Stereochemistry of 1,3-Elimination Reactions[1]

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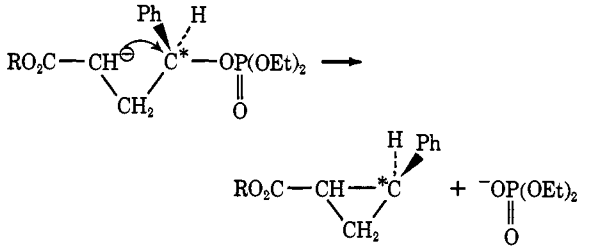
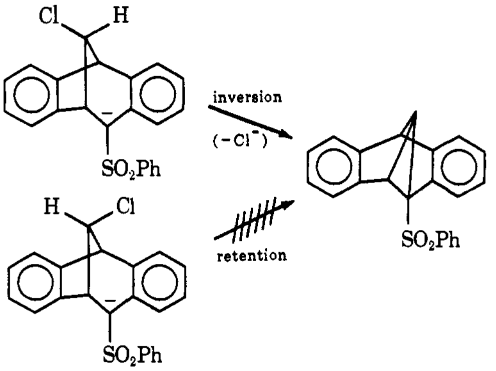
Abstract: Reaction of *dl*-$PhCHBrSO_2CHBrPh$ (**1**) with Ph_3P in refluxing benzene gave 96% of *trans*-stilbene whereas the meso isomer (**2**) gave 95% of *cis*-stilbene under comparable conditions. Trapping experiments showed that these reactions occur *via* α-sulfonyl carbanion intermediates that maintain their configurations and initiate intramolecular nucleophilic displacements at the remaining chiral center. The net result is debromination to form *trans*- and *cis*-2,3-diphenylthiirane 1,1-dioxides, respectively, with inversion at each chiral center. Comparably stereoselective 1,3 eliminations of hydrogen bromide with double inversion occurred on heating **1** or **2** with dimethylformamide. Here too trapping experiments showed the presence of carbanion intermediates. It is concluded that the carbanion intermediates in these reactions must be formed by abstraction of Br^+ (by Ph_3P) or H^+ (by DMF) from a conformation in which these atoms are cis to and flanked by the oxygen atoms of the sulfone group. The stereochemistry of 1,3 debrominations of **1** and **2** with other reagents, including Mg, Zn–Cu, $LiAlH_4$, PhSK, LiI, NaI, KI, CsI, Bu_4NI, and Ph_3PMeI, is described. Some of these reactions are also stereoselective but with others the stereoselectivity is sharply curtailed or lost; this is rationalized in terms of ion-pair intermediates. It is concluded that most, if not all, 1,3 eliminations occur by two-stage mechanisms and that the stereochemistry is dictated by the demands of the individual chiral centers. Since inversion is the rule at the nucleofugal center it is concluded that either double-inversion or retention-inversion geometry will be the rule for base-initiated 1,3-elimination reactions.

Intramolecular SN2-type nucleophilic displacements to form heterocyclic or carbocyclic rings are known to proceed almost invariably with inversion at the carbon atom that is the object of nucleophilic attack (nucleofugal center). Several examples may be cited wherein the nucleophile initiating the attack is a carbanion and the ring being formed has three members. One such is the reaction of $O{=}P(OEt)_2\bar{C}HCO_2R$ with optically active styrene oxide wherein the subsequent ring formation inverts the configuration at the C–O bond, as shown in eq 1.[2]



(1)

Examples are also known where a ring closure of this type fails when retention of configuration would be required,[3] for example,[3d] eq 2. The stereochemistry at the center initiating attack (electrofugal center) in such 1,3-elimination reactions cannot be examined unless the carbanion intermediate reacts prior to epimerization, or unless breaking of the H–C (or like) bond is concerted with formation of the C–C bond and cleavage of the bond between carbon and the leaving group.[4]



(2)

Generation of α-sulfonyl carbanions which are known to maintain configuration, at least long enough for protonation to occur,[7] offers an opportunity to examine this point. This approach has been used in the present paper to examine the overall stereochemistry of several 1,3-elimination reactions.[1]

Results

The *dl* and meso isomers (**1** and **2**, respectively) of bis-α-bromobenzyl sulfone were prepared by the method of Carpino,[8] and separated by chromatography over alumina. Single-crystal X-ray analysis[1,9] of the lower melting isomer showed it to have the meso configuration. Treatment of this isomer (**2**) with triphenylphosphine in refluxing benzene gave 95% of *cis*-stilbene, whereas **1** gave 96% of *trans*-stilbene under comparable conditions.

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(1) For a preliminary account of this work, see F. G. Bordwell, B. B. Jarvis, and P. W. R. Corfield, *J. Amer. Chem. Soc.*, **90**, 5298 (1968).

(2) I. Tomoskozi, *Tetrahedron*, 22, 179 (1966).

(3) (a) J. Meinwald and J. K. Crandall, *J. Amer. Chem. Soc.*, **88**, 1292 (1966); (b) S. J. Cristol and B. B. Jarvis, *ibid.*, **88**, 1529 (1966); (c) S. J. Cristol, J. K. Harrington, and M. S. Singer, *ibid.*, **88**, 3095 (1966); (d) S. J, Cristol and B. B. Jarvis, *ibid.*, **89**, 401 (1967); (e) S. J. Cristol, A. R. Dahl, and W. Y, Lim, *ibid.*, **92**, 5670 (1970).

(4) Notations have been devised for 1,3 eliminations (U, W, *exo*-Sickle, *endo*-Sickle, and *apo*-Sickle)[5] apparently under the assumption that one-stage (concerted) 1,3 eliminations could be realized. Recent developments suggest, however, that most, if not all, 1,3 eliminations occur by two-stage mechanisms, rather than by one-stage mechanisms wherein bond formation aids bond breaking.[3e,6] The Nickon–Werstiuk notations provide a useful shorthand description of the apparent *overall* molecular geometry, but it must be kept in mind that, since the reactions are likely to be two stage rather than one stage, neither the ground state nor the transition state of the reaction in question need necessarily conform to the pictorialization evoked by this notation.

(5) A. Nickon and N. H. Werstiuk, *J. Amer. Chem. Soc.*, **89**, 3914, 3915, 3917 (1967).

(6) F. G. Bordwell, *Accounts Chem. Res.*, **3**, 281 (1970).

(7) See J. N. Roitman and D. J. Cram, *J. Amer. Chem. Soc.*, **93**, 2225 (1971), and references cited therein.

(8) L. A. Carpino, L. V. McAdams, III, R. H. Rynbrandt, and J. W. Spiewak, *ibid.*, **93**, 476 (1971).

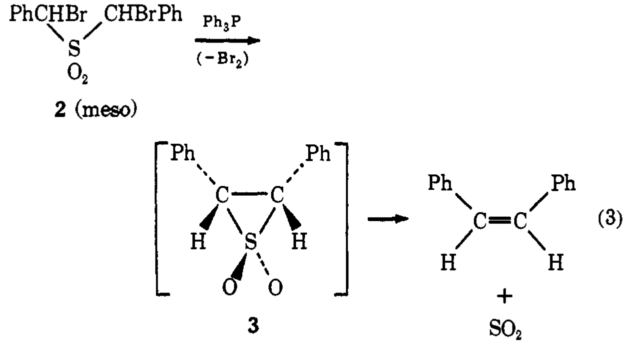
(9) P. W. R. Corfield, unpublished results.

Table I. Products from 1,3 Eliminations from *dl*- and *meso*-$PhCHBrSO_2CHBrPh$ (**1** and **2**, respectively)

				—PhCH=CHPh—		—PhCBr=CHPh—		
Isomer	Solvent	Temp, °C	Nucleo-phile	% cis[a]	% trans[a]	% cis[b]	% trans[b]	Yield (%)
1	C_6H_6	80	Ph_3P	4	96			85–90
2				95	5			85–90
1	2% MeOH in C_6H_6	80	Ph_3P	7	93			90[c]
2				96	4			90[c]
1	5% MeOH in C_6H_6	80	Ph_3P	10	90			90[d,e]
2				93	7			90[d,e]
1	DMF	153	DMF	1[e]	2[e]	79	21	85–90[f]
2				2[e]	4[e]	10	90	85–90[f]
1	DMA	165	DMA	2[e]	6[e]	46	54	85–90[g]
2				2[e]	3[e]	27	73	85–90[g]
1	$C_6H_5CH_3$	111	*d*-PhCH(Me)NMe_2	Trace		87	13	
2						7	93	

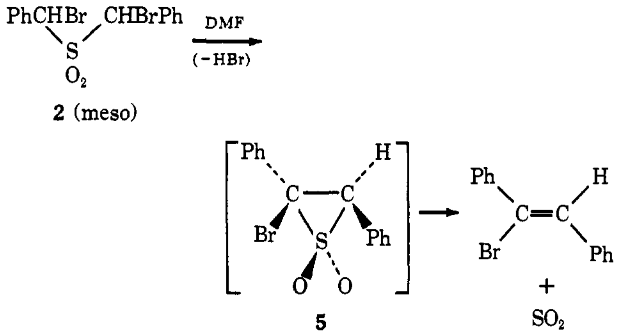
[a] Based on 100% PhCH=CHPh. [b] Based on 100% PhCH=CBrPh. [c] About 40% stilbenes and 60% reduction products. [d] 75–80% reduction. [e] Based on total yield. [f] Consisting of 73–75% PhCH=CBrPh, 2–4% PhCH=CHPh, and 19–24% PhC≡CPh. [g] Consisting of 2–6% PhCH=CHPh, 89–94% PhCH=CBrPh, and 4–5% PhC≡CPh.

