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### Calculations of Kinetic Isotope Effects in the Hofmann Eliminations of Substituted (2-Phenylethyl)trimethylammonium Ions

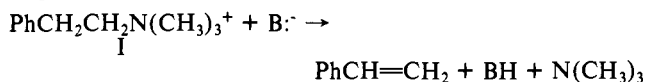
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**Abstract:** Theoretical calculations of kinetic isotope effects (KIE) for the Hofmann elimination of the (2-phenylethyl)trimethylammonium ion (I, Z = H) have been carried out for an extensive series of transition-state models encompassing the E1cB-like region of the E2 mechanistic spectrum. The reaction coordinate employed corresponded to the irreversible fragmentation of the base-H'-C<sub>β</sub>-C<sub>α</sub>-N system, with proton transfer being the dominant contributor. Structural parameters (bond distances and angles) were related to the independent bond orders  $n_{\alpha-N}$  and  $n_{\beta-H'}$  by empirical and semiempirical relationships. The most probable transition-state structure for the reaction was determined by interpolation of the experimental values for the  $\beta$ -D<sub>2</sub> and <sup>15</sup>N KIE into plots of the trends of the calculated KIE. The nonsolvated models obtained in this manner gave only poor agreement between calculated and experimental secondary deuterium ( $\alpha$ -D<sub>2</sub>) and leaving group deuterium [N(CD<sub>3</sub>)<sub>x</sub>(CH<sub>3</sub>)<sub>3-x</sub>, x = 1-3] KIE; explicit consideration of differential solvation of the reactant and transition state afforded the most chemically reasonable resolution of these discrepancies. Using solvated models, transition-state structures were also determined for the Hofmann elimination of parasubstituted derivatives of I (Z = OCH<sub>3</sub>, Cl, CF<sub>3</sub>). These transition states are related by a shift parallel to the central E2 diagonal of an O'Ferrall-Jencks reaction diagram, as predicted by Thornton, indicating that, in the absence of other factors (differing solvent or base, etc.), the extent to which negative charge is accumulated at C<sub>β</sub> in the transition state is solely a factor of the leaving group. Both independent bond orders ( $n_{\alpha-N}$  and  $n_{\beta-H'}$ ) exhibit a linear dependence on the  $\sigma$  value of the substituent, allowing for the first time prediction of transition states for other ring-substituted derivatives of I. These predictions have been checked by calculation of the  $\beta$ -tritium KIE for the extrapolated model for the *p*-NO<sub>2</sub> compound.

#### Introduction

The base-promoted elimination reactions of 2-phenylethyl compounds which have been studied have been shown to exhibit bimolecular kinetics.<sup>2</sup> For the Hofmann elimination of substituted (2-phenylethyl)trimethylammonium ions (I)



in particular, the Hammett<sup>3</sup> plots are linear, with  $\rho$  values usually in excess of +3.0. This has been interpreted as evidence for substantial negative charge development at the  $\beta$ -carbon in the transition state, which, in conjunction with the kinetic order of the reaction, is consistent with either an E1cB mechanism or an E2 mechanism with substantial E1cB character. Stereochemical studies of the reaction<sup>4</sup> have shown that the reaction proceeds almost exclusively by anti elimination.

One of the most useful and probably the most sensitive probe for determining the timing and extent of bonding changes during

Table I. KIE for the Hofmann Elimination of (2-Phenylethyl)trimethylammonium Bromide

isotopic isomer	base/solvent/T (°C)	para subst	k/*k	ref
$\beta$ -D <sub>2</sub>	EtO <sup>-</sup> /EtOH/50	H	2.98 ± 0.08	44
	EtO <sup>-</sup> /EtOH/40	H	3.23 ± 0.04	7, 9b
$\alpha$ -D <sub>2</sub>	OH <sup>-</sup> /H <sub>2</sub> O/97	H	1.02 ± 0.01	7
	EtO <sup>-</sup> /EtOH/40	H	1.03	6
<sup>15</sup> N	EtO <sup>-</sup> /EtOH/40	H	1.0117 ± 0.0007	9a
	EtO <sup>-</sup> /EtOH/40	H	1.0142 ± 0.0004	9b
	EtO <sup>-</sup> /EtOH/40	H	1.0133 ± 0.0002	7
N(CH <sub>3</sub> ) <sub>2</sub> CD <sub>3</sub>	HO <sup>-</sup> /H <sub>2</sub> O/80	H	1.05 ± 0.03	10
N(CD <sub>3</sub> ) <sub>2</sub> CH <sub>3</sub>	HO <sup>-</sup> /H <sub>2</sub> O/80	H	1.10 ± 0.03	10
N(CD <sub>3</sub> ) <sub>3</sub>	HO <sup>-</sup> /H <sub>2</sub> O/80	H	1.12 ± 0.03	10
solvent	DO <sup>-</sup> /D <sub>2</sub> O/80	H	0.56	11

the course of a reaction is the kinetic isotope effect (KIE) or relative rate ratio for isotopic isomers. The bonding changes can be particularly well elucidated by the determination of KIE for reactants labeled at a number of different positions. When coupled with model calculations of KIE, this successive labeling approach<sup>5</sup> offers possibly the most powerful technique currently available for the determination of transition-state structure.

