SN2 products. The presence of a maximum at 11–11.5 μ for each thiuronium salt raised the question of contamination by an SN2′ product, the —CH=CH_2 grouping of which should have a maximum this region (no 10.1 μ band, which is also characteristic of this group, was present). However, a band in the 11–11.5 μ region has been observed for other compounds of type $ArSO_2CH{=}CHCH_2Y$ (Y = OH, Cl, Br, I, SO_2CH_3, $SO_2C_6H_5$), several of which can be shown not to contain the —CH=CH_2 group. Further structural evidence was obtained by hydrolysis of the thiuronium salt from $C_6H_5SO_2CH{=}CHCH_2Br$ (C_7H_7 of III replaced by C_6H_5), and identification of the thiol produced, as shown.



$$C_6H_5SO_2CH{=}CHCH_2Br + \underset{NH_2CNH_2}{\overset{S}{\|}} \longrightarrow C_6H_5SO_2CH{=}CHCH_2\overset{+}{S}C(NH_2)_2Br^-$$

$$\xrightarrow{1,\ OH^-;\ 2,\ CH_3I;\ 3,\ H_2O_2\text{–}HOAc;\ 4,\ H_2 + Pd} C_6H_5SO_2CH_2CH_2CH_2SO_2CH_3$$

$$C_6H_5SCH_2CH_2CH_2Cl \xrightarrow[2,\ H_2O_2\text{–}HOAc]{1,\ CH_3SNa} C_6H_5SO_2CH_2CH_2CH_2SO_2CH_3$$

The rates of reaction for Ia-Ic, IIa-IIc and IIIa-IIIc with excess thiourea in methanol solution were determined conductometrically at 25 and 50°. None of the halides was observed to undergo methanolysis over periods of time equivalent to or longer than those used for determining the rates. Using about a 10-fold excess of thiourea, pseudo first-order plots of log $[R/(R - R_E)]$ against time gave good straight lines for most halides.[4] This es-

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(2) Unpublished work from this Laboratory.

(3) C. C. J. Culvenor, W. Davies and W. E. Savige, *J. Chem. Soc.*, 2198 (1949). The background of information now available on displacement and elimination reactions makes the following mechanistic sequence appear highly probable for the formation of this alcohol from sodium *p*-toluenesulfinate and epichlorohydrin in aqueous alcohol

(4) Alternatively, the rate constants were determined by use of the Guggenheim method, [see "Kinetics and Mechanism," by A. A. Frost and R. G. Pearson, John Wiley and Sons, Inc., New York, N. Y., 1953, pp. 48–49], which avoids errors resulting from the uncertainty in determining the equilibrium resistance.

TABLE I

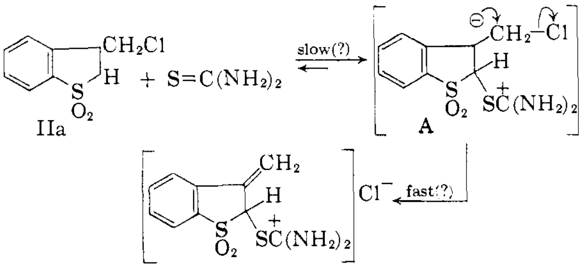
RATES OF REACTION OF *n*-PROPYL AND ALLYL HALIDES WITH THIOUREA IN METHANOL AT 25 AND 50°

Bromide	Reaction type	k_2 at 25°, M^{-1} sec.$^{-1}$	Relative rates at 25°	k_2 at 50°, M^{-1} sec.$^{-1}$	Cl:Br:I	Br:I
$CH_3CH_2CH_2Br$	SN2	1.67×10^{-5}	1.0	1.70×10^{-4}	1.0:128:556	1.0:4.3
$CH_2{=}CHCH_2Br$[a]	SN2	2.28×10^{-3}	137	1.38×10^{-2}	1.0:62:183	1.0:3.0
Ib	SN2	4.92×10^{-3}	295	2.62×10^{-2}	1.0:28:75	1.0:2.7
IIb	SN2′	1.32×10^{-2}	790	6.91×10^{-2}	1.0:79:230	1.0:2.9
IIIb	SN2	8.48×10^{-3}	507	4.68×10^{-2}	1.0:82:312	1.0:3.8

[a] R. G. Pearson, S. H. Langer, F. V. Williams and W. J. McGuire, THIS JOURNAL, 74, 5130 (1952), report $k_2 = 5.5 \times 10^{-3}$ at 35°.

tablishes the reaction as being first order in halide. The second-order constants were calculated by dividing the observed first-order rate constants (2.303 × slope of plotted lines) by the thiourea concentration. Since runs at the same temperature in which the halide and thiourea concentrations were varied gave good agreement in second-order rate constants, the reaction (SN2 and SN2′) must be first order in thiourea as well as halide.

Although SN2′ reactions are logically assumed to be concerted,[5] there is no actual experimental evidence in the literature to exclude an addition–elimination type mechanism, such as that written for the reaction of IIa with thiourea. According to this scheme, addition to the allylic double bond to form intermediate A might occur as the slow, rate-controlling step. A mechanism of this type



must be considered, at least for SN2 reactions of IIa, since the $C_2{=}C_3$ bond in benzothiophene 1,1-dioxide is highly susceptible to addition by nucleophilic reagents.[6]

Concerted Nature of SN2′ Reactions.—One test of a mechanism of the addition–elimination type is to measure the effect on the rate of changing the nature of the leaving group. In SN2 displacements, where bond-making and bond-breaking are known to be simultaneous, changing the leaving group from Cl to Br results in an increase in rate of roughly 30–40-fold.[7] If an intermediate such as A is formed in a slow step the nature of the leaving group would be expected to have relatively little effect. The rate data summarized in Table I provide the information needed to satisfy this test, show the relative rates of systems I, II and III, and allow comparison of these rates with those of *n*-propyl and allyl halides.