The debromination of **1** or **2** with subsequent loss of sulfur dioxide and the ultimate formation of stilbene finds a close analogy in the Ramberg–Bäcklund reaction, wherein hydrogen bromide is eliminated from an α-halo sulfone by the action of base with the formation of a thiirane 1,1-dioxide (episulfone) intermediate. The latter undergoes thermal decomposition to form an alkene.[10] By analogy, there is every reason to believe that the reaction of triphenylphosphine with **2**, for example, proceeds as shown in eq 3. The reaction is represented as forming *cis*-2,3-diphenylthiirane 1,1-dioxide (**3**) since this episulfone is known to decompose thermally and stereospecifically to *cis*-stilbene.[11] It is possible that **3** also may be formed as an intermediate in the Ramberg–Bäcklund dehydrobromination of $PhCH_2SO_2CHBrPh$ (**4**) with bases, such as sodium methoxide in methanol,[10] but it is impossible to tell because under these (basic) conditions **3** is rapidly and completely epimerized to the trans episulfone.[11b] The observed product in this instance, *trans*-stilbene, no doubt arises from decomposition of *trans*-2,3-diphenylthiirane 1,1-dioxide, but it is uncertain whether this was the initial product of the 1,3 elimination or arose from **3** by epimerization. On the other hand, in refluxing dimethylformamide (DMF) which acts as a solvent and base, **4** has now been found to give a mixture consisting of 32% *cis*- and 68% *trans*-stilbene (90% yield), which shows that at least 32% of **3** is formed by Ramberg–Bäcklund dehydrobromination under these conditions.



(3)

Some degree of stereoselectivity also was observed in the 1,3 dehydrobromination of **1** or **2** using DMF as a base and solvent. These reactions gave 73–75% of α-bromostilbenes, 2–4% of stilbenes, and 19–24% of diphenylacetylene. The *dl* isomer (**1**) gave 79% of *cis*- and 21% of *trans*-α-bromostilbene and the meso isomer (**2**) gave 9% of *cis*- and 91% of *trans*-α-bromostilbene. The major initial product formed, for example, in the dehydrobromination of **2** is no doubt *trans*-2-bromo-2,3-diphenylthiirane 1,1-dioxide (**5**) which yields *trans*-α-bromostilbene by thermal loss of sulfur dioxide; **1** reacts by a comparable pathway.



In *N*,*N*-dimethylacetamide (DMA) the yields of α-bromostilbenes increased at the expense of diphenylacetylene, presumably because of the higher reaction temperature, but there was a substantial loss in stereoselectivity (Table I). When *d*-*N*,*N*-dimethyl-α-phenethylamine was the base (in refluxing toluene) the α-bromostilbenes were formed with a high degree of stereoselectivity. This experiment was carried only to partial completion in an attempt to partially resolve **1**, but the recovered starting material failed to exhibit optical activity.

Epimerization and Trapping of Intermediate Carbanions with Protic Solvents. In DMA containing 5% D_2O about 50% deuterium exchange (in the recovered starting material) had occurred in 12 hr at 100° (*ca.* 10% dehydrobromination); *ca.* 90% deuterium exchange occurred in 4 hr at 136° (*ca.* 35%) dehydrobromination). In the latter experiment about 15% epimerization of **1** to **2** (or of **2** to **1** when **2** was the starting

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(10) See (a) F. G. Bordwell and J. M. Williams, Jr., *J. Amer. Chem. Soc.*, **90**, 429 (1968); (b) L. A. Paquette, *Accounts Chem. Res.*, **1**, 209 (1968).

(11) (a) N. Tokura, T. Nagai, and S, Matsumura, *J. Org. Chem.*, **31**, 349 (1966); (b) F. G. Bordwell, J. M. Williams, Jr., E. B. Hoyt, Jr., and B. B. Jarvis, *J. Amer. Chem. Soc.*, **90**, 429 (1968).

Table II. Products from 1,3 Eliminations from *dl*- and *meso*-PhCHBrSO$_2$CHBrPh (**1** and **2**, respectively)

				PhCH═CHPh		
Isomer	Solvent	Temp, °C	Nucleophile	% cis[a]	% trans[a]	Yield (%)
1	DMF	60	Ph$_3$P	4	96	85–90
2				83	17	85–90
1	2% MeOH in DMF	60	Ph$_3$P	5	95	90[b]
2				80	20	90[b]
1	5% MeOH in DMF	60	Ph$_3$P	8	92	90[c]
2				82	18	90[c]
1	DMF	70	Ph$_3$P–I$_2$	18	82	85–90
2				43	57	85–90
1	DMF	70	Ph$_3$P–AgNO$_3$	5	95	85–90[d]
2				11	89	85–90[d]
1	THF	65	Ph$_3$P	4	96	85–90
2				90	10	85–90
1	THF	65	Mg	14	86	65
2				80	20	55
1	THF	65	Zn–Cu	24	76	20
2				75	25	20
1	DMF	153	Zn–Cu	27	73	85–90[e]
2				62	38	85–90[e]
1	THF	25	LiAlH$_4$	10	90	85–90
2				30	70	85–90
1	DMF	60	KSPh	4	96	85–90[f]
2				12	88	85–90[f]
1	DMF	70	LiI	21	79	85–90
2				21	79	85–90
1	DMF	70	NaI	21	79	85–90
2				22	78	85–90
1	DMF	70	KI	22	78	85–90
2				24	76	85–90
1	DMF	70	CsI	24	76	85–90
2				22	78	85–90
1	DMF	70	Bu$_4$NI	24	76	85–90
2				25	75	85–90
1	DMF	70	Ph$_3$PMeI	26	74	85–90
2				25	75	85–90
1	THF	65	LiI	12	88	80[g]
2				18	82	80[g]

[a] Based on 100% PhCH═CHPh. [b] 55% reduction products. [c] 75% reduction products. [d] Consisting of 57–68% stilbenes and 32–43% α-bromostilbenes (88% cis and 12% trans from **1**; 22% cis and 78% trans from **2**). [e] A trace of PhCH═CBrPh and 10–20% of PhC≡CPh were present. [f] 5–10% of reduction products were present. [g] 3–6% of PhCH═CBrPh and 19% of PhC≡CPh were present.

material) was observed. In anhydrous DMA after 30 min at 165° the reaction had gone to about 50% completion and the recovered starting material had undergone about 20% epimerization.

Treatment of **2** with sodium methoxide in methanol also is believed to give **5**, but under these (basic) conditions **5** is rapidly dehydrobrominated to 2,3-diphenylthiirene 1,1-dioxide which, in turn, reacts with the base to give sodium 1,2-diphenylethene-1-sulfonate and diphenylacetylene.[12] About 20% of diphenylacetylene also is formed in the reaction of **1** (or **2**) with DMF, but the low basicity and high temperature of the medium favors thermal decomposition of **5** over dehydrobromination.

When 2% by volume of methanol (20:1 molar ratio of MeOH to dibromide) was included in the benzene solvent in the debromination of **1** or **2** by triphenylphosphine the yield of stilbenes dropped from 85–90% to about 40%. Under these conditions about 60% of reduction products (principally benzyl α-bromobenzyl sulfone and benzyl sulfone) were formed. The relative amounts of *cis*- and *trans*-stilbenes obtained from **1** and **2** were the same in these experiments as obtained in the absence of methanol (Table I). These results appear to be best interpreted as indicating the partial trapping of a carbanion intermediate by protonation. By increasing the amout of methanol to 5% the amount of reduction products increased to 75–80%, and with 25% methanol the formation of stilbenes was almost totally suppressed.

Variation in Reaction Type and Stereoselectivity with Reagents and Conditions. Debrominations of **1** and **2** by triphenylphosphine were also carried out in DMF and tetrahydrofuran (THF) solvents with similar results, although the stereoselectivity was not quite as high. Once again inclusion of methanol brought about partial reduction without changing the stereochemical outcome of the unaffected portion of the reaction (Table II). When iodine was included in the Ph$_3$P–DMF reaction a sharp drop in stereoselectivity was observed. (Neither *cis*- nor *trans*-stilbene was isomerized under these conditions.) Inclusion of silver nitrate in the Ph$_3$P–DMF reaction led to a further drop in stereoselectivity.