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Table II. KIE for the Hofmann Elimination of Substituted (2-Phenylethyl)trimethylammonium Bromides

isotopic isomer	base/solvent/T (°C)	para subst	$k/k^*$	ref
$\beta$ -D <sub>2</sub>	EtO <sup>-</sup> /EtOH/40	OCH <sub>3</sub>	2.64 ± 0.04	7, 9b
	EtO <sup>-</sup> /EtOH/40	Cl	3.48 ± 0.06	9b
	EtO <sup>-</sup> /EtOH/40	CF <sub>3</sub>	4.15 ± 0.05	9b
<sup>15</sup> N	EtO <sup>-</sup> /EtOH/40	OCH <sub>3</sub>	1.0137 ± 0.0009	7, 9b
	EtO <sup>-</sup> /EtOH/40	Cl	1.0114 ± 0.0009	9b
	EtO <sup>-</sup> /EtOH/40	CF <sub>3</sub>	1.0088 ± 0.0006	9b
$\beta$ -T (1°)	MeO <sup>-</sup> /MeOH/22	NO <sub>2</sub>	13.5 ± 4	12
$\beta$ -T (2°)	MeO <sup>-</sup> /MeOH/22	NO <sub>2</sub>	1.18 ± 0.10	12

The Hofmann elimination of the (2-phenylethyl)trimethylammonium ion (I) affords one of the best examples of the successive labeling approach; the literature abounds with experimental KIE for this reaction under a number of conditions: the primary<sup>6a,7</sup> ( $\beta$ -D<sub>2</sub>), and secondary<sup>6,7</sup> ( $\alpha$ -D<sub>2</sub>) deuterium,  $\beta$ -carbon-13,<sup>8</sup> nitrogen-15,<sup>9a</sup> leaving group deuterium [N(CD<sub>3</sub>)<sub>x</sub>(CH<sub>3</sub>)<sub>3-x</sub>, x = 1-3],<sup>10</sup> and solvent deuterium<sup>11</sup> KIE have all been reported. These results are summarized in Table I.

In addition, the effects of para substituents on the primary deuterium<sup>9b</sup> and nitrogen-15<sup>9</sup> KIE have been determined for the *p*-OCH<sub>3</sub>, *p*-Cl, and *p*-CF<sub>3</sub> compounds. The primary and secondary  $\beta$ -tritium KIE have been determined for the *p*-NO<sub>2</sub> compound.<sup>12</sup> These results are summarized in Table II.

The value of the solvent deuterium isotope effect observed<sup>11</sup> for the Hofmann elimination by aqueous hydroxide ion ( $D^k/H^k = 1.79$ ) is considerably larger than that predicted ( $D^k/H^k \approx 1.4$ ) for a transition state in which the proton is half-transferred to the base. Therefore, Thornton and co-workers<sup>11</sup> have proposed that the proton is somewhat more than half-transferred to the base in the transition state. Corroborative evidence for this is afforded by the primary deuterium isotope effect<sup>6a,7</sup> and its variation with para substituent.<sup>9b</sup> The same conclusion has been reached by Saunders and Cockerill<sup>2</sup> on the basis of the Hammett  $\rho$  values (and hence the likely E1cB character of the transition states) for elimination reactions of 2-phenylethyl compounds with the series of leaving groups Br, OTs, S(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>, and N(CH<sub>3</sub>)<sub>3</sub><sup>+</sup>.

The nitrogen-15 KIE for the Hofmann elimination of the (2-phenylethyl)trimethylammonium ion and its substituted analogues are all small (20-40% of the theoretical maximum of  $^{14}k/^{15}k \approx 1.04$ ), and on this basis it has been proposed<sup>2</sup> that the bond to nitrogen is somewhat less than half-ruptured in the transition state.

In discussing the spectrum of elimination reaction mechanisms, we have found it convenient to define transition-state structures in terms of the bond orders of the bonds being broken and formed. In this way, transition-state structures may be conveniently represented as points on a transition state map (Figure 1) based on an adaptation<sup>13</sup> of the More-O'Ferrall potential energy diagram.<sup>14</sup> In Figure 1, the reactant is at the origin and the product at the diagonally opposed corner; the ordinate represents the E1 mechanistic extreme, with the carbocation intermediate at the upper left. The abscissa represents the E1cB mechanistic extreme, with the carbanion intermediate at the lower right. All other points within the diagram correspond to transition states for E2 reactions with varying degrees of E1 or E1cB character, the diagonal

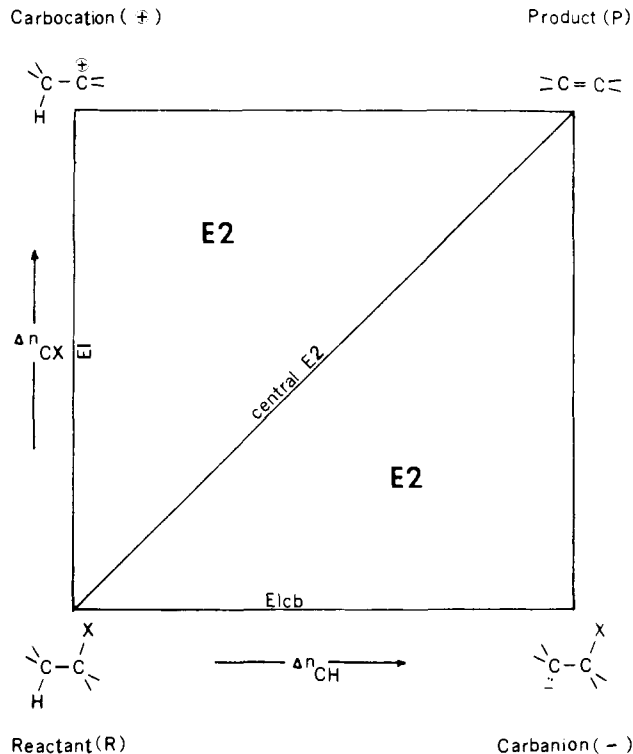


Figure 1. Transition-state map for the elimination reaction mechanistic spectrum.

