# CARBON-13 KINETIC ISOTOPE EFFECTS IN THE SOLVOLYSIS OF 1-BROMO-1-PHENYLETHANE<sup>1</sup>

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#### ABSTRACT

Carbon-13 kinetic isotope effects have been measured for the solvolysis in methanol and ethanol of 1-bromo-1-phenylethane of natural isotopic abundance. Methanolysis of the bromide at 25° C gave a kinetic isotope effect  $(k^{12}/k^{13})$  of  $1.0065\pm0.0006$ , and ethanolysis at 45° C gave  $1.0064\pm0.0010$ . These surprisingly low effects for a bond-rupture process have been interpreted in terms of a model for the transition state in which the bonding of the isotopic carbon is strengthened by conjugation of the electron deficient center with the ring. The results are considered to provide support for the mass fragment model for evaluation of the effective mass term of the Bigeleisen expression for the theoretical calculation of kinetic isotope effects.

#### INTRODUCTION

It has been known for many years that molecules differing only in the isotopic mass of a component atom may react at different rates (1, 2, 3). These kinetic isotope effects are largest when some bond associated with the isotopic atom is undergoing rupture in the rate-determining step of the process. Consequently, isotope effect studies have played an important role in the elucidation of reaction mechanisms (1, 4).

Following the discovery (5, 6, 7) of carbon kinetic isotope effects of considerable magnitude, Bigeleisen (8, 9) proposed equations for the theoretical evaluation of kinetic isotope effects using spectroscopic data. In applying these equations to the rather complex molecular systems for which kinetic isotope effects had been studied experimentally, it was usually found necessary to make the simplifying assumption that the vibrational frequencies of all bonds other than the bond undergoing rupture remain unaltered in the transition state (3, 9). Notwithstanding this and other approximations, surprisingly good agreement has been obtained between calculated and experimental isotope effects in a number of reactions.

Since, in principle, kinetic isotope effects provide information concerning the nature of the transition state, it was decided to undertake a carbon isotope effect study of the reaction of nucleophilic substitution at a saturated carbon atom, a reaction which is one of the most important in organic chemistry and which has been the subject of detailed mechanistic study for over 25 years. At the outset of the investigation it was thought that kinetic isotope effects might provide a useful criterion of mechanism since, on the basis of a simplified theoretical treatment, one might expect that reaction by the unimolecular, or  $S_{\rm N}1$ , mechanism, in which the main covalency change in the rate-determining step is the rupture of a bond associated with the isotopic atom, would give rise to a larger effect than reaction by the bimolecular, or  $S_{\rm N}2$ , mechanism, in which bond formation and bond rupture are synchronous. It was hoped, also, that the investigation might serve as a test for the theoretical equations and, in particular, might help in deciding between the Slater and mass fragment methods for evaluation of the temperature-independent term of these equations.

While this work was in progress two papers by Bender appeared (10, 11) reporting

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the results of a carbon-14 isotope effect study of the displacement reactions of methyl iodide and *tert*-butyl chloride. In the  $S_{\rm N}2$  reaction of methyl iodide with hydroxide ion and with several tertiary amines  $k^{12}/k^{14}$  ratios ranging from 1.09 to 1.14 were observed. Solvolysis of methyl iodide in aqueous ethanol in the presence of silver ion, which was considered to be a borderline case between a  $S_{\rm N}2$  and  $S_{\rm N}1$  reaction, gave an isotope effect which was essentially no different from effects found in the pure  $S_{\rm N}2$  processes. These large effects are of the same magnitude as many effects observed in reactions involving only bond rupture and agree with the predictions of the Bigeleisen equation based on a model for the transition state in which only the bond undergoing fission is considered to have changed in the activation process. Hydrolysis of *tert*-butyl chloride in aqueous dioxane, somewhat surprisingly, gave rise to a smaller effect,  $k^{12}/k^{14} = 1.03$ , than did the reactions proceeding by the bimolecular mechanism. From these results, Bender concluded that kinetic isotope effect studies are of very limited value in differentiating between  $S_{\rm N}1$  and  $S_{\rm N}2$  reactions.

The present paper is concerned with a carbon-13 study of the solvolysis of 1-bromo-1-phenylethane in methanol and ethanol. Carbon-13 was chosen as the heavier isotope rather than carbon-14 since, using mass spectrometry, a higher order of precision in evaluation of the isotope effect is possible ( $\pm 0.001$  in this study, compared with  $\pm 0.005$ to  $\pm 0.015$  in Bender's work), contamination of samples is less likely to give rise to spurious effects, and isotopic labelling is unnecessary. The choice of 1-bromo-1-phenylethane as the reactant was dictated by two considerations. First, depending upon the conditions, the compound may be made to undergo reaction either exclusively by the  $S_{\rm N}1$  or by the  $S_{\rm N}2$  mechanism (12, 13); under solvolytic conditions in solvents of high ionizing power the reaction exhibits characteristics of a unimolecular process, while pure second-order kinetics are observed for reaction in ethanol using ethoxide concentrations of 1.5 *M* or higher. Secondly, the compound and its reaction products, 1-methoxyand 1-ethoxy-1-phenylethane, may be degraded so as to furnish, in good yield for mass spectrometer analysis, carbon dioxide derived exclusively from the carbon at the seat of displacement.