Magnesium in refluxing THF effected debromination to give stilbenes in 55–65% yield with about a 4:1 stereoselectivity (Table II). With zinc–copper couple in THF the yields and stereoselectivity were both lower; in DMF the yields increased, but the stereoselectivity decreased.

Lithium aluminum hydride (LiAlH$_4$) in THF, potassium thiophenoxide in DMF, or lithium iodide in DMF effected debrominations to form stilbenes in high yield,

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(12) F. G. Bordwell, J. M. Williams, Jr., and B. B. Jarvis, *J. Org. Chem.*, **33**, 2026 (1968).

but stereoselectivity was largely lost in these reactions.[13] The degree of stereoselectivity in the iodide ion initiated debrominations appeared to be completely insensitive to the nature of the cation (Table II).

Cadmium iodide or calcium iodide gave no reaction under these conditions, presumably due to their lesser dissociation in DMF as compared to monovalent iodides. Lithium bromide in refluxing THF gave *ca.* 84% α-bromostilbenes and 16% diphenylacetylene.

The reactions of **1** (or **2**) with thiourea, triphenylphosphine sulfide, or potassium thiocyanate were so slow in DMF or DMA that reaction with the solvent prevailed.

Discussion

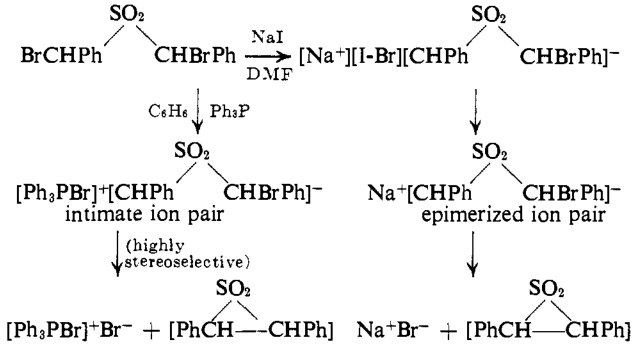
Attack of Nucleophiles on Bromine *vs.* Hydrogen. Nucleophiles effect reaction with **1** (or **2**) by either attack at bromine or at hydrogen. The observed choice can be correlated reasonably well by using Pearson's theory of hard and soft acids and bases.[15] Thus, "soft" bases such as triphenylphosphine, magnesium, zinc, thiophenoxide ion, iodide ion, and hydride ion (in $LiAlH_4$) would be expected to attack the "softer" atom, bromine, whereas "hard" bases such a methoxide ion, DMF, DMA, and tertiary amines would be expected to attack the "harder" atom, hydrogen. It would have been more difficult to predict the behavior of bromide ion, which, as it turns out, attacks hydrogen almost exclusively.

Evidence for Carbanion Intermediates. The formation of appreciable quantities of reduction products, benzyl α-bromobenzyl sulfone and dibenzyl sulfone, when methanol is included in the Ph_3P–C_6H_6 reaction mixtures provides strong evidence for the presence of a carbanion intermediate which is trapped by proton abstraction.[16] Note that the quantity of reduction products increases with increased methanol concentration (Table I); in 25% MeOH–75% C_6H_6 the reaction is almost entirely reduction, only about 4% of stilbenes being formed.[17]

The trapping experiments with D_2O in DMA provide evidence for the formation of carbanion intermediates in the reactions carried out in dipolar aprotic media. The observation that epimerization competes with dehydrobromination indicates that carbanion formation is reversible to at least some extent. The ratio of exchange to epimerization of about 6:1 is of the order of magnitude expected from earlier work wherein rates of exchange to racemization were measured.[7]

Stereoselectivity and Ion-Pair Formation. It is significant that stereoselectivity is greater with neutral than with negatively charged nucleophiles, and that stereoselectivity decreases with increased dissociating ability of the solvent (Table II). Both of these observations are consistent with the presence of ion-pair intermediates. In benzene solution the close proximity of the Ph_3PBr^+ ion to the carbanion generated from **1** (or **2**) prevents its epimerization, whereas with, say, NaI in DMF, both the greater distance of separation of the ion partners and the greater dissociative ability of the solvent (DMF *vs.* C_6H_6) provide a greater opportunity for epimerization of the carbanion (Scheme I).

Scheme I



The influence of iodine and of silver nitrate in lowering the stereoselectivity of the Ph_3P in C_6H_6 reactions may be due to promotion of the loss of configuration of the $[Ph_3PBr]^+[R^-]$ ion pair. With I_2 the effect may be one of trapping the carbanion (as RI). Trapping and regeneration of the carbanion would increase the chances of epimerization at the carbanion center. The effect of silver nitrate may be one of replacement of $[Ph_3PBr]^+$ by $[Ag]^+$ in the ion pair.

The lack of any stereoselectivity in reactions of K^+I^- in DMF with **1** or **2**, and the lower stereoselectivity observed with Zn–Cu couple or Mg in THF, as compared to Ph_3P in THF (Table II) made us think that perhaps the cation associated with the carbanion might have an effect on the configurational stability of the carbanion. However, a series of iodides (lithium, sodium, potassium, cesium, tetra-*n*-butylammonium, and triphenylmethylphosphonium iodides) gave nearly identical results with **1** or **2** in DMF.

Double Inversion *via* a Carbanion Mechanism. The overall stereochemical result of formation of *trans*-stilbene from **1** (or *cis*-stilbene from **2**) by debromination (and subsequent loss of SO_2 with retention) could result *a priori* by retention of configuration at each center or by inversion of configuration at each center (U- and W-type processes, respectively, in the Nickon–Werstiuk classification[4,5]). The dehydrobromination reactions with DMF occur in the same stereochemical sense as the debromination reactions, **1** giving *cis*-α-bromostilbene and **2** giving *trans*-α-bromostilbene. The demonstration that carbanions are formed coincidently with debromination or dehydrobromination makes their intermediacy in the reaction highly probable. It has been pointed out that the presence of carbanions does not necessarily mean that they are on the pathway for elimi-

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[13] Under simulated reaction conditions (iodine–iodide ion in DMF) neither *cis*- nor *trans*-stilbene underwent isomerization. This is not surprising since iodine-catalyzed isomerization of *cis*-stilbene to *trans*-stilbene is known to be slow.[14]

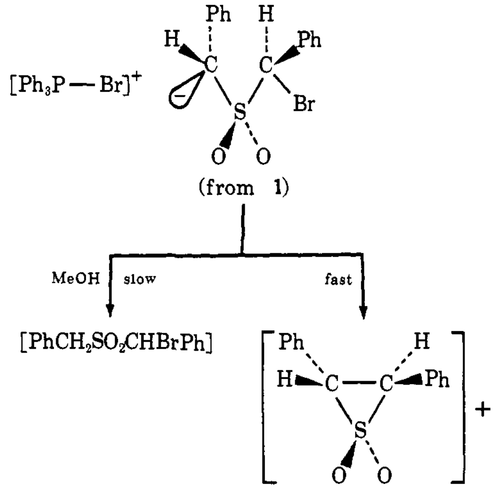
[14] Y. Yamashita, *Bull. Chem. Soc. Jap.*, 34, 487 (1961).

[15] See R. G. Pearson and J. Söngstad, *J. Amer. Chem. Soc.*, 89, 1827 (1967); R. F. Hudson, "Structure and Mechanism in Organo-Phosphorus Chemistry," Academic Press, New York, N. Y., 1965, Chapters 4 and 5.

[16] H. Hoffman and H. Förster, *Tetrahedron Lett.*, 1547 (1963), have observed comparable reductions of α-bromo sulfones and have suggested the intermediacy of carbanions.