representing the central E2 mechanism in which rupture of the C-H and C-leaving group bonds are exactly equal and can be exactly balanced by C-C double-bond formation.

The effects of an electron-withdrawing group at the  $\beta$ -carbon atom have been postulated<sup>11b</sup> to result in a general shift of transition state to a more reactant-like structure for E1cB-like eliminations. Thornton<sup>11,15</sup> has expanded on this view and has proposed that the change in para substituent affects both the C-H and C-leaving group bonds to a very nearly equal degree. The resultant shift in transition-state structure as the substituent becomes more electron withdrawing is thus toward the E1cB mechanistic extreme along a line very nearly parallel to the central E2 mechanism. The variations of both the primary deuterium and nitrogen-15 KIE<sup>7,9</sup> as the substituent becomes more electron withdrawing have been interpreted by Saunders and Cockerill<sup>2</sup> as supporting this hypothesis.

It is evident from the data contained in Tables I and II that although a substantial number of investigations have afforded a large number of experimentally determined KIE, no completely systematic study of any one system (including successive labeling at all positions while maintaining base, solvent, and temperature constant) has been undertaken. Nonetheless, the considerable number of experimental data have enabled some semiquantitative deductions to be made about the structure of the transition states for these reactions: it has been proposed<sup>2</sup> that the reaction mechanism is E2 with considerable E1cB character, the proton being more than half-transferred to the attacking base and the bond to the leaving group remaining largely intact. No quantitative estimates of the bonding in the transition state of the reaction have been proposed.

In view of the abundance of experimental data, we have carried out an extensive series of model calculations of KIE in order to assign transition state structures for the Hofmann eliminations from (2-phenylethyl)trimethylammonium ions.

#### Calculations

The calculations were carried out by using a local modification of program BEBOVIB-IV,<sup>16</sup> which calculates molecular masses and

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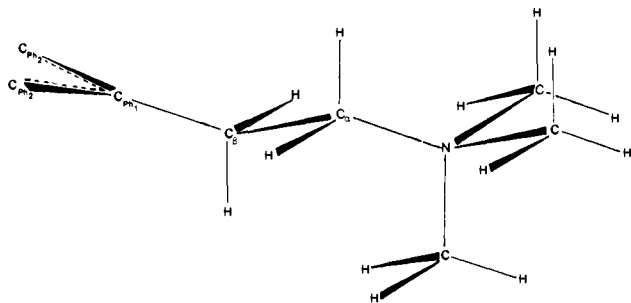


Figure 2. 22-Atom unsolvated reactant model.

moments of inertia from structural parameters (atomic masses and molecular geometry) and vibrational frequencies from bonding parameters and force constants, using a modification<sup>17</sup> of Gwinn's method<sup>18</sup> for determining normal modes and frequencies of vibration. The program calculates KIE by using relationships derived from transition-state theory<sup>19</sup> by Bigeleisen and Mayer,<sup>20</sup> as expressed in the notation of Wolfsberg and Stern<sup>21</sup>

$$\text{KIE} = k/^*k = \text{MMI} \cdot \text{EXC} \cdot \text{ZPE} \quad (1)$$

where the asterisk denotes the heavier isotopic isomer. The MMI term is the mass moment of inertia contribution to the KIE, EXC is the contribution from excited vibrational states, and ZPE is the zero-point energy contribution. When the Teller-Redlich product rule is applied,<sup>22</sup> eq 1 may be expressed in the alternative form (2) in which VP is the vibrational frequency product ratio<sup>21</sup> and

$$k/^*k = (\nu_L/^*\nu_L) \cdot \text{VP} \cdot \text{EXC} \cdot \text{ZPE} \quad (2)$$

$\nu_L^*$  and  $^*\nu_L^*$  are the reaction coordinate frequencies for the light and heavy isotopic isomers of the transition state, respectively. A Bell<sup>23</sup> tunneling correction (with at least four terms in the expansion retained) to the magnitudes of the KIE is carried out by the program. Tunneling factors account for only approximately 3% (for the 4-OCH<sub>3</sub> compound) and 12% (for the 4-CH<sub>3</sub> compound) of the magnitude of the calculated  $\beta$ -D<sub>2</sub> KIE and for approximately 0.5 and 2%, respectively, of the calculated  $\beta$ -<sup>14</sup>C KIE; tunneling corrections were negligible for the other KIE.

