

Figure 3. Representation of the Sims-Fry<sup>13,14</sup> relation between transition-state symmetry and heavy-atom isotope effect ( $k/k^*$ ).

neophyl brosylate, and with the data of Shiner and Sieb,<sup>10</sup> who measured  $\alpha$ -deuterium isotope effects for the solvolyses (25 °C) of a series of para-substituted neophyl methanesulfonates and triflates, the values (per deuterium) lying in the range 1.099–1.134. Our value ( $k_H/k_D = 1.098$ ) for **1-1,1-d<sub>2</sub>** is clearly consistent with those reported<sup>9,10</sup> for the neophyl derivatives. Although slightly higher than expected for typical  $S_N2$  reactions,<sup>11</sup> the out-of-plane bending in a nonlinear transition state such as illustrated in Figure 1 should be greater than in the typical  $S_N2$  case. Thus the higher  $k_H/k_D$  ratios reported here and also by Ando<sup>9</sup> and Shiner<sup>10</sup> are consistent with the Streitwieser<sup>12</sup> explanation for  $\alpha$ -deuterium isotope effects.

A possible explanation of the carbon-14  $k/k^*$ 's is to be found in the treatment of Fry<sup>13</sup> and Sims, Fry, and co-workers,<sup>14</sup> who related the primary heavy atom isotope effects during  $S_N2$  displacements to the bond orders ( $n_2$  and  $n_1$ ) for the developing and disappearing bonds, respectively, of the transition state. The results, for any given entering and leaving group are idealized as shown in Figure 3 (it is assumed that  $n_1 + n_2 = 1$ ). Although Bron's treatment<sup>15</sup> shows no maximum in a similar plot, the Sims-Fry<sup>13,14</sup> calculations have been supported experimentally by Yamataka and Ando<sup>16</sup> in the Menschutkin reaction of para-substituted benzyl arylsulfonates with *N,N*-dimethyl-*p*-toluidine.

Thus, according to Fry,<sup>13</sup> Sims, and co-workers,<sup>14</sup> a maximum, primary heavy-atom isotope effect should be associated with an  $S_N2$  or  $S_N2$ -like reaction only if the transition-state is nearly symmetrical. The observed value [ $k/k^* = 1.048$ ] for **1-1-<sup>14</sup>C** is smaller than that reported<sup>9</sup> for solvolysis of neophyl-**1-<sup>14</sup>C** brosylate (Figure 2), but still much too large to imply a complete loss of  $S_N2$  character. We therefore assume a reasonably unsymmetrical transition state ( $n_1 \neq n_2$ ). The value  $k/k^* = 0.990$  for solvolysis of **1-3-<sup>14</sup>C** seems to indicate that the bond order ( $n_1$ ) for the breaking  $C_1$ -O bond is greater than that ( $n_2$ ) for the developing  $C_3$ -C<sub>1</sub> bond. This would imply that the vibrational stretching frequency and force constants for  $C_3$ -C<sub>1</sub> in the transition state are smaller than those for the  $C_1$ -O and that the activation energy for the solvolysis is lower than it would be in the event the transition state were symmetrical, meaning that anchimeric assistance by the triple bond must be considerable and probably much greater than for the neophyl<sup>9,10</sup> case.