The PrCl:PrBr ratio of 1.0:128 and the PrBr:PrI ratio of 1.0:4.3 given in Table I are considerably outside the 30–40-fold and 2.0–2.5-fold ranges for RCl:RBr and RBr:RI, respectively, mentioned for SN2 reactions of alkyl halides,[7] but this is true for a number of other SN2 reactions,[8] and it seems evident that the range is larger than supposed. The allyl chloride to allyl bromide rate ratio for the reaction of ethoxide ion is 1.0 to 58,[8a] which agrees well with that found with thiourea (Table I).

The results recorded in Table I clearly indicate that bond-breaking is of comparable importance in the SN2′ displacement reaction which II is undergoing as in the SN2 displacements occurring with the other allylic halides (I, III and allyl halides). If II were to react with thiourea by a mechanism involving formation of intermediate A in a rate-determining step its RBr/RCl ratio would be small, possibly even less than one, since the addition step should occur more rapidly with the chloride than with bromide.[9] Actually, the RBr/RCl value for II is about three times as large as that for I and of the same order of magnitude as that found in the simple allyl halides and in III.[10]

We conclude from these data that the SN2′ reaction of II is concerted in nature. Since intermediate formation is much more likely for II, where the electrons of the C=C bond have been delocalized by the presence of the strong electron-withdrawing sulfonyl group, than in other systems known to undergo SN2′ reactions, this provides experimental justification also for the assumption of the concerted nature for SN2′ reactions in general.

Effect of Sulfonyl Group on SN2 and SN2′ Reactivity of Allyl Halides.—Examination of Table I shows that at 25° I, II and III (chlorides, bromides and iodides) are all 2–5 times as reactive as the corresponding unsubstituted allyl halides toward thiourea. This agrees with previous work in which the presence of a γ-sulfonyl group has been shown to activate allyl halides in SN2 reactions where the nucleophile was iodide ion[11] and thiosulfate.[12]

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(5) R. H. DeWolfe and W. G. Young, *Chem. Revs.*, **56**, 753 (1956).

(6) F. G. Bordwell and W. H. McKellin, THIS JOURNAL, **72**, 1985 (1950).

(7) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 339.

(8) (a) M. Conrad and C. Brückner, *Z. physik. Chem.*, **4**, 631 (1889), report RCl:RBr:RI = 1.0:62:131 for OEt^- + PrX; (b) B. V. Tronov and E. A. Krüger, *J. Russ. Phys. Chem. Soc.*, **58**, 1270 (1926); *C. A.*, **21**, 3887 (1927), report RCl:RBr = 1.0:113 for the reaction of piperidine with isobutyl halides.

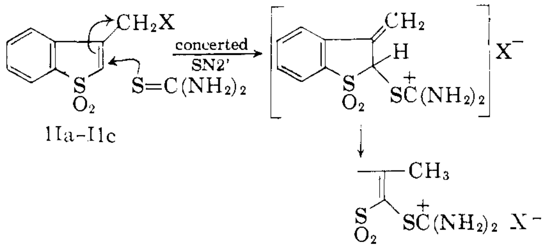
(9) In nucleophilic aromatic substitution, where intermediates similar to A are postulated, chlorides are sometimes of comparable or greater reactivity than are the corresponding bromides; see J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 335 (1951).

(10) It is conceivable, although highly unlikely, that intermediate A could be formed in a rapid reversible step, and that elimination of halide from this carbanion would be rate determining. Again the RBr/RCl ratio would be expected to be lower than that observed, since the rate will then depend on the concentration of intermediate, which will be greater for the chloride (inductive effect of Cl greater than Br), and the sensitivity of the carbanion to changes in the nature of the leaving group would not be high. The failure of thiourea to add to benzothiophene 1,1-dioxide under these conditions is another argument against this reaction path.

(11) F. G. Bordwell and G. D. Cooper, THIS JOURNAL, **73**, 5184 (1951).

(12) K. Akagi, S. Oae and M. Murakami, *ibid.*, **78**, 4034 (1956).

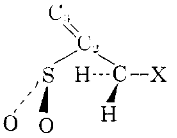
The question arises as to why halides Ia-Ic and IIIa-IIIc react with thiourea and other nucleophiles preferentially by the SN2 pathway, whereas for IIa-IIc the SN2′ mechanism is strongly favored. It seems probable to us that the prime effect in promoting SN2′ reactions in system II is the delocalization of the π-electrons by the sulfonyl group through the β- as well as the γ-position. This effect operates just as strongly to favor the SN2′ mechanism in system I as in system II, but it is opposed in the former by a conjugative effect. An SN2′ mechanism for Ia-Ic would require that conjugation of the $C_2{=}C_3$ bond with both the benzene ring and sulfonyl group be disrupted in the transition state. This could raise the activation energy for this process by several kcal. per mole. In IIa–IIc it will be noted that the SN2′ mechanism can operate without loss of Ar–C=C conjugation, since the C=C bond being formed as well as the one being disrupted is in conjugation with the benzene ring. Direct conjugation with the sulfonyl group is destroyed during the SN2′ reaction (conjugation through the benzene ring remains), but is restored by a subsequent tautomerization.



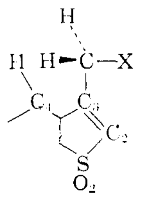
IIa–IIc

In IIIa-IIIc the sulfonyl group probably activates SN2′ displacement by delocalizing the π-electrons of the C=C bond, but SN2 displacement is favored by a conjugative effect, whereas SN2′ displacement can occur only at the expense of destroying the SO_2—C=C conjugation. The observed preference for SN2 displacement of IIIa-IIIc can therefore be rationalized. Since IIa-IIc have an option of SN2 or SN2′ similar to that of IIIa-IIIc, it would appear that delocalization from the β-position may be of considerable importance to SN2′ attack at the C=C bond.