#### EXPERIMENTAL

#### Materials

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Absolute methanol and ethanol were prepared from commercial "absolute" products using magnesium, followed by distillation through a 20-in. Vigreux column.

1-Bromo-1-phenylethane was prepared by passing dry hydrogen bromide into 1-phenylethanol maintained at 0° C (14). The product, purified by fractional distillation, was obtained in 85–93% yields (b.p. 83–84° C (10 mm),  $n_{\rm D}^{25}$  1.5592).

1-Methoxy-1-phenylethane and 1-ethoxy-1-phenylethane, products of the solvolysis reactions, were required for testing the degradation procedures. These were prepared in approximately 75% yield by heating a solution of 1-bromo-1-phenylethane in the anhydrous alcohol for 24 hours at reflux temperatures. The physical constants of the ethers were: 1-methoxy-1-phenylethane, b.p.  $55-56^{\circ}$  C (10 mm),  $n_{\rm D}^{25}$  1.4900; 1-ethoxy-1-phenylethane, b.p.  $65-66^{\circ}$  C (11 mm),  $n_{\rm D}^{25}$  1.4821.

To test for possible isotopic exchange between the ether product and 1-bromo-1phenylethane it was necessary to prepare 1-ethoxy-1-phenylethane-1-C<sup>13</sup>. Acetophenonecarbonyl-C<sup>13</sup> (8.6 g, 0.072 mole), prepared from sodium acetate-1-C<sup>13</sup> by the method of Shantz and Rittenberg (15), was reduced to the carbinol using lithium aluminum hydride

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(2.0 g, 0.053 mole) in anhydrous ether (50 ml). The complex was decomposed with 20% sulphuric acid and the product isolated by ether extraction. The crude carbinol was dissolved in carbon tetrachloride (25 ml) and treated with anhydrous hydrogen bromide until there was no further absorption of gaseous halide. The reaction mixture was poured into water and extracted with carbon tetrachloride. The combined extracts were dried, concentrated, and taken up in absolute ethanol (100 ml). This solution was heated under reflux for 24 hours while small amounts of a solution of sodium ethoxide in ethanol were added periodically to neutralize the hydrogen bromide formed. At the end of this period the solution was poured into cold water and extracted with ether. Fractional distillation gave 1-ethoxy-1-phenylethane-1-C<sup>13</sup> (b.p. 64–65° C (10 mm),  $n_D^{25}$  1.4821) in 65% yield, based on the acetophenone.

# Kinetic Measurements

The rates of solvolysis of 1-bromo-1-phenylethane in absolute methanol and ethanol were followed by acid-base titration of the product, hydrogen bromide. Reaction temperatures were chosen such that there was approximately 5% reaction in 15 minutes. This was a convenient rate for the partial reactions in the subsequent isotope effect experiments. A solution of the bromide in the alcohol was maintained to within  $\pm 0.02^{\circ}$  C of the desired temperature and at appropriate time intervals accurately measured aliquots were removed and quickly placed in a cold mixture of benzene and water. The resulting mixture was immediately titrated with standard sodium hydroxide using phenolphthalein as indicator. The rate constants were obtained from a least-squares plot of reaction time versus log[RBr].

## Isotope Effect Experiments

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In the determination of the carbon-13 isotope effect, 1-bromo-1-phenylethane of normal isotopic abundance was solvolyzed to some small known extent of reaction, the ether product separated from unreacted bromide and degraded so as to furnish carbon dioxide derived exclusively from the alkoxy-bearing carbon. The isotopic ratio for this carbon dioxide and that of the carbon dioxide formed from the original reactant by a similar degradation procedure were measured mass spectrometrically. The rate constant ratios,  $k^{12}/k^{13}$ , were calculated from the isotopic ratios using an expression derived by Stevens and Attree (16), which takes into account the extent of reaction.

The detailed procedure was as follows. One liter of the appropriate alcohol was equilibrated to the desired reaction temperature and a weighed sample of 1-bromo-1-phenylethane was added. The resulting solution, approximately 0.5~M in organic bromide, was allowed to stand in the constant-temperature bath for an accurately measured time corresponding to approximately 5% reaction, and then was quickly poured into a mixture of 3–4 liters of cold water and 600 ml of benzene. The quenched reaction mixture was vigorously shaken, the layers separated, and the aqueous layer extracted with three 300-ml portions of fresh benzene. The combined extracts were thoroughly washed with water and dried over calcium chloride, and the benzene then removed by distillation under reduced pressure. The small amount of product was separated from the large amount of unreacted bromide by careful fractional distillation under reduced pressure using a 50-cm tantalum-wire column described by Cason and Rapoport (17). One such distillation was sufficient to separate the methyl ether; a second distillation was required for 1-ethoxy-1-phenylethane. Trial experiments on synthetic mixtures of 1-ethoxy-1-phenylethane and the organic bromide showed that ether of 93-95% purity could be separated with

better than 90% recovery. The impurity, which was mainly bromide, would not be expected to affect significantly the isotopic ratios subsequently determined.