The transition-state models are constructed according to rules which are similar to Johnston's bond energy-bond order approach<sup>24</sup> for hydrogen-transfer reactions, and we refer to our method of constructing transition-state models as the BEBO method of calculating KIE. The method consists briefly of assigning a (Pauling-type<sup>25</sup>) bond order to each bond in the model; chemical information is used to supply constraints to some of these, so that only a small number of bond orders are independent parameters of the model. Bond distances, bond angles, and force constants are then related to the bond orders by empirical and semiempirical relationships derived from stable molecular species to provide a complete input to a standard molecular vibration program.

The reactant model initially employed was a 22-atom cutoff<sup>26</sup> model shown in Figure 2. The bond between atoms *i* and *j* was

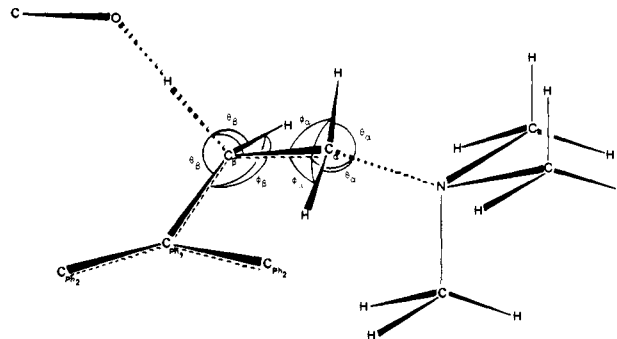


Figure 3. 24-Atom unsolvated transition-state model.

assumed to be a normal single bond of order  $n_{ij} = 1.0$  for all bonds of the molecule except the aromatic C-C bonds, for which  $n_{ij} = 1.67$ .<sup>27</sup> (The sum  $N_{\text{Ph}}$  of bond orders at the phenyl-1 carbon is thus 4.34; the larger value of  $N_{\text{Ph}}$ ,—relative to the value of 4.0 at the sp<sup>3</sup>-hybridized carbon atoms of the model—reflects the aromatic stabilization energy of the ring.) Bond distances for the reactant,  $r^0$ , were chosen by analogy to stable molecules.<sup>28</sup> Bond angles about all sp<sup>3</sup>-hybridized atomic centers were constrained to be tetrahedral (109.47°) and those about the sp<sup>2</sup>-hybridized atomic center, C<sub>Ph1</sub>, to be trigonal planar (120°).

The transition-state model initially employed was the 24-atom cutoff model shown in Figure 3. Bond lengths and bond orders of the methyl groups, the  $\alpha$ -hydrogen atoms, and the nontransferring  $\beta$ -hydrogen atom were retained at their reactant values, as were the bond angles about the methyl carbons, the nitrogen atom, and the phenyl-1 carbon atom. The bond orders of the rupturing C-N bond ( $n_{\alpha\text{-N}}$ ) and the rupturing C-H bond ( $n_{\beta\text{-H}}$ ) were chosen to be the independent bond orders of the model and were allowed to vary between their reactant values (both 1.0) and their values in the product (both 0.0). Other bond orders were related to these two as detailed below.

The extent to which double bond formation can occur between the  $\alpha$ - and  $\beta$ -carbon atoms in the transition state of an E1cB-like E2 reaction is limited by the extent of rupture of the C <sub>$\alpha$</sub> -N bond. It is reasonable to assume that in the absence of steric or electronic factors precluding perfect alignment of the developing p orbitals, bonding between C <sub>$\alpha$</sub>  and C <sub>$\beta$</sub>  would completely compensate for the bonding loss to nitrogen at C <sub>$\alpha$</sub> , as expressed by eq 3, where  $n_{\alpha\text{-}\beta}$

$$n_{\alpha\text{-}\beta} = 1 + \Delta n_{\alpha\text{-N}} \quad (3)$$

is the bond order of the C <sub>$\alpha$</sub> -C <sub>$\beta$</sub>  bond and  $\Delta n_{\alpha\text{-N}}$  is the loss in bond order of the rupturing C <sub>$\alpha$</sub> -N bond ( $\Delta n_{\alpha\text{-N}} = 1.0$  in the product). Under these constraints, the total bond order ( $N_{\alpha}$ ) at C <sub>$\alpha$</sub>  is maintained constant at the reactant value of 4.0 in all transition-state models (constant total bond order at C <sub>$\alpha$</sub> , CTBO <sub>$\alpha$</sub> ). In certain systems, however, particularly those in which there are bulky groups bonded to C <sub>$\alpha$</sub>  and C <sub>$\beta$</sub> , steric interactions may preclude perfect alignment of the p orbitals developing at the  $\alpha$ - and  $\beta$ -carbon atoms. If there is a dihedral angle  $\tau$  between the two developing orbitals (Figure 4), the overlap between the orbitals is reduced<sup>29</sup> by the factor  $\cos \tau$ . It has been proposed<sup>30</sup> that the resonance energy of conjugated  $\pi$  systems is reduced in proportion to  $\cos^2 \tau$  and accordingly the C <sub>$\alpha$</sub> -C <sub>$\beta$</sub>  bond order in the transition state models was calculated from relationship 4. In the reactant,

$$n_{\alpha\text{-}\beta} = 1 + \Delta n_{\alpha\text{-N}} \cos^2 \tau \quad (4)$$

the phenyl and leaving groups are arranged anti to one another (Figure 4a) in the position of minimum steric hindrance, but the reaction is known to proceed by an antielimination of the leaving group and a  $\beta$  proton in which proton transfer is more advanced