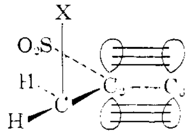
Structure of the Transition State for Allylic SN2 and SN2′ Reactions.—The conformations in which I and II can undergo SN2 attack by nucleophilic reagents are in each instance severely limited by their geometries. The most stable conformations for halides I and II are no doubt conformations I$_1$ and II$_1$ in which the axis of the C–X bond is in the plane of the C–C$_2$–C$_3$ bond or C$_2$–C$_3$–C bond, respectively, and is *perpendicular* to the plane of the π-bond. However, in this conformation the CH_2X group is completely screened from attack of nucleophilic agents by the SO_2 group in I$_1$ and by the *peri* hydrogen on C$_4$ in II$_1$. The magnitude of the steric effect may be judged by the fact that 180° rotation around the C$_2$–CH_2X or C$_3$–CH_2X bonds from conformations I$_1$ and II$_1$ cannot be realized, even when X is chlorine, due to interference of the Cl atom with the SO_2 group in Ia and with the *peri* hydrogen in IIa. This situation is of course intensified in Ib, Ic, IIb and IIc. As a consequence of these steric effects halides I and II can undergo SN2 displacement only in conformations comparable to I$_2$ and II$_2$ *in which the axis of the C–X bond is parallel to the C$_2$–C$_3$ π-bond orbitals.* It is gratifying to find that Winstein has predicted that in the SN2′ transition state the nucleophile will utilize just such a transition state.[13] It is possible to understand, then, the high susceptibility of halides IIa-IIc SN2′ displacement, since the only transition state open to them for reaction is one believed to be favorable to SN2′ displacement. In the reaction of IIa approach of the nucleophile is represented as being *cis* to the leaving Cl group in accordance with Winstein's prediction[13] and the geometry demanded by the experiments of Stork and White.[14]



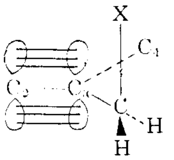
conformation I$_1$



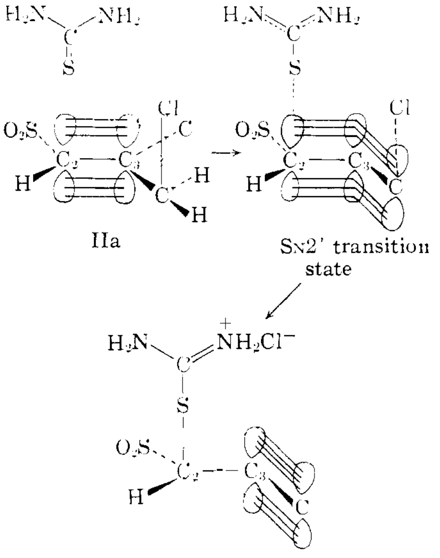
conformation II$_1$



conformation I$_2$



conformation II$_2$



Consideration of the geometry of Ia-Ic shows that for these halides the SN2 displacement must utilize a transition state similar to that of the SN2′ reaction.

The transition states for the SN2 reactions of Ia-Ic and the SN2′ displacements of IIa-IIc were prescribed by the peculiar geometry of these systems. This could conceivably lead to a more negative entropy of activation for these systems than for ordinary allylic systems. Also, these transition

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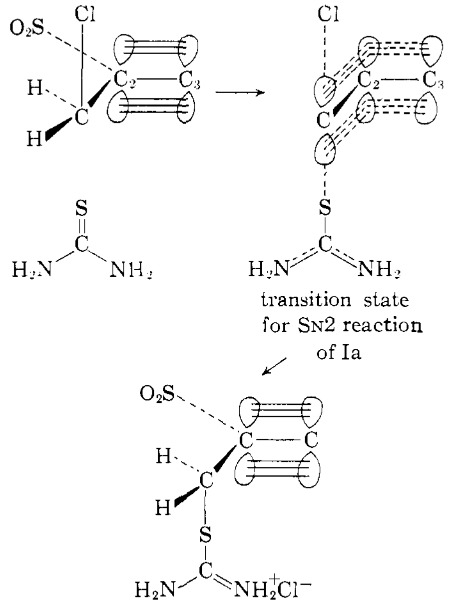
(13) Postulate of S. Winstein cited by W. G. Young, I. D. Webb and H. L. Goering, This Journal, **73**, 1079 (1951).

(14) G. Stork and W. N. White, *ibid.*, **75**, 4119 (1953).



states require the C–X bond to be parallel to orbitals of the π-bond system, and the repulsions so produced could lead to an increase in activation energy over that of ordinary allylic systems if the latter utilize a transition state which avoids such repulsions. Examination of Table II in which the entropies and energies of activation of I and II are compared with III, which does not have the geometric restrictions of I and II, and with ordinary allylic halides, fails to reveal any appreciable differences between the various allylic halides. Indeed, the figures for the simple allylic halides are remarkably close to those for the more complex halides. The 2–5-fold faster rates for the allylic halides containing the sulfonyl group is seen to be due primarily to a small decrease in the activation energy. The 137–507 faster rates for the allylic halides than for propyl halides is caused primarily, at least for the chlorides and bromides, by substantial decreases in the activation energies. These decreases in activation energy can be accounted for on the basis of the transition state shown for reaction of Ia, since this allows conjugation of the orbital system of the bonds being formed and broken during reaction with the π-bond orbitals and those of the sulfonyl group.

TABLE II

ACTIVATION ENERGIES AND ACTIVATION ENTROPIES FOR THE REACTION OF THIOUREA WITH PROPYL AND ALLYL HALIDES IN METHANOL AT 25°

	Ea, kcal. per mole[a]			$\Delta S^{\ddagger}$, e.u.[a]		
Halide	Chloride	Bromide	Iodide	Chloride	Bromide	Iodide
$CH_3CH_2CH_2X$	21.6	17.8	14.6	−19.5	−22.5	−30.5
$CH_2{=}CHCH_2X$	15.8	13.7	13.3	−27.9	−26.5	−25.9
Ia–Ic	14.3	12.8	13.6	−29.9	−28.2	−23.5
IIa–IIc	14.3	12.7	12.5	−29.9	−26.6	−24.8
IIIa–IIIc	13.7	13.1	12.8	−32.9	−25.8	−24.5

[a] The absolute accuracy of these figures is no better than two significant figures, but since all data were compiled by a single investigator the relative accuracy may be great enough to warrant three significant figures.