Under the normal solvolytic conditions, hydrogen bromide concentration builds up as the reaction proceeds and, as a result, there might be some tendency for ether cleavage with the regeneration of starting bromide. If this were to happen, the measured isotopic fractionation would not be that resulting from a strictly unidirectional process but rather from a process tending toward equilibrium. Since, in all experiments, the reaction was stopped before more than 10% of organic halide had been consumed, the back reaction, if it occurred at all, would be expected to make only a very minor contribution to the measured effect. Nevertheless, to establish this point, two isotope effect experiments in methanol were carried out in which sodium methoxide was present in a concentration which was sufficient to neutralize the hydrogen bromide formed in the partial reaction but not sufficient to induce any significant amount of bimolecular reaction (12, 13). The isotope effects obtained in the presence and in the absence of methoxide ion differed only very slightly, if at all.

It was also necessary to establish that no isotopic exchange occurred during the separation of the ether product from the large amount of unreacted organic bromide. This was accomplished by subjecting a mixture of 1-ethoxy-1-phenylethane-1-C<sup>13</sup> and unlabelled 1-bromo-1-phenylethane to the usual separation procedure and determining the loss of label in the recovered ether. It was found that an upper limit for the exchange, if it occurred at all, was 5%. This would have no measurable effect on the results.

## Degradation Method

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Since the isotopic ratio for the carbon atom at the center of displacement must be determined for the reactant and for the product of partial reaction, it was necessary to develop a degradation procedure whereby this atom could be removed from the rest of the molecule and converted in high yield to carbon dioxide for mass spectrometric analysis. The method consisted of oxidation of the bromide and ether to benzoic acid followed by decarboxylation using the Schmidt reaction.

# Oxidation to Benzoic Acid

Best over-all yields of benzoic acid were obtained by a two-stage oxidation procedure. In the first stage, the compounds were oxidized with alkaline permanganate in a pyridine– water solvent to give a mixture of benzoic acid and benzoylformic acid. This acid mixture was then further oxidized with hydrogen peroxide whereby the benzoylformic acid was quantitatively converted to benzoic acid.

1-Bromo-1-phenylethane (1.65 g, 0.0089 mole) was placed in pyridine (50 ml) and water (100 ml) and potassium hydroxide (5 g, 0.089 mole) was added. The mixture was heated under reflux for 15 minutes with vigorous stirring. Solid potassium permanganate (8 g, 0.051 mole) was then added slowly at reflux temperature to the stirred solution over a period of 15 minutes and the reaction mixture heated for an additional 30 minutes with vigorous stirring. The mixture was cooled to about 50° C and excess potassium permanganate destroyed by the addition of ethanol. The inorganic solids were removed by filtration and washed thoroughly with hot water. The filtrate was cooled, acidified with concentrated hydrochloric acid, and extracted four times with ether. Ether was removed and the residue stirred vigorously for 2 to 3 hours with 5% hydrogen peroxide (30 ml). The reaction mixture was allowed to stand overnight and then heated under reflux to destroy excess peroxide, additional water being added to

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effect complete solution of the benzoic acid. The solution was allowed to cool and the benzoic acid collected. Additional acid was recovered by ether extraction of the filtrate. Total yield of pure acid was 0.909 g (84%), m.p.  $121.5^{\circ}$ - $121.8^{\circ}$  C (corr.).

A similar procedure using, however, 50% more oxidizing agent was followed for the two ether products. Yields of benzoic acid were generally slightly higher than those obtained from the bromide.

## Decarboxylation of Benzoic Acid

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An apparatus similar to that described by Phares (18) was used. A solution containing approximately 1 millimole of benzoic acid in 3–4 ml of concentrated sulphuric acid was placed in the reaction flask and cooled to 0° C. Approximately 80 mg of sodium azide was added and the flask connected to the absorption traps. The reaction mixture was maintained at about 40° C for 2 hours while the carbon dioxide was swept by means of a slow stream of purified nitrogen into 0.2 M carbonate-free sodium hydroxide. The trapped gas was precipitated as barium carbonate (19). Great care was taken in all operations to avoid contamination with atmospheric carbon dioxide. Yields of barium carbonate were in the range 91-93%.