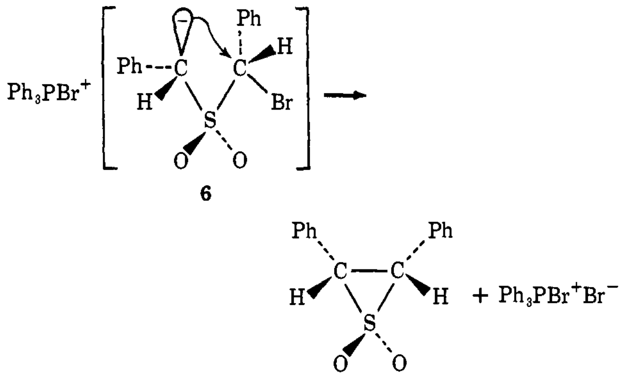
[17] The rate constant for the intramolecular displacement step whereby the carbanion $[PhCHSO_2CHBrPh]^-$ derived from $PhCH_2SO_2$-CHBrPh gives 2,3-diphenylthiirane 1,1-dioxide has been estimated to be about 1.5×10^2 sec^{-1} at 25° in methanol, as compared with 2×10^4 sec^{-1} for protonation in methanol of this carbanion.[10a] The latter is a pseudo-first-order rate constant obtained by multiplying the second-order constant by the solvent concentration. In the present instance the solvent concentration is 0.05 *M* (in 2% MeOH) as compared with 25 *M* (in 100% MeOH), which reduces the proton abstraction rate to 4×10^1 sec^{-1}, making the intramolecular displacement rate about four times faster than the proton abstraction rate. This calculation therefore is consistent with the two processes being competitive, but, of course, differences in solvation effects on the rates have not been taken into account.

nation,[18] but, on the other hand, no examples appear to be known of reactions wherein carbanions have been demonstrated to be present yet shown *not* to participate in 1,3 or 1,2 eliminations. Furthermore, there is evidence to indicate that such eliminations from anions have larger driving forces than do concerted eliminations.[19] In the present study the fact that carbanion trapping agents decrease the yield of alkene but do not alter the stereoselectivity indicates that if both carbanion and concerted eliminations are occurring they must exhibit the same stereochemistry. If a concerted process is operative it must not have much driving force since $PhCHBrSO_2Ph$ and $PhCHBrSO_2CH_2Ph$ are less reactive toward Ph_3P in 5% MeOH in C_6H_6 by only factors of *ca.* 5 and 25, respectively, than is $PhCHBrSO_2CHBrPh$ (**1** or **2**), and this difference is explicable as an inductive effect. We conclude that the reactions of **1** and **2** are best represented as abstractions of Br^+ (by Ph_3P or the like) or H^+ (by DMF) to form a chiral carbanion as one partner of an ion pair. The carbanion then usually initiates an intramolecular S_N2-type reaction at the second chiral center before losing its asymmetric character. Intramolecular displacement from the carbanion is rapid compared to exchange of the cation with solvent since a 20:1 molar ratio of MeOH to dibromide is required to realize *ca.* 50% reduction (eq 4).



(4)

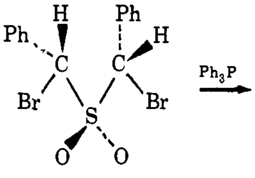
Analogies showing that inversion of configuration at the carbon atom from which the leaving group departs has overwhelming precedent for intramolecular nucleophilic displacements were cited in the preliminary account,[1] and in the introduction to this paper.[2,3] Accepting inversion as the stereochemical result at one chiral center *requires* that inversion of configuration occur also at the other chiral center since the overall stereochemical product result is consistent only with a double inversion or double retention mechanism. Since the backside of the C–Br bond at the nucleofugal center is accessible to intramolecular attack only when the C–Br bond is flanked by the two oxygen atoms of the sulfonyl group this fixes the transition state geometry, assuming attack by the carbanion part of an ion pair, as shown in **6**.



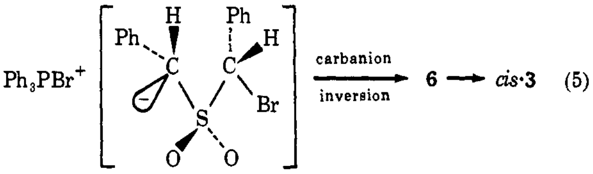
6

cis-**3** (90%)

Structure **6** must be an inverted form of the carbanion, however, in order to satisfy the requirement of double inversion. A possible formulation of the reaction would then be one where overall W geometry obtains (eq 5).[4,5]

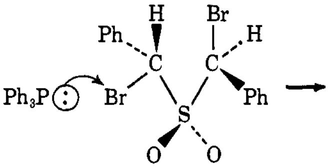


2a (eclipsed Ph's)

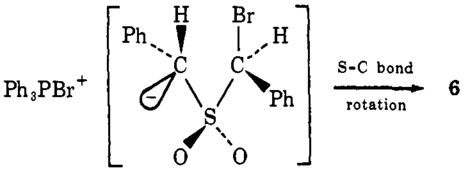


(5)

Examination of models shows, however, that there are severe phenyl–phenyl repulsions in this eclipsed conformation of **2**. A much more likely mode of generation of **6** would be from a conformation wherein the phenyl groups are staggered, *e.g.*, **2b**.



2b (staggered Ph's)



In this representation it is assumed that Ph_3P attacks the bromine atom flanked by the two oxygen atoms of the sulfonyl group, and that rotation around the S–CH(Br)Ph bond occurs to give **6**. Rotation around the S–$\bar{C}$HPh bond presumably does not occur to any appreciable extent since this would give **7**, which could account for no more than 10% of the observed product. Note also that attack of Ph_3P on the bromine atom anti to the oxygen atoms in **2b** will also lead to **7**. The minor (trans) product from **2** is probably formed from **7**.

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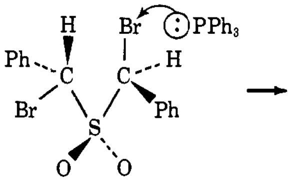
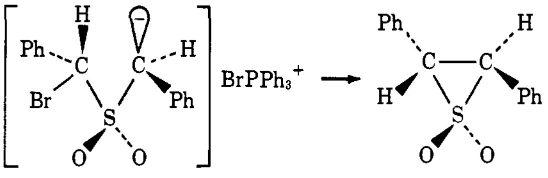
[18] J. Hine, R. Weisboeck, and O. B. Ramsay, *J. Amer. Chem. Soc.*, **83**, 1222 (1961); R. Breslow, *Tetrahedron Lett.*, 399 (1964).

[19] (a) F. G. Bordwell, D. A. R. Happer, and G. D. Cooper, *Tetrahedron Lett.*, 2759 (1972); (b) F. G. Bordwell, *Accounts Chem. Res.*, **5**, 374 (1972).



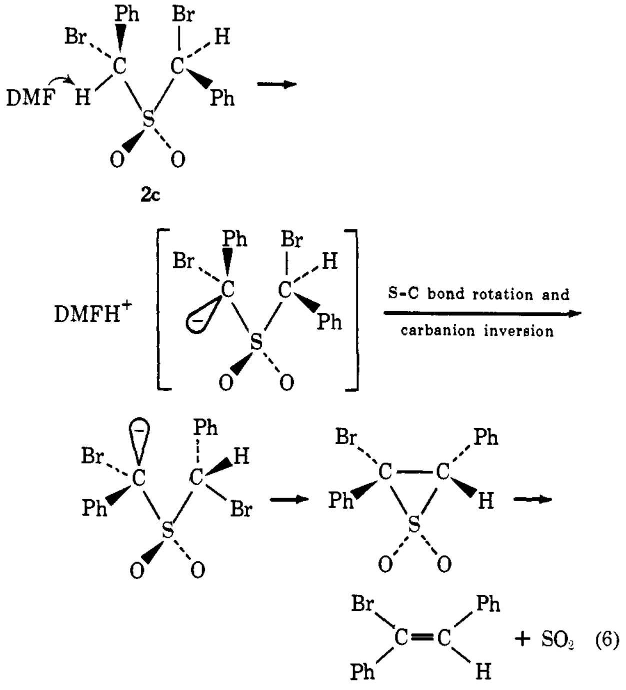
2b (staggered Ph's)



7

trans isomer

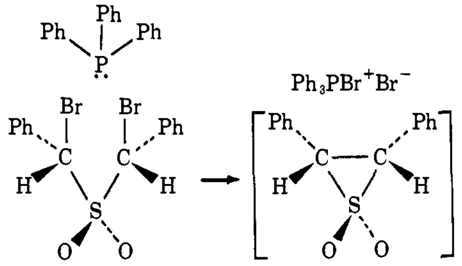
The major isomer formed on dehydrobromination of 2 most likely follows a course similar to debromination (2b → 6 → *cis*-3) except that a hydrogen flanked by the two oxygen atoms of the sulfonyl group is removed selectively (eq 6).