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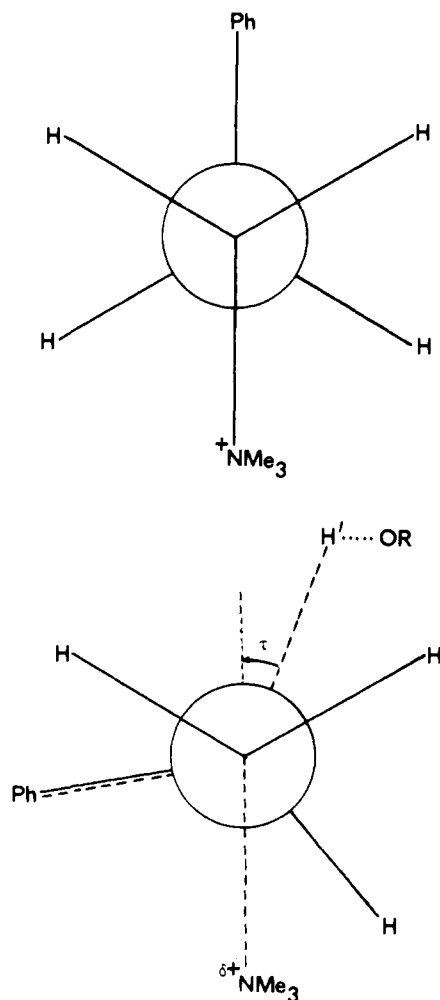


Figure 4. Newman projections along the  $C_{\alpha}$ - $C_{\beta}$  bond for (top) reactant model and (bottom) transition-state model.

than bond rupture to the leaving group. However, an anti arrangement of the transferring  $\beta$  proton and leaving group leads to a severe gauche interaction between the phenyl and leaving group unless the transition state is very product-like (largely broken  $C_{\alpha}$  leaving group bond) which would allow correct alignment ( $\tau = 0^\circ$ ) of the p orbitals for double-bond formation. For more reactant-like transition states, the gauche interaction can be relieved only by twisting about the  $C_{\alpha}$ - $C_{\beta}$  bond ( $\tau > 0^\circ$ ); a twist of  $45^\circ$  reduces the p orbital overlap by 50%, at which point the syn hydrogen becomes better disposed for elimination. Thus, the angle  $\tau$  was limited to  $\tau \approx 45^\circ$  for a very reactant-like (or a very carbanion-like) transition state and decreases as the transition state becomes more product-like. Clearly,  $\tau$  is related to the extent of both the  $C_{\beta}$ - $H'$  and  $C_{\alpha}$ -leaving group bonds and can approach  $\tau \approx 0^\circ$  for a very product-like transition state only if both bonds are largely broken ( $\Delta n_{\alpha-N} \approx \Delta n_{\beta-H'} \approx 1$ ). Equation 5 is a simple

$$\cos \tau = (0.5 + 0.5 \Delta n_{\alpha-N} \Delta n_{\beta-H'})^{1/2} \quad (5)$$

empirical expression which has the proper behavior for  $\tau$  and which is simple to substitute into eq 4; the calculated KIE are not very sensitive to the form of eq 5. In cases where steric hindrance precludes perfect alignment of the developing p orbitals at  $C_{\alpha}$  and  $C_{\beta}$ , double-bond formation does not completely compensate for  $C_{\alpha}$ -N bond cleavage (i.e., the total bond order at  $C_{\alpha}$  is decreased—DTBO $_{\alpha}$ —and  $N_{\alpha} < 4.0$ ), and there is development of a partial positive charge  $q^+$  at  $C_{\alpha}$  in the transition state of magnitude

$$q^+ = 2.0 - (n_{\alpha-N} + n_{\alpha-\beta}) \quad (6)$$

By definition, C-H bond rupture precedes C-leaving group bond rupture and C-C double-bond formation in an E1cB-like mech-

anism, and therefore negative charge  $q^-$  will develop at the  $\beta$ -carbon atom according to eq 7. In systems such as I some fraction

$$q^- = 2.0 - (n_{\beta-H'} + n_{\alpha-\beta}) \quad (7)$$

of this charge can be delocalized by the aromatic ring system, depending on the substituent carried by the ring; this delocalization may be represented as an increase in the importance of quinoid-type resonance contributors, leading to an increase in the  $C_{\beta}$ - $C_{Ph_1}$  bond order and a concomitant decrease in the  $C_{Ph_1}$ - $C_{Ph_2}$  bond orders (such that the sum,  $N_{Ph_1}$ , of bond orders at  $C_{Ph_1}$  remains 4.34 during the course of the reaction, CTBO $_{Ph_1}$ ). The evidence from proton<sup>31</sup> and carbon-13<sup>32</sup> NMR studies of metal benzyls suggests that in the benzyl anion  $\sim 50\%$  of the negative charge at the benzylic position is delocalized into the aromatic ring; unfortunately similar data for other para-substituted analogues are unavailable. It does, however, seem reasonable to assert that the ability of a substituted aromatic ring to delocalize charge should be dependent upon the electronic character of the substituent. Accordingly, the increase in the  $C_{\beta}$ - $C_{Ph_1}$  bond order was assumed to be given by eq 8, which corresponds to 50% delo-

$$\Delta n_{\beta-Ph_1} = 0.5q^-(1.0 + \sigma) \quad (8)$$

calization of the partial charge at  $C_{\beta}$  in the unsubstituted compound and  $\sim 90\%$  for the *p*-nitro analogue. Although there is no direct experimental evidence for this dependence on the Hammett parameter  $\sigma$ , only the  $\beta$ -carbon and  $\beta$ -hydrogen KIE are even slightly dependent upon this assumption, and the effect is added only because it seems to be required in any reasonable model.