## Tests for Rearrangement and Isotopic Fractionation in the Degradation Reactions

There is a possibility, albeit an unlikely one, that rearrangement might occur during the two-stage oxidation of bromide and ether to benzoic acid, with the result that the carbon atom in the carboxyl group of the acid would not be the atom originally joined to the benzene ring. To test for this, some labelled ether, 1-ethoxy-1-phenylethane-1-C<sup>13</sup>, was subjected to the usual alkaline oxidation while another sample was oxidized by chromic anhydride to acetophenone, which was then converted to benzoic acid by means of the haloform reaction. Carbon dioxide samples were prepared in the usual way from each benzoic acid sample and analyzed mass spectrometrically. The isotopic ratios obtained for the two samples were identical within the precision limits of the measurements and they corresponded closely to the ratio expected on the basis of the carbon-13 content of the barium carbonate used in the synthesis of the labelled ether. From this result it may be concluded that no rearrangement occurred during the degradation.

Although the yields in each of the degradation steps were good, the possibility remained that isotopic fractionation during the conversion of bromide or ether to carbon dioxide might affect, to a measurable extent, the isotopic abundance of this gas. To test for this possibility the following interconversions were carried out: (1) 1-phenylethanol of normal isotopic abundance to 1-bromo-1-phenylethane using dry hydrogen bromide; (2) a sample of this bromide to 1-methoxy-1-phenylethane by methanolysis; and, (3) a further sample of the 1-phenylethanol to 1-methoxy-1-phenylethane using methyl sulphate. Since conversion (3) involved no change in the bonding of the carbon atom alpha to the ring, the isotopic abundance for this carbon should be identical in the alcohol and the ether product. Furthermore, since conversion (1) proceeded in better than 90% yield the isotopic ratio of the bromide should correspond very closely to that of the alcohol. One or more samples of the alcohol, ether, and bromide were oxidized in the usual way to benzoic acid, samples of which were then converted in duplicate or triplicate to carbon dioxide for mass spectrometric analysis. The fourteen carbon dioxide samples prepared in this way gave  $C^{12}/C^{13}$  ratios which were the same within the limits of the mass spectrometric analysis. These results definitely establish that either there was no isotopic fractionation in the degradation reactions or that any small fractionation

that did occur was the same for the ether and the bromide. In either case, the degradations were entirely suitable for the isotope effect studies in which an intercomparison of isotopic ratios was being made.

## Preparation of Carbon Dioxide Samples for Mass Spectrometric Analysis

Carbon dioxide was liberated from the barium carbonate samples by means of concentrated sulphuric acid using standard high vacuum techniques. The gas was trapped at liquid nitrogen temperatures, distilled at  $-78^{\circ}$  C through an "anhydrone" drying tube, and condensed into a standard mass spectrometer sample tube.

## Mass Spectrometry

All carbon dioxide samples were analyzed in a 180° direction-focussing mass spectrometer. The C<sup>12</sup>/C<sup>13</sup> ratios were obtained from the mass 44 / mass 45 ion current ratio after applying a suitable correction for the contribution to mass 45 of the molecule species C<sup>12</sup>O<sup>16</sup>O<sup>17</sup>. Each carbon dioxide sample in a given series of experiments was analyzed relative to a standard, the standard being one of the samples of carbon dioxide prepared from the reactant used in that series. An arbitrary value of 85.00 for the mass 44/45 ratio was assigned to these standards. The procedure was to analyze the standard, the unknown, and the standard again all in the shortest possible time. A single analysis consisted of a series of at least six double spectrograms, each double spectrogram being obtained from a scan of the masses in the order 44, 45, 45, 44. A single analysis was considered satisfactory if the mean deviation of the 44/45 ratios was less than 0.1%, and the mean for the unknown was accepted if the mean for the standard, before and after analysis of unknown, differed by no more than this value.

## RESULTS

The results of the kinetic measurements for the solvolysis of 1-bromo-1-phenylethane in absolute methanol and in absolute ethanol are summarized in Table I.

Solvent	Temp., ℃	Concn. of RBr, M	$k_1 \times 10^5 \text{ sec}^{-1}$
Methanol	25.0	$\begin{array}{c} 0.112 \\ 0.114 \\ 0.303 \end{array}$	5.70 5.72 5.57 Average 5.67
Ethanol	45.0	$\begin{array}{c} 0.486\\ 0.525\\ 0.512 \end{array}$	5.87 6.07 6.07 Average 6.00

T	ABLE I
Kinetic results for solvoly	yses of 1-bromo-1-phenylethane

The results of the isotope effect experiments on the methanolysis and the ethanolysis of 1-bromo-1-phenylethane are given in Tables II and III, respectively. Each individual experiment consisted of a partial reaction of bromide to ether followed by parallel degradations to carbon dioxide of a sample of the original reactant and of the product. The rate constant ratios,  $k^{12}/k^{13}$ , were calculated from the C<sup>12</sup>/C<sup>13</sup> ratios and the percentage of reaction (16).