Note that, although the *overall* geometry can be described as W in the Nickon–Werstiuk notation, the ground-state conformation is probably *endo*-S and the transition state geometry is probably *exo*-S.[4]

According to the above analysis the stereochemical course of the reaction is dictated by two factors: (a) a preference for inversion at the nucleofugal chiral center being attacked in the intramolecular displacement reaction and (b) a preference for removal of the electrofugal atom from a conformation wherein it is flanked by the two sulfonyl oxygen atoms. It is noteworthy that Corey and Lowry have obtained evidence from a quite different type of experiment for preferential removal of a proton flanked by the sulfonyl oxygen atoms in the formation of an α-sulfonyl carbanion. They showed when the carbanion was generated so that it was anti to the sulfonyl oxygen atoms that the resulting protonated product had the proton in an *inverted* configuration.[20] Their result is unique since exchange involving α-sulfonyl carbanions ordinarily occurs with retention of configuration.[7] It suggests that protonation occurs selectively to a position flanked by the sulfonyl oxygen atoms. It follows from the principal of microscopic reversibility that deprotonation must also occur preferentially from this position, and this is the presently accepted explanation of exchange with retention of configuration.[7] To summarize, in the Corey–Lowry example[20] inversion of the α-sulfonyl carbanion is observed because the carbanion is generated in an unfavored conformation; in our example inversion occurs because, although the carbanion is generated in a favored conformation, it must undergo inversion in order to initiate the intramolecular displacement. It is also possible to rationalize the preferential removal of Br^+ (or H^+) from the position wherein it is flanked by the two sulfonyl oxygen atoms in terms of "thermodynamic control" since *ab initio* calculations indicate that α-sulfonyl carbanions in which the electron pair on carbon is gauche to the two sulfonyl oxygen atoms lies at an energy minimum.[21] These calculations of course necessarily ignore solvation forces, which is unfortunate, since these must play a major role.[7]

Double Retention Mechanism. The double retention mechanism can be formulated in an overall sense by a U-type pictorialization,[4,5] utilizing conformation **2d**.



2d 3

A mechanism involving carbanion formation followed by intramolecular nucleophilic displacement with retention is unprecedented. A more likely two-stage mechanism to rationalize double retention geometry would be to assume dissociation of bromide ion from the carbanion to give a dipolar ion intermediate, $Ph\bar{C}HSO_2\overset{+}{C}HPh$, which collapses to form **3** stereoselectively. This reaction path is rendered highly unlikely, however, by studies of the Ramberg–Bäcklund which show that methyl substitution α to the C–Br function, as in the series $PhCH_2SO_2CH_2Br$, $PhCH_2SO_2CH(CH_3)Br$, $PhCH_2SO_2C(CH_3)_2Br$, does not cause rate acceleration.[22] A marked accelerating effect on methyl substitution would be expected if the mechanism involved a rate-limiting dissociation of bromide ion from the carbanion. Finally, we think a one-stage mechanism wherein P–Br and C–C bonds are formed simultaneously with the breaking of two C–Br bond (concerted U mechanism[4,5]) is highly unlikely, not only because of the demonstration of the presence of carbanion intermediates, but also because mechanisms of this type for both 1,3- and 1,2-elimination reactions appear to be rare.[19b]

Stereochemistry of 1,3 Eliminations. Conclusions.

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(20) E. J. Corey and T. H. Lowry, *Tetrahedron Lett.*, 793 (1965).

(21) S. Wolfe, A. Rauk, and I. G. Csizmadia, *J. Amer. Chem. Soc.*, **91**, 1467 (1969); S. Wolfe, *Accounts Chem. Res.*, **5**, 102 (1972).

(22) M. D. Wolfinger, Ph.D. Dissertation, Northwestern University, 1968.

From the results reported to date it would appear that for base-initiated 1,3 eliminations stereoselectivity is usually not high and that no one pattern of stereochemistry is dominant. In 1,3 elimination of TsOH from 6-*exo-d-exo*-2-norbornyl tosylate and the 6-*endo-d* epimer initiated by *t*-BuOK in *t*-BuOH *exo*-Sickle geometry is favored over W, and U geometry is favored over *endo*-Sickle;[4,5] the preference is not high in either instance, however.[5] In alkylboronate 1,3 eliminations W is favored over *exo*-S geometry.[23] 1,3 Debrominations from *cis*- and *trans*-2,8-dibromo-3,6-dibenzobicyclo[3.3.0]octadienes initiated by lithium aluminum hydride in ether, magnesium in ether, or sodium in glyme–toluene show no stereochemical preference, but zinc in ethanol gives a 1,3-elimination product only from the trans isomer, suggesting a preference for *exo*-S over W.[3e] In contrast, we find in 1,3 debrominations of **1** and **2** initiated by zinc in aprotic solvents that W geometry is preferred (Table II). This is true also for 1,3 debrominations with triphenylphosphine in DMF or benzene, or with magnesium in THF; on the other hand, there is little or no stereochemical preference when lithium aluminum hydride in THF, potassium thiophenoxide in DMF, or metal iodides in DMF are used (Table II). In 1,3 debrominations of 2,4-dibromopentanes with butyllithium it has been concluded that W geometry prevails,[24] but arguments for a U geometry have also been presented.[3e] In 1,3 dehydrobrominations of **1** and **2** initiated by DMF W geometry is preferred. Furthermore, analogous 1,3 dehydrobrominations in cyclic systems which require a W geometry are known to occur readily,[25a] and the W geometry has been shown to be preferred in a similar reaction in an acyclic system.[25b] Finally, in 1,3 debrominations with α,α'-dibromo sulfoxides initiated by hexamethylphosphoric triamide in benzene W geometry is preferred.[26]

The lack of a high degree of stereoselectivity for most 1,3 eliminations and the failure of a preferred stereochemical pathway to emerge support the conclusion that 1,3 eliminations generally occur by two-stage mechanisms, and that the one-stage, concerted mechanism is rare or nonexistent.[6,19b] In the two-stage mechanism the stereochemistry will be dictated by the stereochemical behavior at the individual chiral centers. Since inversion is known to be highly preferred at the nucleofugal carbon atom, the two-stage mechanism will, in general, require either double-inversion or retention-inversion geometry (overall W or *exo*-S geometry, rather than overall U, *endo*-S, or *apo*-S geometry[4,5]). It appears significant in this regard that W and *exo*-S geometries have been found to be preferred in most studies to date. The choice between W and *exo*-S will usually be dictated by the stereochemical behavior at the electrofugal center. Epimerization at this center is often rapid, which accounts for the scarcity of systems where the stereochemistry can be observed and the low degree of stereoselectivity usually found.

Inversion at the electrofugal center α to sulfonyl or sulfoxide is apparently dictated by a preference for generation of the carbanion in a configuration where it is flanked by two oxygen atoms (sulfone) or an oxygen atom and a lone pair (sulfoxide). In this configuration the carbanion is prevented from attacking the nucleofugal center, and it must invert its configuration in order to do so.[27]

In reactions such as those studied by Nickon and Werstiuk,[5] it seems likely that an ion pair is formed at the nucleofugal center prior to deprotonation at the electrofugal center. It is difficult to know what stereochemistry to expect in this system, particularly in view of its proclivity to rearrangement. Since, for reasons presented above, we feel that overall W and *exo*-S geometry will be the rule for base-initiated 1,3 eliminations, we agree with Trost in favoring the W over the U pathway for the 1,3 debromination of 2,4-dibromopentanes.[24]

Experimental Section[29]

Solvents and Reagents. Thiophene-free benzene was distilled from potassium metal. Tetrahydrofuran (THF) was distilled from lithium aluminum hydride and stored in a tightly stoppered vessel under an atmosphere of nitrogen. Both dimethylformamide (DMF) and dimethylacetamide (DMA) were distilled from phosphorus pentoxide under reduced pressure (*ca.* 12 mm) and stored in tightly stoppered vessels under an atmosphere of nitrogen. Dimethyl sulfoxide was distilled from calcium hydride under reduced pressure (*ca.* 12 mm) and stored in a tightly stoppered vessel under an atmosphere of nitrogen.

Triphenylphosphine was recrystallized from hexane and dried under vacuum at 60°. Lithium iodide trihydrate was ground to a fine powder and dried under vacuum at 60°. The other iodide salts were dried under vacuum at 100° and stored in a desiccator in the presence of phosphorus pentoxide. The zinc–copper couple was prepared by washing zinc powder with 2% aqueous copper sulfate until the blue color persisted, followed by three washings (15 ml of solvent for 1 g of zinc powder) each with first distilled water followed by absolute ethanol and finally with anhydrous ether. The zinc–copper couple was dried under vacuum at 100° and stored in a desiccator in the presence of phosphorus pentoxide.

Bis-α-bromobenzyl Sulfone.[30] To a solution of 50.0 g (0.23 mol) of α-bromophenylacetic acid and 35 g of sodium carbonate dissolved in 250 ml of water was added over a period of about 10 min 31.2 g (0.13 mol) of sodium sulfide nonahydrate dissolved in 100 ml of water. After standing at 20° for 18 hr the mixture was acidified with dilute hydrochloric acid to pH 2, and the resulting mixture was extracted with two 250-ml portions of ether. The ether extracts were combined, washed with a saturated salt solution, and dried. The oil resulting from solvent removal was crystallized from methylene chloride–hexane to give 24.8 g (71%) of bis-α-carboxybenzyl sulfide, mp 177–180°. To a solution of 22.6 g (0.15 mol) of the latter in 230 ml of glacial acetic acid at 0° was added dropwise 40 ml of 30% hydrogen peroxide. A milky solution developed after 4 hr but became clear after *ca.* 30 hr. After standing at 20° for a total of 60 hr the solution was treated with 30 g of potassium bromide in 130 ml of water, followed by 9.0 ml of bromine in 25 ml of glacial acetic acid. The solution was stirred

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[23] J. A. Marshall and J. H. Babler, *Chem. Commun.*, 993 (1968).