The sum of bond orders to the transferring proton,  $H'$ , was assumed to be unity, as for hydrogen atom transfer reactions,<sup>33</sup> and the proton transfer was assumed to be linear.

$$n_{\beta-H'} + n_{H'-O} = 1.0 \quad (9)$$

The C-O-H' angle at the oxygen atom of the base was assumed to be tetrahedral.

As the reaction proceeds, the hybridization of the orbitals used by  $C_{\alpha}$  and  $C_{\beta}$  for bonding to the departing groups [ $N(CH_3)_3$  at  $C_{\alpha}$ ,  $H'$  at  $C_{\beta}$ ] is changing from  $sp^3$  to  $p$ . In order to simulate this change, which preserves in the product the threefold symmetry of angles about  $C_{\alpha}$  and  $C_{\beta}$  in the reactant, the departing groups were constrained to leave at angles  $\theta_{\alpha}$  and  $\theta_{\beta}$ , respectively, such that this symmetry was preserved in the transition state (see Figure 3). The complementary angles  $\Phi$ , to which the angles  $\theta$  are related by trigonometry, were calculated from the bond orders about the carbon atoms by expressions 10 and 11. These expressions give

$$\cos \Phi_{\alpha} = -0.5 + 0.16667(n_{\alpha-N}^2 n_{\alpha-H'}^2)^{1/2} \quad (10)$$

$$\cos \Phi_{\beta} = -0.5 + 0.16667[(2 - n_{\alpha-\beta})(2 - n_{\beta-Ph_1})(3 - n_{\alpha-\beta} - n_{\beta-Ph_1})n_{\beta-H'}]^{1/2} \quad (11)$$

tetrahedral angles for  $\Phi_{\alpha}$  and  $\Phi_{\beta}$  in the reactant and trigonal planar angles ( $120^\circ$ ) in the product. The differences between the two expressions are most easily accounted for in terms of the difference in the nature of  $C_{\alpha}$  and of  $C_{\beta}$  in the transition state: in the absence of total compensation for  $C_{\alpha}$ -N bond rupture by  $C_{\alpha}$ - $C_{\beta}$  double-bond formation,  $C_{\alpha}$  acquires some carbocation character in the transition state; conversely, under the same circumstances  $C_{\beta}$  acquires some carbanion character in the transition state. Carbocations are known to be planar trigonal, whereas alkyl anions are known to be planar trigonal if conjugated and isostructural with amines if nonconjugated. Consequently, eq 10 gives planar-trigonal angles for the carbocation whereas eq 11 gives tetrahedral angles for nonconjugated anions (for which  $n_{\beta-Ph_1} = 1.0$ ) and planar-trigonal angles for the fully conjugated anion ( $n_{\beta-Ph_1} = 2.0$ ).

(31) (a) Waack, R.; McKeever, L. D.; Doran, M. H. *Chem. Commun.* 1969, 117; (b) Sandel, V. R.; Freedman, H. H. *J. Am. Chem. Soc.* 1963, 85, 2328; (c) Waack, R.; Doran, M. H. *Ibid.* 1963, 85, 1651.

(32) Takahashi, K.; Kondo, Y.; Asami, R. *J. Chem. Soc., Perkin Trans. 2* 1978, 577.

(33) Reference 24, pp 180-209.

Bond distances for the reacting bonds in the transition state were calculated by using a modification of Pauling's rule,<sup>25</sup> eq 12, where  $n_{ij}$  is the bond order for bond  $i-j$  in the transition state.

$$r_{ij} = r_{ij}^0 - 0.3 \ln n_{ij} \quad (12)$$

Molecular vibrations of the model were defined in terms of the five types of internal coordinates of Decius<sup>34</sup> (bond stretching, valence angle bending, out-of-plane wagging, linear bending, and torsion). The neglect of off-diagonal (interaction) force constants has been shown<sup>35</sup> to have little effect upon calculated KIE, and consequently a simple valence force field (SVFF, diagonal potential energy matrix) was used for both the reactant and transition-state models except that four interaction constants were used to generate a reaction coordinate frequency in the transition state.

Stretching force constants of C-H and C-C single bonds are dependent on the hybridization of the carbon atoms; for ethane, ethylene, and acetylene these are reproduced by expressions 13 and 14, where  $\Phi_i$  and  $\Phi_j$  are tetrahedral for  $sp^3$  centers,  $120^\circ$  for

$$F_{C-H}^0 = 4.6 - 1.2 \cos \Phi_i \text{ mdyn}\cdot\text{\AA}^{-1} \quad (13)$$

$$F_{C-C_j}^0 = 3.5 - 1.5 (\cos \Phi_i + \cos \Phi_j) \text{ mdyn}\cdot\text{\AA}^{-1} \quad (14)$$