TABLE II
C12/C13 ratios and kinetic isotope effects in the methanolysis
of 1-bromo-1-phenylethane at 25° C

Expt. No.	Compound degraded	Reaction, %	C <sup>12</sup> /C <sup>13</sup> ratios	k <sup>12</sup> /k <sup>13</sup>	
1	RBr ROCH₃	5.1	$91.16\\91.72$	1.0063	
2	RBr ROCH₃	5.1	$\begin{array}{c} 91.13\\ 91.75\end{array}$	1.0070	
3	RBr ROCH₃	4.7	$\begin{array}{c} 90.95 \\ 91.49 \end{array}$	1.0061	
Ŧ	RBr ROCH₃	4.8	$\begin{array}{c} 91.00\\91.60\end{array}$	1.0068	
5	RBr ROCH₃	4.8	$\begin{array}{c} 90.94 \\ 91.56 \end{array}$	1.0070	
6	RBr ROCH₃	4.7	$\begin{array}{c} 90.87\\91.54 \end{array}$	1.0076	
7ª	RBr ROCH₃	5.0	$\begin{array}{c} 91.07\\91.54 \end{array}$	1.0054	
$8^a$	RBr ROCH₃	5.0	$\begin{array}{c} 90.99\\91.52 \end{array}$	1.0060	
	Ν	Iean value of	isotope effect	$1.0065^{b}$	

<sup>*a*</sup>Experiments carried out in the presence of  $\sim 0.03 M$  NaOCH<sub>3</sub>. <sup>*b*</sup>Standard deviation 0.0007; 95% confidence limit 0.0006.

of 1-bromo-1-phenylethane at 45° C				
Expt. No.	Compound degraded	Reaction,	C <sup>12</sup> /C <sup>13</sup> ratios	$k^{12}/k^{13}$
1	RBr ROC₂H₅	4.9	$\begin{array}{c} 90.86\\ 91.45 \end{array}$	1.0067
<b>2</b>	RBr ROC₂H₅	4.9	$90.88 \\ 91.35$	1.0054
3	RBr ROC₂H₅	5.8	$90.97 \\ 91.59$	1.0070
4	RBr ROC₂H₅	5.6	$\begin{array}{c} 91.02\\91.59\end{array}$	1.0065
Mean value of isotope effect			$1.0064^a$	

TABLE III

C<sup>12</sup>/C<sup>13</sup> ratios and kinetic isotope effects in the ethanolysis of 1-bromo-1-phenylethane at 45° C

<sup>a</sup>Standard deviation 0.0007; 95% confidence limit 0.0011.

## DISCUSSION

It seems reasonable to assume on the basis of the results of extensive kinetic and stereochemical studies (12, 13, 20, 21) that the solvolysis of 1-phenylethyl halides in good ionizing solvents, including methanol and ethanol, proceeds by a  $S_{\rm N}1$  mechanism in the sense that some type of carbonium ion intermediate is involved. Winstein and co-workers (22, 23) have recently proposed that the ionization process for a compound RX can involve two discrete ion pair intermediates, as well as dissociated carbonium ions, and that one or all of these ion types may interact with solvent to form product.



Grunwald and co-workers (24) have presented cogent arguments in support of the idea that for 1-phenylethyl compounds the ratio  $k_2/k_s^{II}$  is small and, therefore, that substitution occurs mainly at the intimate ion pair stage. This seems reasonable since the 1-phenylethyl carbonium ion should be very reactive, particularly in the moderately nucleophilic solvents, methanol and ethanol, used in the present investigation.

There remains the question of the relative rates of reaction of the intimate ion pair with solvent and its collapse to re-form RX (internal return). Winstein (25) has reported that in the acetolysis of 1-bromo-1-phenylethane the true ionization rate is about seven times greater than the titrimetric solvolysis rate. Assuming that product is formed mainly by interaction of solvent with the intimate ion pair, the ratio  $k_{-1}/k_{\rm g}^{\rm II}$  in acetolysis is therefore 6. In methanol and ethanol, which are more nucleophilic solvents (26), there should be a smaller tendency for internal return. One cannot assume, however, that the alcoholysis rates will be determined solely by the ionization step.

On the basis of these considerations the mechanism of solvolysis of 1-phenylethyl bromide may be formulated as follows:

$$RX \xrightarrow{k_1}_{k_{-1}} \underset{\text{Intimate}}{\overset{R^+}{\underset{\text{ion pair}}{x^-}}} R^+ X^- \xrightarrow{k_s^{\text{II}}} ROS + HX$$

For a theoretical evaluation of the carbon isotope effect in this reaction, it is useful to examine two limiting cases, one in which the ionization step is rate determining  $(k_s^{II} \gg k_{-1})$ , and the other in which the intimate ion pair is in equilibrium with the organic halide  $(k_s^{II} \ll k_{-1})$ . In the former case, the observed isotope effect will be the kinetic isotope effect associated with the ionization process. In the latter case, the observed effect will be the result of two fractionation processes, that associated with the interaction of intimate ion pair and that associated with the interaction of intimate ion pair with solvent. It may be readily shown in this case that the over-all isotope effect is given by the expression

$$k/k' = K_{\mathrm{exch}} \cdot \frac{k_{\mathrm{g}}^{\mathrm{II}}}{k_{\mathrm{g}}^{\mathrm{II}}}$$

where k and k' are the specific reaction rate constants for solvolysis of the light and heavy isotopic organic halides, RX and R'X, respectively,  $k_s^{II}$  and  $k_s^{II'}$  are the corresponding rate constants for interaction of the intimate ion pairs, R+X<sup>-</sup> and R+'X<sup>-</sup>, with solvent, and  $K_{exeh}$  is the equilibrium constant for the isotopic exchange process

$$RX + R^{+'}X^{-} \rightleftharpoons R'X + R^{+}X^{-}.$$

Bigeleisen and Mayer (27) have shown that the equilibrium constant for an isotopic exchange process can be expressed as the ratio of the so-called isotopic partition functions ratios, f, for the reacting species. For the exchange process given above,