[24] B. M. Trost, W. L. Schinski, F. Chen, and I. R. Mantz, *J. Amer. Chem. Soc.*, **93**, 676 (1971).

[25] (a) E. J. Corey and E. Block, *J. Org. Chem.*, **34**, 1233 (1969); L. A, Paquette and R. W. Houser, *J. Amer. Chem. Soc.*, 91, 3870 (1969); (b) F. G. Bordwell, E. Doomes, and P. W. R. Corfield, *ibid.*, **92**, 2581 (1970).

[26] B. B. Jarvis, S. D. Dutkey, and H. L. Ammon, *ibid.*, **94**, 2136 (1972).

[27] Preference for generation of the carbanions in these configurations does not appear to be large, however, particularly for the sulfoxide function, and may be solvent dependent.[28] Loss of stereoselectivity is therefore not surprising, and we can anticipate that in suitable systems retention-inversion rather double-inversion geometry will be observed. This point is under investigation.

[28] D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965; B. J. Hutchinson, K. K. Anderson, and A. R. Katritsky, *J. Amer. Chem. Soc.*, **91**, 3839 (1969); T. Durst, R. R. Fraser, M. R. McClory, R. B. Swingle, R. Viau, and Y. Y. Wigfield, *Can. J. Chem.*, **48**, 2148 (1970).

[29] Microanalyses were performed by H. Beck, Northwestern University, and by Micro-Tech Laboratories, Skokie, Ill.

[30] This is a modification of a procedure kindly supplied by Professor L. A. Carpino; see L. A. Carpino and L. V. McAdams, III, *J. Amer. Chem. Soc.*, **87**, 5804 (1965).

at room temperature for 20 min and was then heated at 80° (sun lamp) for 15 min and at 100° for 15 min. To this solution was added 10 g of sodium thiosulfate dissolved in 25 ml of water. The solid resulting from solvent removal was taken up in 300 ml of methylene chloride. The methylene chloride solution was washed with water and with saturated sodium carbonate until basic. The oil resulting by removal of the (dried) solvent was crystallized from methylene chloride–hexane to give 23.0 g (77%) of bis-α-bromobenzyl sulfone, mp 132–144°. Analysis by nmr indicated the presence of *ca.* 55% of diastereomer **1** and 45% of diastereomer **2**.[31]

Separation of Diastereomers (1 and 2) of Bis-α-bromobenzyl Sulfone (A).[32] Attempts to fractionally crystallize the diastereomers from various solvents meet with little success as did column chromatography using silica gel. However, using Woelm acid washed alumina (grade II) as the column substrate, the diastereomers could be separated quite cleanly with 80 g of alumina/1 g of A. The dibromide mixture (A) was put on the column with the minimum amount of chloroform followed by elution with carbon tetrachloride. Diastereomer **1** (*dl*) came off the column first and was recrystallized from chloroform–ethanol, mp 163–164°. Diastereomer **2** (meso) was eluted by additional carbon tetrachloride; **2** was recrystallized from chloroform–ethanol, mp 158.5–159.5°. The progress of the chromatography was followed conveniently by nmr spectroscopy (deuteriochloroform solvent) since **1** and **2** exhibited well-separated sharp singlets (**1** at δ 6.3 and **2** at δ 5.8) outside the aromatic region.

The vpc analyses were performed on an F&M Model 5750 with a 6 ft × $^1/_8$ in. o. d. stainless steel column with 10% vc 98 W silicone gum rubber on Diaport P support; column temperature was 180°. The retention times were compared with those of authentic samples of *cis*- and *trans*-stilbene,[33] *cis*-[32] and *trans*-bromostilbene,[34] and diphenylacetylene.[33] The peak areas were compared directly with a standard solution of *trans*-stilbene.

Reactions of the Diastereomeric Mixture (A) and the Individual Diastereomers (1 and 2). With Triphenylphosphine in Dry Benzene. A solution of 215 mg (0.53 mmol) of **1** (or **2**) and 1.0 g (3.8 mmol) of triphenylphosphine in 15 ml of dry benzene was refluxed for 4 hr. The precipitate of triphenylphosphine dibromide was collected on a filter and washed with 10 ml of pentane; on standing it turned orange and decomposed in the characteristic manner described previously.[35] The filtrate was concentrated under vacuum to *ca.* 5 ml and passed over 30 g of silica gel[36] eluting with benzene in hexane. The resulting material, after removal of solvent, was diluted to 2.0 ml with ether and analyzed by vpc (see Table I). If the benzene solvent used was not scrupulously dry, bromobenzyl benzyl sulfone and benzyl sulfone were always present in the reaction mixture. They were isolated by chromatography over silica gel, bromobenzyl benzyl sulfone being eluted with 20% ether in hexane and benzyl sulfone with 50% ether in hexane.

With Triphenylphosphine in Methanol–Benzene. A solution of 2.0 g (4.9 mmol) of A[31] and 3.5 g (13.3 mmol) of triphenylphosphine in 10 ml of absolute methanol and 30 ml of benzene was refluxed for 15 hr. The volume of the solution was reduced to about 5–10 ml and the triphenylphosphine dibromide was removed by filtration. The filtrate was passed over 100 g of silica gel eluting first with 5% benzene in hexane (30 mg, 4%) of *cis*- and *trans*-stilbene in the ratio of 4:1, respectively); 10% ether in hexane gave 250 mg of recovered triphenylphosphine, 20% ether in hexane gave 650 mg (41%) of bromobenzyl benzyl sulfone,[12] mp and mmp 107–108°, and 50% ether in hexane gave 505 mg (42%) of benzyl sulfone, mp and mmp 151–152°.

Treatment of 215 mg (0.5 mmol) of **1** (or **2**) with 1.0 g (3.9 mmol) of triphenylphosphine in 20 ml of 2% (by volume) methanol (10 mmol) in benzene and also with 20 ml of 5% (by volume) methanol (25 mmol) in benzene was carried out at reflux for 12 hr and analyzed as above (no precipitate of triphenylphosphine dibromide was formed). The results are listed in Table I.

With Triphenylphosphine in DMF. A solution of 215 mg (0.53 mmol) of **1** (or **2**) and 190 mg (0.72 mmol) of triphenylphosphine in 7.2 ml of dry DMF was heated at 60° for 1 hr. The reaction mixture was poured into 25 ml of water, and this was extracted with three 25-ml portions of ether. The ether extracts were combined, washed with water and a saturated salt solution, and dried over anhydrous magnesium sulfate. The magnesium sulfate was removed by filtration and the resulting filtrate was analyzed as described above (see Table I).

When this reaction was repeated using 215 mg of **1** (or **2**) and 300 mg of triphenylphosphine in 8 ml of 2 and 5% (by volume) methanol in DMF at 60° for 1 hr, the yield of stilbenes decreased markably and the yield of benzyl sulfone rose (see Table I).

With Triphenylphosphine in THF. A solution of 215 mg (0.53 mmol) of **1** (or **2**) and 1.0 g (3.9 mmol) of triphenylphosphine was heated at reflux in dry THF for 20 hr. The mixture was allowed to cool to room temperature, and the solid was collected on a filter and recrystallized from water and then ethanol–ethyl acetate to give 60 mg of tetramethylenebis(triphenylphosphonium bromide), mp 294–296° (lit.[37] 292–293°). The filtrate was processed as described above. The results are summarized in Table II. Using THF that had not been carefully dried led to varying amounts of bromobenzyl benzyl sulfone and benzyl sulfone depending upon the amount of moisture present.

With Zinc–Copper Couple in DMF. A mixture of 215 mg (0.53 mmol) of **1** (or **2**) and 150 mg of zinc–copper couple was stirred and heated at reflux for 1 min and cooled to room temperature, and the copper colored solid removed by filtration. The filtrate was worked up as usual and the results are shown in Table II.

With Zinc–Copper Couple in THF. A solution of 300 mg of **1** (or **2**) and 250 mg of zinc–copper couple in 6 ml of dry THF was heated at reflux for 15 hr. The solid was removed by filtration, and chromatography over silica gel gave *ca.* 20% yield of stilbenes (see Table II) and 200 mg (68%) of recovered **1** (off with 10% ether in hexane).

With Magnesium Metal in THF. A solution of 300 mg of **1** (or **2**) was treated with 25 mg of magnesium turnings in 10 ml of dry THF in an atmosphere of nitrogen at reflux for 3 days. (The reaction was initiated with a crystal of iodine.) The resulting gray solution was filtered and the filtrate worked up as usual (see Table II). Chromatography yielded, along with the stilbenes, 30 mg of recovered **1** (and 50 mg of recovered **2**). Traces of moisture completely inhibited this reaction.