It may be concluded from the close correspondence of the entropies and energies of activation that the transition states demanded for halides I and II by their peculiar geometry are identical with those used by other allylic halides which have a freer choice. The energetic advantages of this transition state for SN2 displacements in allylic halides were pointed out some time ago by Dewar.[15] The assumption of this transition state for SN2 displacements in allylic and benzyl systems has since been put to good advantage by Streitwieser.[16]

Adopting this transition state, SN2 rate accelerations produced in allylic systems by electron-withdrawing γ-substituents, such as $ArSO_2$ (ref. 11 and 12 and halides I, II, and III), CN[11] and Cl[5], could operate by decreasing the C–X *vs.* π-bond repulsions and by increasing the extent of conjugation. Furthermore, this transition state explains the relative unimportance of the bulk of the nucleophile in SN2′ displacements,[5] and predicts no interference in SN2 displacements from γ-substituents which are *cis* to the $-CH_2X$ group. In contrast, the assumption of other transition states for allylic SN2 displacements leads to the conclusion that the reaction of the *cis* isomer should be less favored than the *trans*.[12] A near equivalence of rates and activation energies, such as observed in the reaction of sodium thiosulfate in 50% alcohol with *cis*- and *trans*-1,3-dichloropropenes,[12] thus finds a ready explanation. The fact that the *cis* isomer in allylic systems often reacts more rapidly than the *trans*[5] can be accommodated, and perhaps may find explanation as a polarizability effect.[17]

The effect of the $ArSO_2$ group on the rates of SN2 and SN2′ reactions of allylic halides is worthy of special comment. The 2–5-fold increase in SN2 rate and the decrease in activation energy on substitution of γ-$ArSO_2$ into the allylic system (compare allyl bromide with Ib and IIIb in Table I) supports our previous conclusion[11] that the greater than 100-fold retarding effect of an α-$ArSO_2$ group on SN2 reactions of alkyl halides is not caused by an electronic effect, but rather by a steric effect. The $ArSO_2$ group when operating from β-and/or γ-positions in II must accelerate the SN2′ displacements much more than it does SN2 displacements. This conclusion comes from the fact that IIb reacts 5.8 times as rapidly with thiourea by an SN2′ mechanism as allyl bromide does by an SN2 mechanism. The extent of SN2′ reaction of thiourea with allyl bromide is unknown,[18] but is probably small. It seems likely that the $ArSO_2$ group in IIb has increased the rate of the SN2′ reaction by a factor of 20–500 or more, whereas the $ArSO_2$ group in Ib and IIIb causes only a 2–5-fold increase in SN2 rate relative to allyl bromide. If, as we have concluded, the SN2 and SN2′ displacements have similar transition states, a γ-$ArSO_2$ group performs the same functions for the two processes, but, by delocalization of the electrons, γ and β-$ArSO_2$ groups render the C=C bond much more susceptible to attack by the nucleophile, and

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[15] M. J. S. Dewar, "Electronic Theory of Organic Chemistry," Oxford University Press, Amen House, London, E.C. 4, 1949, p. 73.

[16] A. Streitwieser, Jr., *Chem. Revs.*, **56**, 574 (1956).

[17] J. F. Bunnett, THIS JOURNAL, **79**, 5969 (1957).

[18] Using C^{14}-labeled allyl chloride W. G. Young and I. J. Wilk have shown that some SN2′ displacement occurs between allyl bromide and dimethylamine (25% SN2′), and trimethylamine (7% SN2′) in benzene solution (see p. 773 of ref. 5).

in this way the SN2′ process can be accelerated more than the SN2 process.[19]

Experimental[20]

2-Bromomethylbenzothiophene 1,1-Dioxide (Ib). Method A.—A mixture of 2.6 g. (0.016 mole) of 2-hydroxymethylbenzothiophene[21] and 8.1 g. (0.03 mole) of phosphorous tribromide was heated for 5 minutes and then poured onto 200 ml. of ice-water. Three extractions with 20-ml. portions of ether followed by drying over anhydrous sodium sulfate and evaporation afforded a brown oil which gave a positive test with silver nitrate. The oil was dissolved in 10 ml. of glacial acetic acid and then cooled. To this solution was added 5.3 g. (0.10 mole) of 40% peracetic acid and the resulting solution was allowed to sit at room temperature overnight. Treatment with 150 ml. of ice-water followed by filtration and drying yielded 3.5 g. (85%) of an amorphous yellow solid melting at 120–130°. Recrystallization from a benzene–hexane mixture raised the melting point to 128–130° and a second recrystallization from methanol afforded a pale yellow crystalline material melting at 129–130°.

Anal. Calcd. for $C_9H_7BrO_2S$: C, 41.71; H, 2.72. Found: C, 41.62; H, 2.82.

Method B.—A solution of 1.0 g. (0.0044 mole) of 2-chloromethylbenzothiophene 1,1-dioxide, 3.0 g. (0.03 mole) of sodium bromide and 50 ml. of dry acetone was refluxed for 72 hours and then poured onto 200 ml. of ice-water to give a pale yellow solid. Filtration and drying yielded 0.9 g. (78%) of a solid melting at 110–114°. Two recrystallizations from methanol afforded yellow crystals melting at 129–130° which did not depress the melting point of the material prepared in (A).

2-Iodomethylbenzothiophene 1,1-Dioxide (Ic).—A solution of 2.0 g. (0.0077 mole) of 2-chloromethylbenzothiophene 1,1-dioxide in 25 ml. of dry acetone was added to 10.0 g. (0.067 mole) of sodium iodide in 35 ml. of dry acetone. The reaction mixture was allowed to sit in the cold room for 3 hours, giving a brown solution and a yellow precipitate at the end of the reaction time. After pouring onto 200 ml. of ice-water, filtering and drying, 2.2 g. (93%) of a yellow solid melting at 133–143° was obtained. Recrystallization from a benzene–hexane mixture raised the melting point to 147–148° and a second recrystallization afforded pale yellow crystals melting at 150–151°.