$sp^2$  centers, and  $180^\circ$  for  $sp$  centers. Equations 13 and 14 provide reasonable estimates of stretching force constants for many other molecules as well. For bonds of order  $n_{ij}$ , the stretching force constants  $F_{ij}$  are related to the single bond values,  $F_{ij}^0$ , by the Pauling-Badger relations,<sup>36</sup> eq 15, where the single bond values  $F_{ij}^0$  are given by eq 13 and 14 or taken from standard sources for stable molecules.<sup>37</sup>

$$F_{ij} = n_{ij} F_{ij}^0 \quad (15)$$

All angle bending force constants were related to standard values,<sup>37</sup>  $F_{ijk}^0(T_d)$ , for tetrahedral angles subtended by single bonds  $i-j$  and  $j-k$ , by the empirical relation<sup>35</sup> given in eq 16, where  $g_\alpha$  is a geometry or hybridization factor given by eq 17. The value of  $g_\alpha$  is unity for  $\alpha = 109.47^\circ$  and decreases as  $\alpha$  increases.

$$F_{ijk}(\alpha) = g_\alpha (n_{ij} n_{jk})^{1/2} F_{ijk}^0(T_d) \quad (16)$$

$$g_\alpha = 1.39 - 1.17 \cos \alpha \quad (17)$$

The torsional force constant about a bond  $i-j$  depends on the order  $n_{ij}$  and hybridization of the atoms  $i$  and  $j$ , but no empirical relations have been suggested between the torsional force constant and these parameters. Data from representative molecules are reproduced quite well by eq 18

$$F_{\text{tors}} = h_i h_j (n_{ij})^4 F_{\text{tors}}^0 \quad (18)$$

where

$$h_i = [T_d \sin \Phi_i / \Phi_i \sin T_d]^2 \quad (19)$$

represents the hybridization factor for atom  $i$  and  $F_{\text{tors}}^0 = 0.072$  mdyn $\cdot\text{\AA}\cdot\text{rad}^{-2}$ , the torsional force constant for torsion about a single bond between two  $sp^3$ -hybridized atoms, as in ethane.<sup>37c</sup> The angles  $\Phi_i$  and  $\Phi_j$  have the same values as in eq 13 and 14. The torsional force constant about the  $C_\beta$ -H'-O moiety in the transition-state model was arbitrarily assumed to be 0.036 mdyn $\cdot\text{\AA}\cdot\text{rad}^{-2}$  (half the value for ethane) in the absence of any suitable stable species with which to compare. Although the

calculated KIE are all insensitive to the magnitude of torsional force constants, eq 18 (and the assumption about the C-H'-O torsion) provides reasonable estimates of torsional force constants for the models and is included to make the model physically reasonable (the torsion about the  $C_\alpha$ - $C_\beta$  bond should significantly increase with double-bond formation).

The out-of-plane force constant at the phenyl-1 carbon was retained at the representative reactant value of 0.2 mdyn $\cdot\text{\AA}\cdot\text{rad}^{-2}$  in the transition state and had no effect on the calculated KIE.

The reaction coordinate motion was chosen to correspond to an irreversible overall asymmetric stretching motion of the O-H'- $C_\alpha$ - $C_\beta$ -N system, leading to fragmentation of the transition state to products, with a small contribution to the reaction coordinate motion from asymmetric stretching of the  $C_{\text{Ph}_1}$ - $C_\beta$ -H' system, simulating the increased conjugation in the transition state and the product. The reaction coordinate was generated by the use of four off-diagonal (interaction) force constants, each of the form

$$f_{ik} = a_{ik} (F_{ij} F_{jk})^{1/2} \quad (20)$$

representing the asymmetric (for  $a_{ik} > 0$ ) stretching motion of adjacent bonds  $i-j$  and  $j-k$  with stretching force constants  $F_{ij}$  and  $F_{jk}$ , respectively. In subsequent discussion, the proportionality constants  $a_{ik}$  are denoted by  $A$  (the O-H', H'- $C_\beta$  interaction),  $B$  (the H'- $C_\beta$ ,  $C_\beta$ - $C_\alpha$  interaction),  $C$  (the  $C_\beta$ - $C_\alpha$ ,  $C_\alpha$ -N interaction), and  $E$  (the  $C_{\text{Ph}_1}$ - $C_\beta$ ,  $C_\beta$ -H' interaction). For  $A$ ,  $B$ ,  $C$ , and  $E$  all positive, the reaction coordinate motion corresponds approximately to the overall asymmetric stretching motion described above.

The condition that the reaction coordinate motion correspond to an imaginary frequency is that the determinant of the transition-state force constant matrix be negative,  $|F^\ddagger| < 0$ , which when expanded affords the following relationship between the proportionality constants.

$$1 - A^2 - B^2 - C^2 - E^2 + A^2 C^2 + C^2 E^2 = D < 0 \quad (21)$$

$D$  is the barrier curvature parameter.<sup>38</sup> This procedure is similar to that used by Saunders and co-workers<sup>39,40</sup> to generate an imaginary reaction coordinate frequency in model calculations of KIE for elimination reactions.