With Lithium Aluminum Hydride. A solution of 100 mg of lithium aluminum hydride in 15 ml of dry THF was stirred at room temperature and 215 mg (0.53 mmol) of solid **1** (or **2**) was added slowly. A vigorous reaction ensued. The solution was stirred for an additional 1 hr, and the excess lithium aluminum hydride destroyed by addition of 2 ml of ethyl acetate and then 2 ml of methanol. The resulting solution was poured into 5% hydrochloric acid solution and extracted well with ether. The usual work-up followed (see Table II).

With Iodide Ion. A solution of 215 mg (0.53 mmol) of **1** (or **2**) and 500 mg (3.0 mmol) of potassium iodide was heated in 7 ml of dry DMF at 65–70° in the dark for 12 hr. The reaction mixture was poured into an aqueous solution of sodium bisulfite and extracted well with ether. The ether extracts were combined and treated in the usual manner (see Table I). The reactions involving lithium iodide, sodium iodide, cesium iodide, and *n*-tetrabutylammonium iodide were all run in the same above manner using 3.0 mmol of the iodides (see Table II). Triphenylmethylphosphonium iodide was made *in situ* by the addition of 790 mg (3.0 mmol) of triphenylphosphine to 500 mg (3.4 mmol) of methyl iodide in 7 ml of dry DMF in the dark.[38] This mixture was warmed to 70° and held there for 5 min before the introduction of 215 mg of **1** (or **2**). The resulting mixture was treated as in the previous iodides (see Table II). If moisture was present, bromobenzyl benzyl sulfone and benzyl sulfone resulted. If the concentration of iodide ion was below *ca.* 0.25 *M*, diphenylacetylene and the bromostilbenes were found in the reaction products, in addition to stilbenes. [These compounds presumably arose by the competitive reaction of **1** (and **2**) with DMF solvent (see Table I).]

Treating A[31] with 1 *M* cadium or calcium iodide in DMF at 80° for reaction times up to 2 days gave starting material and small amounts of $\mathrm{PhC{\equiv}CPh}$ and $\mathrm{PhCH{=}CBrPh}$.

Treatment of *cis*-stilbene or *trans*-stilbene with 0.05 *M* iodine in

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[31] This mixture is referred to hereafter by the symbol A.

[32] J. Wislicenos and F. Seeler, *Chem. Ber.*, 28, 2693 (1895).

[33] Aldrich Chemical Co., Milwaukee, Wis.

[34] G. Drefahl and C. Zimmer, *J. Amer. Chem. Soc.*, **93**, 505 (1960).

[35] I. J. Borowitz, K. C. Kirby, and R. Virkhaus, *J. Org. Chem.*, **31**, 4036 (1966).

[36] Vpc analyses for *cis*-stilbene in this and comparable reaction mixtures came out higher after silica gel chromatography than on the crude reaction mixtures. Apparently by-products in the latter interfere with the analysis since the ratio of *cis*- to *trans*-stilbene in a standard mixture was not changed by chromatography.

[37] G. Wittig, H. Eggers, and P. Duffner, *Justus Liebigs Ann. Chem.*, 619, 10 (1958).

[38] W. C. Davies and W. P. G. Lewis, *J. Chem. Soc.*, 1599 (1934).

0.5 *M* potassium iodide in DMF at 80° in the dark for 12 hr gave no sign of isomerization of either of the stilbenes.

With Potassium Thiophenoxide in DMF. To a solution of 215 mg (0.53 mmol) of **1** (or **2**) in 7.5 ml of DMF was added 170 mg (1.15 mmol) of potassium thiophenoxide. This mixture was stirred under nitrogen at 60° for 30 min, poured into water, and worked up in the usual manner. Chromatography over silica gel gave diphenyl disulfide (120 mg, 0.55 mmol, by vpc analysis) and stilbenes along with *ca.* 5% bromobenzyl benzyl sulfone and *ca.* 1% benzyl sulfone (see Table II).

This same reaction repeated using just one-half the amount of potassium thiophenoxide gave the same relative percentages of *cis*- and *trans*-stilbene and no observable isomerization of the recovered **1** or **2**.

Use of higher concentrations of potassium thiophenoxide gave correspondingly higher yields of bromobenzyl and benzyl sulfone, *e.g.*, 1.5 g (5.35 mmol) of A in 40 ml of dry DMF under nitrogen was treated with 4.0 g (25 mmol) of potassium thiophenoxide at 60° for 15 min and cooled to room temperature, and 2 ml of deuterium oxide (99.8%) was added. The usual work-up followed by chromatography gave trace amounts of *cis*-stilbene and bromobenzyl benzyl sulfone, 58 mg (6%) of *trans*-stilbene, and 790 mg (86%) of benzyl sulfone which from nmr analysis showed less than 3% deuterium incorporation. Freshly dried potassium thiophenoxide gave less benzyl sulfone and correspondingly higher yields of stilbenes. Although the potassium thiophenoxide was always quickly transferred to the reaction vessel, it apparently was always able to pick up some moisture from the air. No attempt was made to run these reactions in an enclosed dry area (drybox).

With DMF Solvent. A solution of 200 mg of **1** (or **2**) in 30 ml of dry DMF was held at reflux for 3 hr and then worked up in the usual manner (see Table I).

Attempted Reactions of Nucleophiles. Solutions of A in DMF or *N*,*N*-dimethylacetamide (DMA) were treated with up to 1 *M* potassium thiocyanate, thiourea, or triphenylphosphine sulfide at temperatures that ranged up to reflux. These experiments yielded recovered starting material and/or products derived from the reaction of solvent with A.

With DMA Solvent. A solution of 215 mg of **1** (or **2**) in 5 ml of dry DMA was refluxed for 6 hr and worked up as usual. An nmr spectrum of the crude reaction mixture showed no starting material present. Chromatography yielded a mixture of diphenylacetylene, *cis*- and *trans*-stilbene, and *cis*- and *trans*-bromostilbene (see Table I).

When this reaction was quenched after 30 min, vpc analysis indicated that the reaction had proceeded to about 50% completion. The nmr spectrum of the crude reaction mixture indicated that in the case of both **1** and **2** *ca.* 20% epimerization had taken place to yield 80% recovered starting material and 20% of its diastereomer.

With 5% Aqueous DMA. A solution of 500 mg of **1** (or **2**) in 9.5 ml of DMA and 0.5 ml of water was held at reflux (165°) for 4 hr. The reaction was worked up as usual. Chromatography over silica gel gave the hydrocarbon fraction which showed by vpc analysis that the reaction had proceeded to *ca.* 35% reaction (30% in the case of **2**). Recovered starting material was *ca.* 15% epimerized (nmr analysis). An identical reaction using deuterium oxide in the place of water yielded recovered starting material (recrystallized twice from methylene chloride–hexane) with *ca.* 90% deuterium incorporation in the case of both **1** and **2**.

A solution of 500 mg of A in 9.5 ml of DMA and 0.5 ml of water was heated at 100° for 12 hr. The work-up and analysis were the same as above and showed *ca.* 10% reaction with 50% deuterium exchange (nmr analysis).

With Triphenylphosphine in the Presence of Silver Nitrate. A solution of 215 mg (0.53 mmol) of **1** (or **2**), 210 mg (1.23 mmol) of silver nitrate, and 500 mg (1.9 mmol) of triphenylphosphine was heated at 70° in 8 ml of dry DMF for 2 hr. The resulting precipitate was removed by filtration, and the filtrate was worked up as usual (see Table II).

With Triphenylphosphine in the Presence of Iodine. A solution of 215 mg (0.53 mmol) of **1** (or **2**), 510 mg (2.0 mmol) of iodine, and 800 mg (3.0 mmol) of triphenylphosphine was heated at 70° in 8 ml of dry DMF for 2 hr in the dark. The mixture was poured into dilute aqueous sodium bisulfite and then worked up as usual (see Table II).

Treatment of *cis*- or *trans*-stilbene under the above condition gave no isomerization.

With Lithium Iodide in THF. A solution of 215 mg (0.53 mmol) of **1** (or **2**) and 500 mg (3.7 mmol) of lithium iodide in 8 ml of dry THF was held at reflux in the dark for 18 hr. The reaction was worked up as usual (see Table II).

With Lithium Bromide in THF. A solution of 1.0 g of A and 2.5 g of lithium bromide in 2 ml of dry THF was held at reflux for 1.5 days. The mixture was worked up as usual; vpc analysis showed that *ca.* 20% reaction had taken place. From the crude reaction mixture, 650 mg of A was recovered by crystallization from ethanol. Vpc analysis showed a trace of stilbenes, diphenylacetylene (16%), *cis*-bromostilbene (42%), and *trans*-bromostilbene (42%) in *ca.* 20% overall yield.