Anal. Calcd for $C_9H_7IO_2S$: C, 35.30; H, 2.30. Found: C, 35.87; H, 2.26.

3-Bromomethylbenzothiophene 1,1-Dioxide (IIb).—A mixture of 5.0 g. (0.023 mole) of 3-chloromethylbenzothiophene 1,1-dioxide, 10.0 g. (0.097 mole) of sodium bromide and 300 ml. of dry acetone was refluxed for 43 hours. After pouring onto 700 ml. of ice-water, filtering, and drying 5.5. g. (92%) of white crystals melting at 133–135° were obtained which did not depress the melting point of a sample of IIb prepared by a bromomethylation reaction.[22] Recrystallization from a benzene–hexane mixture yielded colorless crystals melting at 138–139°.

Anal. Calcd. for $C_9H_7BrO_2S$: C, 41.71; H, 2.72. Found: C, 41.37; H, 2.80.

3-Iodomethylbenzothiophene 1,1-Dioxide (IIc).—A solution of 12.0 g. (0.056 mole) of 3-chloromethylbenzothiophene 1,1-dioxide in 50 ml. of dry acetone was mixed with 30 g. (0.20 mole) of sodium iodide in 100 ml. of acetone. The reaction mixture was allowed to stand at room temperature for 4 hours and was then poured onto 500 g. of crushed ice. After allowing the ice to melt, the solid was separated by filtration and air-dried to give 16.0 g. (93%) of a pale brown solid melting at 144–148° dec. Recrystallization was effected from 95% ethanol to give pale yellow cottony crystals melting at 151–152° dec. The analytical sample prepared by a second recrystallization also melted at 151–152° dec.

Anal. Calcd. for $C_9H_7IO_2S$: C, 35.30; H, 2.30. Found: C, 35.55; H, 2.31.

2-Mercuriacetoxy-3-methylbenzothiophene.—A solution of 4.9 g. (0.033 mole) of 3-methylbenzothiophene, 15.9 g. (0.050 mole) of mercuric acetate and 70 ml. of methanol was refluxed for one hour. A solid settled out after about 10 minutes. At the end of the reflux period the reaction mixture was cooled and filtered. The white solid thus obtained was boiled with 200 ml. of 95% ethanol for 2 hours and then filtered hot through a büchner funnel filled with Filter-cel. Upon cooling, 8.0 g. of a white solid settled out. Filtration and concentration yielded an additional 2.0 g. The total yield was 10.0 g. (75%) which melted at 190–191°.

Anal. Calcd. for $C_{11}H_{10}O_2SHg$: C, 32.47; H, 2.48. Found: C, 32.60; H, 2.58.

2-Iodo-3-methylbenzothiophene 1,1-Dioxide.—To a solution of 8.0 g. (0.02 mole) of the mercury compound in 100 ml. of chloroform was added a mixture of 5.1 g. (0.02 mole) of iodine in 25 ml. of chloroform. The resulting reaction mixture was stirred overnight and filtered, and the filtrate was washed with 10% sodium thiosulfate and water. After drying over sodium sulfate and removing solvent under reduced pressure, a dark brown oil (2-iodo-3-methylbenzothiophene) was obtained.

The oil was dissolved in 50 ml. of glacial acetic acid and 10 ml. of 30% hydrogen peroxide. After refluxing for 45 minutes the reaction mixture was poured onto 200 g. of crushed ice. A brown solid weighing 4.3 g. (70%) was obtained which melted at 145–155° dec. Two recrystallizations from methanol afforded a very pale brown crystalline material melting at 172–173° dec.

Anal. Calcd. for $C_9H_7IO_2S$: C, 35.30; H, 2.30. Found: C, 35.00; H, 2.32.

Attempted Reaction of 2-Iodo-3-methylbenzothiophene 1,1-Dioxide with Thiourea.—A solution of 0.25 g. of the iodosulfone, 0.25 g. of thiourea and 15 ml. of absolute ethanol was refluxed for 2 hours and then poured into 100 ml. of water. The solid obtained after filtration melted at 172–173° dec. and did not depress the melting point of the starting material.

3-Chloro-1-*p*-toluenesulfonyl-1-propene (IIIa).—Using a variation of the method described[3] a mixture of 2.0 g. of 3-*p*-toluenesulfonyl-2-propen-1-ol and 2.5 g. of phosphorus pentachloride was heated for 10 minutes and then poured onto 50 ml. of ice-water. After waiting 5 minutes the water-halide mixture was extracted with three 15-ml. portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate and filtered. The ether filtrate was cooled in an ice-bath and 200 ml. of dry pentane was added slowly with swirling. Fifteen minutes after addition large feathery white crystals settled out. Filtration afforded 1.3 g. (65%) of a crystalline material melting at 53–54° (reptd.[3] m.p. 58°). Evaporation of the mother liquors yielded 0.3 g. (15%) of white crystals melting at 50–53°. A second recrystallization from ether–pentane gave the material melting at 53–54° used in the kinetic studies.

3-Bromo-1-*p*-toluenesulfonyl-1-propene (IIIb).—In a manner similar to the preparation of IIIa, 5.0 g. (0.024 mole) of the alcohol and 15 g. (0.055 mole) of phosphorus tribromide gave a total yield of 4.6 g. (70%) of IIIb melting at 65–66° (reptd.[3] m.p. 65–66°).

3-Iodo-1-*p*-toluenesulfonyl-1-propene (IIIc).—A solution of 1.0 g. (0.0043 mole) of IIIa, 3.0 g. (0.02 mole) of sodium iodide and 25 ml. of dry acetone was refluxed for 24 hours, poured onto ice, and then filtered to give 1.2 g. (86%) of a brown amorphous solid melting at 65–70°. Two recrystallizations from ether–pentane, as previously described, afforded colorless crystals melting at 73–74° (reptd.[3] m.p. 75°).