## References and Notes

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- The authors acknowledge, with thanks, travel funds generously provided through the Scientific Affairs Division of the North Atlantic Treaty Organization (Research Grant No. 814). Financial help of the "Fonds der Chemischen Industrie" is gratefully acknowledged.
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- (a) The syntheses of all isotope position isomers of 1-pent-3-ynol begin with triphenylphosphine and methylbromoacetate which are condensed and then allowed to react with propionyl chloride. The Wittig reagent, on pyrolysis, yields methyl pent-2-ynoate, which is hydrolyzed in base, then isomerized with sodium hydroxide to yield  $CH_3C\equiv CCH_2COOH$ ; esterification with diazomethane followed by treatment with lithium aluminum hydride or deuteride produces the alcohols which are then converted to triflates. For the synthesis of 1-1-<sup>14</sup>C, methyl bromoacetate-1-<sup>14</sup>C was employed, whereas for 1-3-<sup>14</sup>C we used propionyl-1-<sup>14</sup>C chloride. (b) Experimental details are as described in the following references: G. Märkl, *Chem. Ber.*, **94**, 3005 (1961); R. J. Bushby and G. H. Whitham, *J. Chem. Soc. B*, 233 (1969); E. R. H. Jones, G. H. Whitham, and M. C. Whiting, *J. Chem. Soc.*, 3201 (1954). (c) The triflate was prepared as described in ref 5. (d) Isotope effects were determined at low conversion by the method of competing reactions (see, for example, V. F. Raaen and C. J. Collins, *Pure Appl. Chem.*, **8**, 347 (1964); V. F. Raaen, T. K. Dunham, D. D. Thompson, and C. J. Collins, *J. Am. Chem. Soc.*, **85**, 3497 (1963)). Deuterium-labeled reactant was also labeled at C<sub>3</sub> with <sup>14</sup>C, and the change in <sup>14</sup>C content was used as a measure of  $k_H/k_D$ . All determinations of  $k_H/k_D$  and  $k/k^*$  were run in triplicate. The fractions (*f*) of reaction were calculated from the (known) reaction kinetics. Products (ketone **5**) were isolated at *f* = 0.10 and at *f* = 1.00; comparisons of their <sup>14</sup>C contents allowed calculation of the isotope effects. With one exception, radioactivity assays were run in triplicate.
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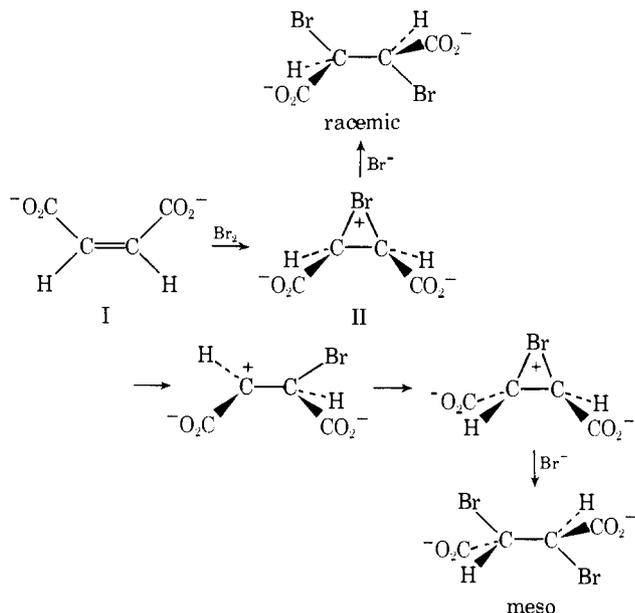
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## On the Aqueous Bromination of Maleate and Fumarate Ions

Sir:

In a classic paper by Roberts and Kimball,<sup>1</sup> the cyclic bromonium ion was first postulated in order to explain the stereospecific addition of bromine to the diethyl esters and the

disodium salts of maleic and fumaric acids. The fact that disodium maleate (I), gave primarily<sup>2</sup> (78%) meso product was attributed to the instability of the bromonium ion (II) derived from maleate with its two eclipsed carboxylate groups. The repulsion of these groups caused opening of the ring, rotation, and formation of the meso product.



In subsequent years, this mechanism became generally accepted and was broadened to include numerous electrophilic additions to alkenes which proceed with trans stereospecificity. While considerable evidence was amassed which fitted such a mechanism of addition, there was little evidence which had the cyclic ion as an obligatory intermediate. Bell and Pring<sup>3</sup> have pointed out that "The main evidence adduced to support the bromonium ion hypothesis is the preponderance of trans addition, though an exception has to be made for addition to the doubly charged maleate ion."

In an attempt to gather more information on the aqueous bromination of maleate, we reinvestigated<sup>4</sup> the effect of temperature and bromide ion concentration on the proportion of stereoisomeric products. If the product composition were a result of a partitioning of the cyclic bromonium ion between unimolecular ring opening and the attack by bromide ion, running the reaction at a lower temperature should diminish the ring opening (which would presumably<sup>5</sup> have a more positive entropy of activation than attack by bromide ion) and therefore produce a greater proportion of trans addition racemic product. As can be seen from Table I, the opposite result was found. At the lowest reaction temperature, the distribution of products was virtually identical with that obtained from the bromination of fumarate ion. The energetically preferred pathway for bromination of these compounds is therefore stereoselective for the meso product rather than stereospecific trans addition. At the higher temperatures, a trans addition pathway becomes significant and is assumed to involve the bromonium ion intermediate.