With (−)-Brucine in Benzene. A solution of 500 mg (1.24 mmol) of **1** and 300 mg (0.76 mmol) of anhydrous brucine[39] in 10 ml of dry benzene was held at reflux under nitrogen for 40 min. The solution was cooled and filtered. The filtrate was washed with five 30-ml portions of 5% hydrochloric acid. The benzene was removed by rotary evaporation and a nmr spectrum of the resulting solid showed **1** but no **2** present. This material was recrystallized from carbon tetrachloride to give 280 mg of **1**, mp 162–164°. This was dissolved in 5.0 ml of benzene and the optical rotation was measured ($\alpha = 0.0°$) in a 2-dm tube.

The same reaction with **2** gave 310 mg of recovered **2**, mp 158–159°, with no observable amount of **1** present. The recovered **2** dissolved in 5.0 ml of benzene in a 2-dm tube showed no optical rotation.

These same reactions repeated on a larger scale (1.0 g) still led to no observable optical rotation.

With *d*-*N*,*N*-Dimethyl-α-phenethylamine. A solution of 1.00 g (2.47 mmol) of **1** (or **2**) and 360 mg (2.40 mmol) of *d*-*N*,*N*-dimethyl-α-phenethylamine[40] was heated at reflux in 25 ml of dry toluene under a nitrogen atmosphere for 6 hr. The solution was cooled and decanted from the red oil that had formed. The reaction mixture was worked up as in the case of the brucine reaction. The results of this experiment varied from run to run; *i.e.*, recovered **1** exhibited optical activity in some cases but not in others. When recovered **1** was purified by chromatography over silica gel, no optical activity was retained: **2** also exhibited no optical activity. The products of this reaction are listed in Table I.

Attempted Reaction with Triphenylamine. A solution of 1.0 g of A and 5.0 g of triphenylamine in 25 ml of dry benzene was held at reflux for 3 days. The usual work-up followed by chromatography from silica gel gave only recovered starting material.

Reaction of Benzyl α-Bromobenzyl Sulfone (13) with DMF Solvent. A solution of 100 mg of **13** in 15 ml of dry DMF was heated at reflux for 10 hr. The reaction was worked up as usual to give a 90% yield of stilbenes (32% *cis*- and 68% *trans*-stilbene).

α-Bromobenzyl Phenyl Sulfone. A solution of 25.0 g (0.116 mol) of α-bromophenylacetic acid and 12.8 g (0.116 mmol) of thiophenol in 250 ml of ethanol in which 9.0 g (0.39 g-atom) of sodium metal had been dissolved was held at reflux for 30 min and then allowed to stand at room temperature for 12 hr. The solution was reduced *in vacuo* to *ca.* 100 ml, poured into water, and extracted well with ether. The ether extracts were combined, washed with water and saturated salt solution, and then dried over anhydrous magnesium sulfate. The ether was removed *in vacuo*, and the resulting oil was dissolved in 250 ml of acetic acid. To this solution was added 100 ml of 30% hydrogen peroxide, and the mixture was allowed to stand at *ca.* 70° for 8 hr. The solution was cooled to room temperature, and the solid was removed by filtration. The crystals were washed with 100 ml of water and then with 50 ml of ethanol and 50 ml of ether to give 24.5 g of α-phenylsulfonylphenylacetic acid, mp 170–180° (with loss of carbon dioxide: lit.[41] mp 142–143° with decarboxylation). To a solution of 11.0 g (40.5 mmol) of α-phenylsulfonylacetic acid in 100 ml of water containing 25 g of potassium carbonate was added 8.0 g (50 mmol) of bromine dissolved in 50 ml of 20% aqueous potassium bromide. The resulting mixture stood at room temperature for 6 hr and was filtered. The solid was collected on a filter and recrystallized from methylene chloride–ethanol to give 6.5 g (50% overall yield) of α-bromobenzyl phenyl sulfone, mp 193–194°.

Anal. Calcd for $C_{13}H_{11}BrO_2S$: C, 50.16; H, 3.56. Found: C, 50.31; H, 3.48.

Reduction of α-Bromobenzyl Phenyl Sulfone and Benzyl α-Bromobenzyl Sulfone with Triphenylphosphine. Treatment of 500

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[39] Fischer Chemical Co.

[40] D. N. Kursanov and S. V. Vitt, *Dokl. Akad. Nauk SSSR*, **113**, 607 (1957); *Chem. Abstr.*, **51**, 14598.

[41] E. A. Lehto and D. A. Shirley, *J. Org. Chem.*, **22**, 989 (1957).

mg (1.6 mmol) of α-bromobenzyl phenyl sulfone with 3.0 g of triphenylphosphine in 15 ml of 5% methanol in benzene at reflux for 20 hr gave *ca.* 15% reduction (benzyl phenyl sulfone) and 80% recovered starting material. Essentially the same result was obtained using 5% acetic acid in benzene as the solvent.

This same reaction with benzyl α-bromobenzyl sulfone (500 mg) and 3.0 g of triphenylphosphine gave 80% reduction after 30 hr in 20 ml of 5% methanol in benzene at reflux.

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Semiempirical Models for Substituent Effects in Electrophilic Aromatic Substitution and Side-Chain Reactions

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Abstract: Semiempirical substituent effect models are formulated which successfully predict relative rates of reaction for a wide variety of substituted aromatic systems, in both electrophilic aromatic substitution and electrophilic side-chain reactions. The semiempirical equations are based on the separation of effects into field and resonance terms. The approach treats the effects of substituents as perturbations affecting the reactivity of parent aromatic systems through the mechanisms of substituent interaction with the charge developed in the transition state. The approach is evaluated on the basis of success in handling the available data for protodetritiation and solvolysis in substituted aromatic systems. New quantitative data are reported for the solvolysis of a series of substituted 1-(2-benzo[*b*]thienyl)ethyl *p*-nitrobenzoates.

The modification of the Hammett equation introduced by Brown and Okamoto by the definition of σ^+ constants[2] has proven remarkably useful for the treatment of substituent effects in benzene for reactions in which a positive charge developed in the transition state is stabilized by delocalization into the aromatic ring. However, in extending the Hammett equation to other aromatic systems, an approach based on empirically defined constants would necessitate establishing a very large number of substituent constants to cover all possible positional orientations of substituent site and reaction center in every aromatic nucleus. Capabilities for prediction of reaction rates in new systems are obviously limited if restricted to dependence upon previously determined, purely empirical σ^+ constants. Furthermore, such a purely empirical approach contributes little to the understanding of the relationships underlying the effects of substituents.

On the other hand, the strictly nonempirical approach of calculating energy differences between ground states and transition states for each substituted molecule by quantum-mechanical means also has limitations of practicality. Approximate quantum-mechanical methods have shown some success in treating the reactivity of substituted benzenes,[3,4] but in one sense the totally quantum-mechanical approach is similar to the totally empirical approach: independent operations must be performed for each situation, *i.e.*, costly calculations are necessary for every substituent in each arrangement of substituent site and reaction center in every aromatic system considered. Neither the quantum-mechanical approach nor the purely empirical method takes advantage of the expected similarities in the effect of substituents on a variety of aromatic systems.

We wish to report in this paper a semiempirical approach for the quantitative correlation and prediction of aromatic substituent effects for electrophilic substitution and solvolysis reactions. This semiempirical approach treats the effects of substituents as perturbations affecting the reactivity of the parent aromatic systems. By identifying the mechanisms of substituent perturbations and by referring to observed effects in a basis system (benzene), mathematical models are developed to estimate the perturbations for other aromatic molecules. These semiempirical models combine fundamental theoretical concepts with empirically derived parameters to produce a method more practical than either purely empirical or purely theoretical treatments. The approach will be evaluated on the basis of success in handling the available data for protodetritiation and solvolysis in substituted aromatic systems and will be compared with previously used methods.

In using the modified Hammett equation for the correlation

$$\log k/k_0 = \sigma^+\rho \qquad (1)$$

of relative rates of electrophilic reactions for substituted benzenes, it is necessary to know either σ_p^+ or σ_m^+ constants for the substituents involved, depending upon the site of substitution relative to the reaction center. To use the Hammett equation to predict relative rates, it is necessary to know both the σ^+ constants and the ρ value for the reaction being considered. Clearly, in extending the Hammett equation to other aromatic systems, the desirable approach is one which

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(1) National Institutes of Health Predoctoral Fellow, 1970–date (GM-49,851).

(2) H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, 80, 4979 (1958).

(3) A. Streitwieser, Jr., H. A. Hammond, R. J. Jagow, R. M. Williams, R. G. Jesaitis, C. J. Chang, and R. Wolf, *J. Amer. Chem. Soc.*, 92, 5141 (1970).

(4) G. R. Howe, *J. Chem. Soc. B*, 984 (1971).