Reaction of Ib with Thiourea.—A mixture of 0.60 g. (0.0023 mole) of Ib, 0.50 g. (0.0066 mole) of thiourea, 5 ml. of benzene and 5 ml. of absolute ethanol was refluxed for 2 hours and then cooled. The solid thus deposited weighed 0.6 g. (78%) and melted at 205–212°. Two recrystallizations from methanol afforded the analytical sample melting at 220–222° dec. whose ultraviolet spectrum had no maximum in the 250–330 mμ region.

Anal. Calcd. for $C_{10}H_{11}S_2O_2N_2Br$: C, 35.82; H, 3.31; N, 8.36. Found: C, 35.79; H, 3.11; N, 8.06.

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(19) P. B. D. de la Mare and C. A. Vernon, *J. Chem. Soc.*, 3628 (1952), have shown that electron-withdrawing α-substituents (Cl) may also accelerate SN2′ processes by reducing the C=C bond electron density through induction.

(20) Carbon, hydrogen and nitrogen analyses were performed by Miss Hilda Beck. Ultraviolet spectra were determined on a Beckman DK recording spectrophotometer. Infrared spectra were determined on a Baird recording spectrophotometer using potassium bromide pellets or chloroform as the medium for solution. Melting points and boiling points are uncorrected.

(21) F. F. Blicke and D. G. Sheets, This Journal, **71**, 2856 (1949).

(22) J. Weinstock, unpublished results.

Reaction of Ic with Thiourea.—A mixture of 1.0 g. (0.0033 mole) of Ic, 0.6 g. (0.0079 mole) of thiourea, 10 ml. of benzene and 7 ml. of absolute ethanol was refluxed for 0.5 hour and then cooled. The reaction mixture deposited 1.0 g. (79%) of a yellow-brown solid melting at 165–175°. Recrystallization from absolute ethanol gave colorless crystals melting at 184–185°. This compound also failed to display an absorption maximum in the 250–330 mμ region.

Anal. Calcd. for $C_{10}H_{11}IN_2O_2S_2$: C, 31.42; H, 2.90; N, 7.34. Found: C, 31.70; H, 2.77; N, 7.35.

Reaction of IIb with Thiourea.—A solution of 1.0 g. (0.013 mole) of thiourea, 1.0 g. (0.0039 mole) of IIb and 20 ml. of absolute ethanol was refluxed for 2 hours. Upon cooling, the solution deposited 1.2 g. (92%) of a solid melting at 205–215°. Two recrystallizations from a benzene–methanol–hexane mixture gave the analytical sample of S-[2-(3-methyl-1,1-dioxybenzothienyl)]-isothiuronium bromide melting at 234–235° dec.; λ_{max} 286 mμ, log ϵ_{max} 4.33 (in ethanol).

Anal. Calcd. for $C_{10}H_{11}BrN_2O_2S_2$: C, 35.82; H, 3.31; N, 8.36. Found: C, 36.18; H, 3.27; N, 8.19.

Reaction of IIc with Thiourea.—In a manner similar to its bromo-analog 1.0 g. (0.0033 mole) of IIc, 1.0 g. (0.013 mole) of thiourea and 20 ml. of absolute ethanol gave a 69% yield of **S-[2-(3-methyl-1,1-dioxybenzothienyl)]-isothiuronium iodide**. The analytical sample melted at 215–216° dec.; λ_{max} 286 mμ, log ϵ_{max} 4.37 (in ethanol).

Anal. Calcd. for $C_{10}H_{11}IN_2O_2S_2$: C, 31.42; H, 2.90; N, 7.34. Found: C, 30.91; H, 2.91; N, 7.20.

Reaction of IIIa with Thiourea.—A solution of 2.308 g. (0.0100 mole) of IIIa, 0.761 g. (0.0100 mole) of thiourea and 20 ml. of absolute methanol was refluxed for 2 hours and then evaporated under a stream of air to give a colorless oil. Addition of 4 ml. of ethyl acetate and 4 ml. of anhydrous ether followed by evaporation under an air stream with simultaneous scratching afforded a quantitative yield of S-[3-(1-*p*-toluenesulfonyl-1-propenyl)]-isothiuronium chloride melting at 199–202°. Two recrystallizations from ethanol–water mixtures gave white crystals melting at 206–207°.

Anal. Calcd. for $C_{11}H_{15}ClN_2O_2S_2$: C, 43.05; H, 4.93; N, 9.13. Found: C, 42.46; H, 4.86; N, 8.98.

Reaction of IIIb with Thiourea.—A solution of 1.376 g. (0.00500 mole) of IIIb, 0.381 g. (0.00500 mole) of thiourea and 10 ml. of absolute ethanol was refluxed for 2 hours and then evaporated under a stream of air to yield an oil which solidified on addition of ethyl acetate followed by scratching. A solid weighing 1.30 g. (74) and melting at 160–170° was isolated and melted at 170–171° after two recrystallizations from a mixture of ethanol and ethyl acetate.

Anal. Calcd. for $C_{11}H_{15}BrN_2O_2S_2$: C, 37.61; H, 4.30; N, 7.98. Found: C, 37.40; H, 4.13; N, 7.86.

Reaction of 3-Bromo-1-benzenesulfonyl-1-propene with Thiourea.—In a manner similar to the reaction with IIIb, a quantitative yield of S-[3-(1-benzenesulfonyl-1-propenyl)]-isothiuronium bromide was obtained. Recrystallization from an ethanol–ethyl acetate mixture afforded the analytical sample melting at 188–180°.

Anal. Calcd. for $C_{10}H_{13}BrN_2O_2S_2$: C, 35.61; H, 3.88; N, 8.31. Found: C, 35.59; H, 3.84.