[1]

[2]

$$K_{\rm exch} = \frac{f_{\rm RX}}{f_{\rm R^+X^-}}$$

where  $f_{RX}$  is the isotopic partition function ratio for organic halide and  $f_{R+X-}$  the ratio for the intimate ion pair. For a rate process, the ratio of the rate constants for the isotopic molecules is given by an expression developed by Bigeleisen (8), which, for the present case of the interaction of solvent molecules with the intimate ion pair, takes the form

[3] 
$$\frac{k_{\rm s}^{\rm II}}{k_{\rm s}^{\rm II'}} = \frac{K}{K'} \cdot \left[\frac{m_{\rm ROS}^{\pm'}}{m_{\rm ROS}^{\pm}}\right]^{\frac{1}{2}} \cdot \frac{f_{\rm R+X^-}}{f_{\rm ROS}^{\pm}}$$

where the K's are transmission coefficients, the ratio of which may be taken as unity,  $m_{\text{Ros}}^{\pm}$  and  $m_{\text{Ros}}^{\pm'}$  are, respectively, the effective masses of the light and heavy transition states in the direction of the reaction co-ordinate, and  $f_{\text{Ros}}^{\pm}$  is the isotopic partition function ratio for these states.

The over-all isotope effect for solvolysis proceeding through an intimate ion pair in equilibrium with undissociated organic halide is, therefore,

[4] 
$$\frac{k}{k'} = K_{\text{exch}} \cdot \frac{k_{\text{s}}^{\text{II}}}{k_{\text{s}}^{\text{II}'}} = \left[\frac{m_{\text{ROS}}^{\pm'}}{m_{\text{ROS}}^{\pm}}\right]^{\frac{1}{2}} \cdot \frac{f_{\text{RX}}}{f_{\text{ROS}}^{\pm}}.$$

If, on the other hand, there is little or no internal return, the rate of solvolysis will be equal to the rate of ionization and, therefore, the istope effect will be given by

$$\frac{k}{k'} = \left[\frac{m_{\rm RX}^{\pm'}}{m_{\rm RX}^{\pm}}\right]^{\frac{1}{2}} \cdot \frac{f_{\rm RX}}{f_{\rm RX}^{\pm}}$$

where the m's and  $f_{RX}^{\pm}$  refer to the isotopic transition states for the ionization step.

The f functions appearing in these equations depend upon molecular vibrations only (27) and are of the form

[6] 
$$f = 1 + \sum_{i=1}^{3n-6} G(u_i) \Delta u$$

where

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$$G(u_{1}) = \frac{1}{2} - \frac{1}{u_{1}} - \frac{1}{e^{u_{1}} - 1}$$
$$u_{1} = \frac{h\nu}{kT}$$
$$\Delta u_{1} = \frac{h}{kT}(\nu_{1} - \nu_{1}').$$

The  $\nu$  and  $\nu'$  quantities are fundamental vibrations of the light and heavy isotopic species, respectively.

The rate constant ratio, k/k', for the solvolysis reaction proceeding through an intimate ion pair in equilibrium with RX now becomes

[7] 
$$k/k' = \left[\frac{m_{\rm ROS}^{\pm}}{m_{\rm ROS}^{\pm}}\right]^{\frac{1}{2}} \left[1 + \sum_{1}^{3n-6} G(u_{\rm RX_1}) \Delta u_{\rm RX_1} - \sum_{1}^{3n-6} G(u_{\rm ROS_1}^{\pm}) \Delta u_{\rm ROS_1}^{\pm}\right]$$

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whereas this rate ratio for solvolysis in which the ionization step is rate determining takes the form

$$] k/k' = \left[\frac{m_{\rm RX}^{\pm'}}{m_{\rm RX}^{\pm}}\right]^{\frac{1}{2}} \left[1 + \sum_{1}^{3n-6} G(u_{\rm RX_{1}})\Delta u_{\rm RX_{1}} - \sum_{1}^{3n-6} G(u_{\rm RX_{1}}^{\pm})\Delta u_{\rm RX_{1}}^{\pm}\right]$$

It can be seen that equations [7] and [8] differ in the effective mass term and in the second summation of the free energy term. In equation [7] these quantities refer to the transition state for covalent bond formation between carbonium ion and solvent; in equation [8] they refer instead to the transition state of the ionization process. It is, therefore, important to compare the nature of these transition states.