A second test of the Roberts and Kimball mechanism was tried by performing the reaction with varying amounts of added bromide ion. If bromide ion attacks the bromonium ion to produce trans addition, a high concentration of bromide should favor this pathway leading to racemic dibromide from the bromination of maleate. As can be seen from Table II, added bromide ion produced the opposite result. A high concentration of bromide encouraged the stereoselective mechanism and was presumably involved in the formation of an intermediate which had lost its stereochemical identity. Fur-

Table I. Bromination of Maleate ( $\text{Br}^- = 0.8 \text{ M}$ )

Reaction temp, °C	% meso product
-5	90
40	56
65	46

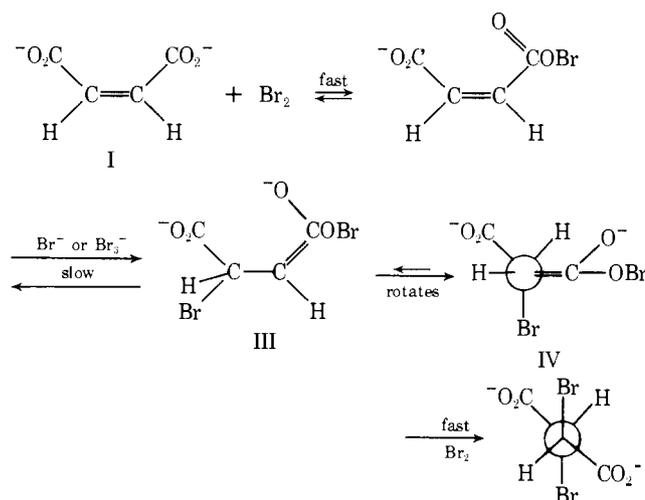
Table II. Bromination of Maleate at 40 °C

Molarity of $\text{Br}^-$	% meso product
0.0	32
0.2	38 <sup>6</sup>
0.8	56
4.0	73

thermore, this intermediate must proceed quickly to product since no isomerization of starting material was found in these reactions under the usual reaction conditions. When, however, the bromine was added to the reaction very slowly, the starting material was found to be 37% isomerized to fumarate indicating that the production of intermediate was reversible but that it reacted quickly with bromine to form the dibromide products.

Bromination of fumarate at various temperatures and bromide concentrations always led to a product mixture which contained  $93 \pm 3\%$  meso dibromide.

All of these results are consistent with a mechanism analogous to that postulated<sup>7a</sup> for the acid catalyzed bromination of maleic acid in glacial acetic acid.<sup>7b</sup>



The attack of bromine upon the carboxylate oxygen has been postulated in other reactions<sup>8</sup> and acyl hypobromites are well-known compounds.<sup>9</sup> It has also been shown that other halogens complex preferentially to the oxygen<sup>10</sup> in  $\alpha, \beta$  unsaturated aldehydes. The nucleophilic attack at the  $\beta$  position is also well documented for a number of  $\alpha, \beta$  unsaturated derivatives.<sup>11</sup> This leads to an enolate ion (III) which rotates around the central bond to the preferred conformation (IV). Bromination of this enolate from the more open side leads to the meso product. Nucleophilic attack on the enolate seems an unlikely alternative as no meso dichloride was found in the bromination of maleate in the presence of a large excess of chloride ion. In a more acidic solution, the enolate ion would be uncharged and therefore less reactive toward bromine. As expected, bromination of maleic acid in water was accompanied by a considerable isomerization to fumaric acid.

The above mechanism also explains the much greater reactivity found for the anions of  $\alpha,\beta$  unsaturated acids.<sup>12</sup> An additional advantage of this mechanism is that it escapes the unstable carbonium ion adjacent to the carboxylate group. Not only would such an intermediate be difficult to form, but it would be expected to react with solvent to produce bromohydrin and no such product is found. Bromohydrins would be less likely from the 1,4 addition mechanism as water is not sufficiently nucleophilic to attack the hypobromite. A similar argument<sup>13</sup> was invoked to explain why dilute HBr, but not dilute H<sub>2</sub>SO<sub>4</sub>, can isomerize maleic acid.

We therefore suggest that two mechanisms are operating in the aqueous bromination of maleate (and presumably fumarate): (1) the higher energy bromonium ion mechanism which effects a trans addition and (2) the lower energy 1,4 addition which produces primarily meso product. It should be noted that Atkinson and Bell,<sup>14</sup> on the basis of a kinetic study, have postulated that two pathways operate concurrently in the aqueous bromination of olefins. They suggest that the intermediate RBr<sup>+</sup> predominates in the bromination of simple alkenes whereas an intermediate RBr<sub>2</sub> is predominant in the bromination of diethyl fumarate. A later study<sup>3</sup> showed that the aqueous bromination of diethyl maleate and diethyl fumarate both gave the meso dibromide.