Degradation and Identification of the Product from Thiourea and 3-Bromo-1-benzenesulfonyl-1-propene. (A) Reaction with Base in the Presence of Methyl Iodide.—A solution of 4.624 g. (0.0200 mole) of 1-benzenesulfonyl-3-bromo-1-propene, 1.522 g. (0.0200 mole) of thiourea and 10 ml. of absolute methanol was refluxed for one hour. To the cooled solution was added 4 ml. of methyl iodide followed by 2.0 g. (0.040 mole) of sodium hydroxide. After another 0.5 hour of refluxing the reaction mixture was poured into 150 ml. of water. Extraction with three 25-ml. portions of ether followed by drying and evaporation afforded an oil whose infrared spectrum had absorption peaks at 10.4 and 11.1 μ.

(B) **Oxidation** of the oil was effected by dissolving it in 30 ml. of acetic acid, 20 ml. of acetic anhydride and 10 ml. of 30% hydrogen peroxide, and refluxing for 25 minutes. Pouring into 200 ml. of water yielded a milky solution which yielded 1.9 g. (40%) of a white solid melting at 140–143° after the solution had been evaporated to half its volume under a stream of air. Additional evaporation afforded another 1.3 g. (25%) of material melting at 130–140°. Two recrystallizations from ethanol gave the analytical sample of 1-benzenesulfonyl-3-methanesulfonyl-1-propene melting at 142–143°.

Anal. Calcd. for $C_{10}H_{12}O_4S$: C, 46.13; H, 4.65. Found: C, 46.21; H, 4.45.

(**C**) **Hydrogenation** of 0.6 g. of the above compound in 60 ml. absolute ethanol with 0.1 g. 10% palladium-on-charcoal in a Parr hydrogenation apparatus afforded a quantitative yield of 1-benzenesulfonyl-3-methanesulfonylpropane melting at 136–137°, identical with a sample of authentic material in melting point, mixed melting point and infrared spectrum.

1-Benzenesulfonyl-3-methanesulfonylpropane.—3-Phenylthiopropanol was prepared in a 76% yield from the reaction of sodium thiophenoxide and 3-bromo-1-propanol in methanol and distilled at 137–139° (3 mm.) (reptd.[23] b.p. 134–135° (2 mm.)). The alcohol was converted to the chloride in a 23% yield by reaction with thionyl chloride and pyridine; b.p. 118–120° (2 mm.) (reptd.[23] b.p. 116–117° (4 mm.) A sodium methanethiolate solution was prepared by refluxing a mixture of 15.2 g. (0.2 mole) of thiourea, 28.4 g. (0.2 mole) of methyl iodide and 250 ml. of methanol for one hour, and then adding 16.0 g. (0.4 mole) of sodium hydroxide and refluxing an additional 0.5 hour. To this thiolate solution was added 8.0 g. (0.043 mole) of 3-phenylthio-1-chloropropane and the resulting solution was stirred and refluxed overnight. Addition of 1000 ml. of water followed by extraction with three 40-ml. portions of ether, drying over anhydrous sodium sulfate, and removal of solvent gave a brown liquid which was dissolved in 40 ml. of acetic acid, 20 ml. of acetic anhydride and 20 ml. of 30% hydrogen peroxide. Refluxing of the latter solution for 25 minutes followed by pouring onto ice and filtering gave 7.6 g. (68%) of a white solid melting at 134–136°. Two recrystallizations from ethanol yielded the analytical sample melting at 137–138°.

Anal. Calcd. for $C_{10}H_{14}O_4S_2$: C, 45.76; H, 5.38. Found: C, 45.82; H, 5.13.

Kinetic Procedure.—The *n*-propyl halides, allyl chloride and allyl bromide used were commercial samples distilled before use. Allyl iodide was prepared from allyl alcohol and 47% hydriodic acid and was distilled immediately before use. Commercial reagent grade absolute methanol (Baker and Adamson) was used as solvent without any prior purification. Standard thiourea solutions were prepared and could be used over a two-week period without decomposition as evidenced by the reproducibility of rate constants at the beginning and end of this interval. It was also found that there was no difference in rate constants when thiourea solutions were prepared either from C. P. thiourea (The Coleman and Bell Co.) or from a recrystallized sample.

Solutions of the halide prepared immediately before use, and thiourea (10- to 20-fold greater in concentration than the halide) were placed in separate arms of Y-shaped cells,[24] one of the arms containing a pair of platinized platinum electrodes. The cells were placed in a constant temperature bath, controlled to ±0.05°, and allowed to come to temperature equilibrium for 20 minutes. The contents of the arms were mixed quickly and then drained into the electrode arm and the resistance was then recorded as a function of time. Concentrations were not corrected for solvent expansion.

Plots of the logarithm of the resistance at a given time divided by the difference between the resistance at that time and the equilibrium resistance [log $R/(R - R_E)$] *vs.* time gave straight lines where the pseudo-first-order rate constant equals the slope times 2.303. Division of the first-order constant by the thiourea concentration yielded the second-order constants. The time to reach the equilibrium resistance was chosen to be between 9 and 11 half-lives. For the Guggenheim procedure the time interval was chosen so as to correspond to about two half-lives of the reaction. Plots of log $(I/R\Delta_t - I/R_t)$ *vs.* time gave straight lines where the pseudo-first-order rate constant equals the slope times 2.303.

Activation energies were calculated from the equation

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(23) W. R. Kirner and G. H. Richter, THIS JOURNAL, **51**, 3414 (1929).