Since the intimate ion pair formed from 1-bromo-1-phenylethane is a high-energy intermediate, the energy of activation both for its reaction with solvent and for internal return to organic halide will be very small. Both transition states, therefore, will resemble the intimate ion pair (28). In other words, the carbon-bromine bond of the halide should be almost completely broken in the transition state for the first step and the carbonoxygen bond should be only starting to form in the transition state of the second step. As a result, the change in vibrational energy resulting from the substitution of carbon-13 for carbon-12 will be much the same for the two transition states and will correspond closely to the change in energy resulting from isotopic substitution in the intermediate itself. The only significant difference then in the magnitude of the isotope effect for reaction in which the intimate ion pair is in equilibrium with RX and for reaction in which it is not, should arise from a difference in the effective mass factor.\*

For calculation of the effective mass term Bigeleisen (8) originally applied a theorem of Slater (29) which in effect considers the reaction to be simply the formation or dissociation of a hypothetical diatomic molecule consisting of the two atoms between which the bond change is taking place. Each value of  $m^{\pm}$  is then the reduced mass,  $\mu$ , of the corresponding diatomic molecule and the effective mass term is the square root of the ratio of the reduced masses of the two isotopic molecules,

$$[9] \qquad \qquad \left[\frac{m^{\pm\prime}}{m^{\pm}}\right]^{\frac{1}{2}} = \left[\frac{\mu'}{\mu}\right]^{\frac{1}{2}} = \left[\left(\frac{1}{m_{\rm A}} + \frac{1}{m_{\rm B}}\right) \middle/ \left(\frac{1}{m_{\rm A}} + \frac{1}{m_{\rm B}}\right)\right]^{\frac{1}{2}}.$$

For rupture of a C—Br bond  $m_A = 12$ ,  $m'_A = 13$ , and  $m_B = 80$ ; for formation of a C—O bond  $m_A = 12$ ,  $m'_A = 13$ , and  $m_B = 16$ .

Recently Bigeleisen (9) has suggested that since the reaction path for a polyatomic molecule involves not merely motion of individual atoms A and B, but rather motion of whole reacting fragments  $\alpha$  and  $\beta$ , a more reasonable formulation of the mass term is

$$\begin{bmatrix} \frac{m^{\pm'}}{m^{\pm}} \end{bmatrix}^{\frac{1}{2}} = \left[ \left( \frac{1}{M_{\alpha}} + \frac{1}{M_{\beta}} \right) \middle/ \left( \frac{1}{M_{\alpha}'} + \frac{1}{M_{\beta}} \right) \right]^{\frac{1}{2}}.$$

For ionization of 1-bromo-1-phenylethane  $M_{\alpha} = 105$ ,  $M'_{\alpha} = 106$ , and  $M_{\beta} = 80$ ; for bond formation between 1-phenylethyl carbonium ion and methanol  $M_{\alpha} = 105$ ,  $M'_{\alpha} = 106$ , and  $M_{\beta} = 32$ . In ethanol,  $M_{\beta}$  equals 46.

The effective mass terms for each transition state of the solvolytic reaction, calculated both from the Slater and the mass fragment models, are given in Table IV. It is of interest

\*Since the vibrational stretching frequency of a carbon-oxygen bond is higher than that of a carbon-bromine bond, the summation for the transition state for covalent bond formation might be slightly higher than that for ionization.

[8]

# TABLE IV

Effective mass and free energy values for the transition states of 1-bromo-1-phenylethane solvolysis

	Effective mass term		$(k^{12}/k^{13})_{expt^b}/(m^{\pm 13}/m^{\pm 12})^{\frac{1}{2}}$	
Reaction®	Slater	Mass fragment	Slater	Mass fragment.
$\begin{array}{l} R \longrightarrow R^+ Br^- \\ R^+ Br^- \longrightarrow ROCH_3 \\ R^+ Br^- \longrightarrow ROC_2 H_5 \end{array}$	$\begin{array}{c}1.0352\\1.0227\\1.0227\end{array}$	1.0021 1.0011 1.0014	$0.972 \\ 0.984 \\ 0.984$	$     \begin{array}{r}       1.004 \\       1.005 \\       1.005     \end{array} $

 ${}^{a}R = C_{6}H_{5}CHCH_{3}, \quad {}^{b}(k^{12}/k^{13})_{expt}$  taken as 1.006.

to calculate from these mass terms the values of the free energy terms,

$$\left[1+\sum_{i}^{3n-6}G(u_{i})\Delta u_{i}-\sum_{i}^{3n-6}G(u_{i}^{\dagger})\Delta u_{i}^{\dagger}\right],$$

which would be required to produce the experimentally observed isotope effect of 1.006 These are shown in the last two columns of the Table IV.