A typical experiment was done as follows: Maleic acid (2.9 g, 25 mmol) was dissolved in 25 mL of 2 M NaOH (50 mmol) and 2.0 g of sodium bromide (20 mmol) was added. This solution was mechanically stirred in a constant temperature bath while 25 mL of 1.0 M (25 mmol) bromine in carbon tetrachloride was added. When the bromine color disappeared, the organic layer was removed and the aqueous layer was acidified with 7 mL of concentrated hydrochloric acid and extracted with 2 × 75 mL of ether. The ether extracts were combined, dried over sodium sulfate, and evaporated on a steam bath. After further drying in a desiccator, these mixtures were dissolved in 12 mL of acetone and analyzed by proton NMR. Integration of the two peaks around 260 Hz indicated the proportion of isomers in the mixture (the racemic dibromide absorbing downfield of the meso product). In some cases, mixtures were also analyzed in basic D<sub>2</sub>O solution. The identity of the peaks in the NMR spectrum was checked by the addition of authentic samples of each product. In some cases, the products were isolated, purified, and checked with mixture melting points.

The use of bromine in aqueous bromide solution in place of the two-phase addition of bromine in carbon tetrachloride was less convenient but gave similar amounts of products. The bromination using half molar amounts of base (producing sodium hydrogen maleate) appeared to go slower but gave similar data. The bromination using no base went much slower and caused precipitation of fumaric acid.

The stability of the products under reaction conditions was also checked.

## References and Notes

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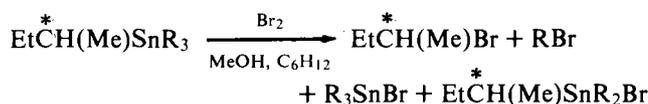
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## Stereochemistry of the Bromine Cleavage of Organotin Compounds

Sir:

On the basis of experiments with a single compound, optically active *sec*-butyltrineopentyltin,<sup>1</sup> the stereochemistry of bromodestannylation is generally described as involving inversion of configuration at carbon, with all the mechanistic consequences of such a statement.<sup>2</sup> Previously retention of configuration was found only in the case of optically active cyclopropyltin compounds.<sup>3</sup> This was easily rationalized in terms of the known resistance of cyclopropyl derivatives to react with inversion of configuration.<sup>1</sup> We report here some results which demonstrate clearly that inversion is *not* a general trend for *sec*-butyltrialkyltin compounds and, by extension, for other tetraalkyltins. Indeed retention of configuration appears to be the predominant mode of reaction and the steric requirements of the neopentyl group most probably are responsible for the special behavior of *sec*-butyltrineopentyltin.

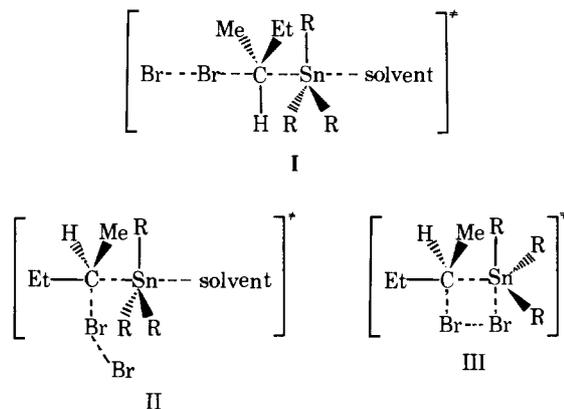
Our bromodestannylation experiments were carried out in the dark with 1:1 stoichiometry. The solution of bromine in methanol was added to the organotin compounds<sup>4</sup> in a 1:1 cyclohexane-methanol mixture at -10 °C and stirred for 12 h at 20 °C.<sup>8</sup>



Isopropyl and 3-pentyl (and 2-butyl) were selected as the R groups in *sec*-BuSnR<sub>3</sub> in order to ensure a rate of cleavage comparable to that of the *sec*-butyl group.<sup>9</sup> The results obtained, cleavage with predominant retention of configuration at carbon, prompted us to reexamine the cleavage of *sec*-butyltrineopentyltin (Table I).

Our experiments confirmed the experiment reported previously.

It would appear in the brominolysis of R<sub>4</sub>Sn that at least two mechanisms, with opposite stereochemistry, are competing,<sup>12</sup> and the following transition states may be considered:



Transition states I<sup>1</sup> and II,<sup>9</sup> with nucleophilic assistance of methanol at tin, correspond respectively to inversion and re-