(24) The kinetics of the *n*-propyl chloride reaction were determined in a single arm cell fitted with a pressure cap to prevent evaporation of solvent and halide at the elevated temperatures needed to follow the kinetics conveniently.

$$E_a = \frac{2.303RT_1T_2}{T_2 - T_1}\log k_2/k_1$$

Entropies of activation were calculated from the equation

$$\Delta S^{\ddagger}_{T_1} = \frac{(E_a - RT_1) + 2.303RT_1\left(\log\frac{k_{\text{rate}}h}{kT_1}\right)}{T_1}$$

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EVANSTON, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

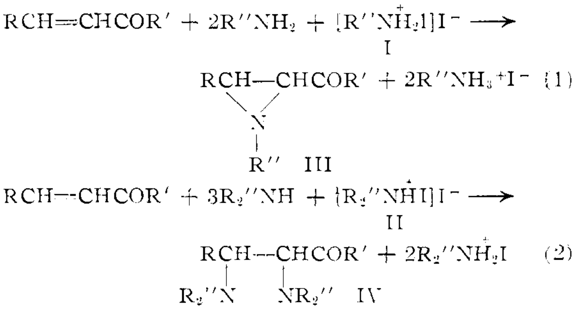
The Stereochemistry of Conjugate Additions. The Methanol Solvent Effect on Configuration Control in Additions of Amines, N-Bromoamines and Iodine–Amine Complexes[1]

BY PHILIP L. SOUTHWICK AND RAYMOND J. SHOZDA[2]

RECEIVED OCTOBER 8, 1959

When ethylenimine ketones are formed by the action of primary amines and iodine–primary amine complexes or N-bromo primary amines on chalcones, or by the action of primary amines on α-bromochalcones, the nature of the solvent may have a decisive influence upon the determination of the configuration of the product. Substitution of methanol for benzene as the solvent in the reaction increased greatly the proportion of *trans*-ethylenimine ketone formed in reactions of *trans*-chalcone or *trans*-4-nitrochalcone with cyclohexylamine and the iodine–cyclohexylamine complex or N-bromocyclohexylamine. On the other hand, substitution of methanol for benzene in reactions of cyclohexylamine with *trans*-α-bromochalcone or *trans*-α-bromo-4-nitrochalcone greatly increased the proportion of *cis*-ethylenimine ketone obtained. It was not possible to demonstrate a difference in the isomeric composition of the ethylenimine ketone product obtained from *cis*-4-nitrochalcone as compared with *trans*-4-nitrochalcone in reactions with cyclohexylamine and the iodine–cyclohexylamine complex. An electronic effect of the nitro group is made evident in a change in the *cis–trans* isomer ratios observed in the ethylenimine ketones obtained from *trans*-4-nitrochalcone and *trans*-α-bromo-4-nitrochalcone as compared with those obtained by the same reactions from *trans*-chalcone and *trans*-α-bromochalcone. The observed solvent and electronic effects are discussed in terms of the hypothesis that under suitable conditions configuration control is determined by asymmetric steric hindrance to protonation or halogenation of intermediate chelated amino enols.

When an α,β-unsaturated ketone is treated with iodine and an excess of a primary or secondary amine, the olefinic bond of the unsaturated ketone may undergo attack by the amine and the iodine–amine complex (I or II) with the formation of an ethylenimine ketone (III) or an α,β-diamino ketone



$$\mathrm{RCH{=}CHCOR' + 2R''NH_2 + [R''\overset{+}{N}H_2I]I^- \longrightarrow}$$ (I)

$$\mathrm{RCH{-}CHCOR'\ (N{-}R'' \text{ bridging}) + 2R''NH_3^+I^-} \quad (1)$$ (III)

$$\mathrm{RCH{=}CHCOR' + 3R_2''NH + [R_2''\overset{+}{N}HI]I^- \longrightarrow}$$ (II)

$$\mathrm{R_2''N{-}CH(R){-}CH(NR_2'')COR' + 2R_2''\overset{+}{N}H_2I} \quad (2)$$ (IV)

(IV). In the original papers[3] on these reactions it was pointed out that a relatively high degree of configuration control seemed evident. For example, in reactions of the benzylamine and cyclohexylamine–iodine reagents with chalcone, only the *trans*-ethylenimine ketone was isolated.[3] Moreover, in the case of a number of other α,β-unsaturated ketones examined more recently by Cromwell and his associates,[4] only the *trans*-ethylenimine ketones were found to result from the iodine–amine additions, even when efficient chromatographic methods were applied in the effort to separate any *cis* isomer which might have been formed. The basis of such configuration control has been the subject of conjecture,[5,6] but more information is needed to establish the correct explanation.

The purpose of the present investigation was threefold. It was desired first to establish whether or not the iodine–amine additions were stereospecific in the same sense as halogen additions to simple olefins, and hence capable of yielding products having different configurations (or ratios of configurations) when applied to a *cis*-unsaturated ketone as opposed to a *trans*-unsaturated ketone. It was also considered of interest to test the hypothesis[5] that intermediate chelated amino enols play a part in the configuration control observed in these reactions by the expedient of introducing an electronic effect which might influence the stability of the assumed chelate ring. Finally, since several details of procedure had been varied in the original investigation without determining quantitatively the effects of such variation on the proportion of diastereoisomers formed, it was desired to examine in more detail one of the addition reactions reported in the first paper. This last line of investigation disclosed a pronounced solvent effect on configuration control in the reactions of chalcones with the

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(1) For the previous paper in this series see P. L. Southwick and R. J. Shozda, THIS JOURNAL, **81**, 5435 (1959).

(2) National Science Foundation Fellow, 1956–1957. This paper is abstracted from a thesis submitted by Raymond J. Shozda in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the Carnegie Institute of Technology, June, 1957.

(3) (a) P. L. Southwick and D. R. Christman, THIS JOURNAL, **74**, 1886 (1952); (b) **75**, 629 (1953).

(4) (a) N. H. Cromwell, R. P. Cahoy, W. E. Franklin and G. D. Mercer, *ibid.*, **79**, 922 (1957); (b) N. H. Cromwell and R. J. Mohrbacher, *ibid.*, **75**, 6252 (1953).

(5) P. L. Southwick and J. E. Anderson, *ibid.*, **79**, 6222 (1957).

(6) See (a) N. H. Cromwell, *ibid.*, **81**, 4702 (1959), and (b) H. E. Zimmerman and W. H. Chang, *ibid.*, **81**, 3634 (1959). These investigators have arrived independently at theories which provide a similar basis for predicting the configurational outcome in ketonizations of unchelated acyclic enols. Cromwell directs his attention mainly to the types of reactions under consideration here, and they are also discussed by Zimmerman.