The values of less than unity for the free energy term, which are obtained by dividing the experimental isotope effect by mass terms calculated from the Slater model, require that the difference in the vibrational energies for the isotopic transition states be greater than the corresponding difference for the isotopic RX molecules,

$$\sum_{1}^{3n-6} G(u_1^{\ddagger}) \Delta u_1^{\ddagger} \ge \sum_{1}^{3n-6} G(u_1) \Delta u_1.$$

This could only come about if the isotopic atom were considerably more "tightly bound" in the transition state than in the initial state (8), a situation which would seem most unlikely in the present reaction system in which the transition state in both the ionization step and the bond formation step closely resembles the carbonium ion intermediate.

The low isotope effect observed in the solvolysis of 1-bromo-1-phenylethane, therefore, lends support to the mass fragment method of evaluating the effective mass term.

A common procedure in calculating from vibrational frequency data the free energy term of the Bigeleisen equation is to assume a model for the transition state in which the force constant for the bond being broken is equal to zero and the vibrational frequencies of all other bonds are the same as those for the initial state (3). The summations for the transition state in equations [7] and [8] then become zero and the initial state term can be readily calculated from the vibrational stretching frequency of the isotopic bond which is undergoing rupture in the reaction. To the extent that the bond in question is less than completely broken in the transition state, or other bonds associated with the isotopic atom are formed or strengthened, the over-all free energy term, calculated on the assumption of a zero value for the transition state summation, will be too high.

Using this very approximate method, one obtains a theoretical value of 1.018 for the free energy term in equations [7] and [8] at 25° C.\* Comparison with the values given in the last two columns of Table IV shows that this value is much too high to account for the observed isotope effect. Even when combined with the low mass term given by the mass fragment theory it leads to an isotope effect of about 2%, and when combined with a mass term calculated on the basis of the Slater theorem it gives an effect of over 4%.

\*An even larger value is given by a more recent equation which makes use of the theorem of the trace (9).

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It is suggested that the origin of this discrepancy arises mainly from the complete neglect of the transition state term.

Of the two simplifying assumptions upon which neglect of this term was based, that involving the assignment of a zero force constant to the carbon-bromine bond in the transition state of the ionization step and to the carbon-oxygen bond in the transition state of the second step would seem justified since, for reasons already given, the two transition states must closely resemble the intimate ion pair intermediate. What undoubtedly is not justified is the assumption that the vibrational frequencies of all other bonds associated with the isotopic carbon will remain unchanged in the transition state. Indeed, the bonding of this carbon to the benzene ring will be considerably strengthened as a result of overlap of its fairly well-developed vacant p orbital with the  $\pi$  orbitals of the benzene ring. Added to this, but of lesser importance, will be hyperconjugative interaction with the attached methyl group. The low isotope effect observed in the reaction would suggest that this conjugation in the transition state compensates to a considerable degree for the loss of the carbon-bromine vibration.

Some support for this interpretation of the low isotope effect is found in a recent study by Magee and Daniels (30) of the carbon-13 isotope effect in the unimolecular decomposition of substituted ureas, the results of which are summarized in Table V. Given also in

TABLE V			
Unimolecular decomposition of substituted ureas			

Reactant	$(k^{12}/k^{13})_{expt}$	$(k^{12}/k^{13})_{\text{expt}}/(m^{\pm 13}/m^{\pm 12})^{\frac{1}{2}}$
sym-Dimethylurea Phenylurea sym-Diphenylurea 3,3'-Dimethylcarbanilide	$1.027 \\ 1.016 \\ 1.008 \\ 1.007$	$1.024 \\ 1.015 \\ 1.006 \\ 1.005$

this table are the  $(k^{12}/k^{13})_{\exp t}/(m^{\pm 13}/m^{\pm 12})^{\frac{1}{2}}$  values calculated using the mass fragment model for evaluation of the effective mass term. These authors attribute the effect of phenyl substitution on the magnitude of the isotope effect to resonance stabilization of the transition state resulting in a strengthening of a bond associated with isotopic carbon. This would tend to increase the  $G(u_1^{\pm})\Delta u_1^{\pm}$  term and result in a lowering of the over-all free energy term.

It may be noted also that the carbon-14 isotope effect observed by Bender and Buist (11) in the hydrolysis of *tert*-butyl chloride is lower than would be predicted on the assumption of a zero transition state term. Using a mass term calculated from the mass fragment hypothesis one obtains a value for  $(k^{12}/k^{14})_{expt}/(m^{\pm 14}/m^{\pm 12})^{\frac{1}{2}}$  of  $1.014\pm0.015$ , whereas the free energy term calculated on the assumption of complete carbon-chlorine bond rupture and no change in other vibrational frequencies is 1.045. It has been suggested that the low effect may be due in part to the electron-releasing effect of the three methyl groups which would tend to loosen the carbon-chlorine bond in the initial state resulting in a lower free-energy term. Another possibility is that hyperconjugative interaction of the three methyl groups with the isotopic carbon tends to strengthen the bonding of this atom in the transition state, hence increasing the free energy term for this state.

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