The relative change in bond length ( $\Delta r$ ) of bonds  $i-j$  and  $j-k$  in the reaction coordinate is given approximately by eq 22, and consequently the magnitudes of the proportionality constants were chosen to reflect the relative contribution of each coupled motion to the overall reaction coordinate motion.

$$|\Delta r_{ij} / \Delta r_{jk}| \propto a_{ik}^2 \quad (22)$$

There are thus two distinct sets of parameters which are required to completely define the model: the proportionality constants  $a_{ik}$  which define the directions and magnitudes of the motions of the atoms in the reaction coordinate; and the bond orders and bond angles which define the structure of the transition state model. Because of constraints among the bond orders and bond angles (eq 3-11) and the empirical relationships between bond orders and bond distances,<sup>33,35</sup> there are three independent parameters which completely define the structure:  $n_{\alpha-N}$ ,  $n_{\beta-H}$ , and  $\sigma$ . The equations of constraints and empirical relationships used are based on currently accepted theories and available chemical data for stable molecules, and we have confidence that they are good first approximations for the transition states.

## Results and Discussion

Carbon-14 ( $\alpha$ -<sup>14</sup>C and  $\beta$ -<sup>14</sup>C), deuterium ( $\alpha$ -D<sub>2</sub> and  $\beta$ -D<sub>2</sub>) and nitrogen-15 KIE were calculated for the transition-state models indicated by points in Figure 5, in order to determine trends in the calculated KIE. The reaction coordinate employed ( $A = 1.04$ ,  $B = C = 0.35$ ,  $E = 0.10$ ,  $D = -0.2$ ) was very similar to that determined by Saunders<sup>39,40</sup> as necessary to produce calculated KIE encompassing the experimentally observed range for elim-

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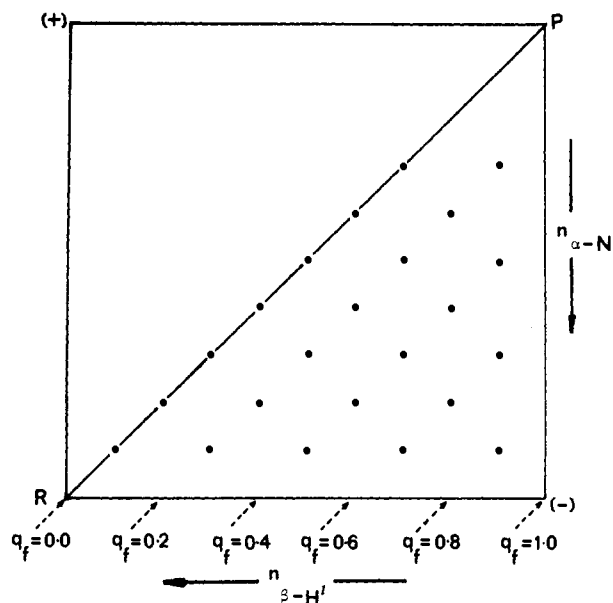
(36) Reference 24, pp 72-83.

(37) (a) Wilson, E. B., Jr.; Decius, J. C.; Cross, P. C. "Molecular Vibrations"; McGraw-Hill: New York, 1955; pp 175-176. (b) Herzberg, G. "Molecular Spectra and Structure, Part II Infrared and Raman Spectra of Polyatomic Molecules"; D. Van Nostrand: Princeton, NJ, 1945. (c) Schachtschneider, J. H.; Snyder, R. G. *Spectrochim. Acta* **1963**, *19*, 117. Snyder, R. G.; Schachtschneider, J. H., *J. Mol. Spectrosc.* **1969**, *30*, 290. *Spectrochim. Acta* **1965**, *21*, 169. (d) Hartshorn, S. R.; Shiner, V. J. *J. Am. Chem. Soc.* **1972**, *94*, 9002.

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(39) Katz, A. M.; Saunders, W. H. Jr. *J. Am. Chem. Soc.* **1969**, *91*, 4469.

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**Figure 5.** Transition-state map indicating transition-state structures for which KIE were calculated (dots) and the net negative charge ( $q_f$ ) developed at carbon.  $q_f$  is a constant as indicated along lines parallel to the central E2 diagonal.

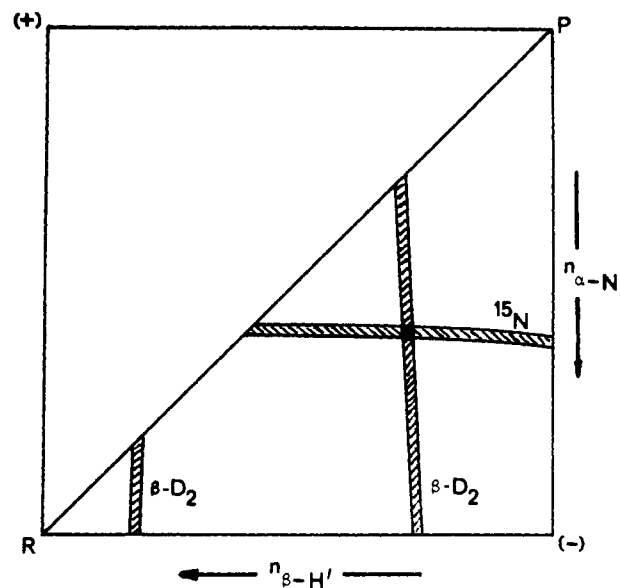
ination reactions of ethyl derivatives. These calculations were carried out in order to determine trends in KIE for the parent compound ( $p$ -H) for which  $\sigma = 0$ . Preliminary calculations indicated that only the  $\beta$ -carbon-14 KIE and, to a lesser extent, the  $\beta$ -deuterium KIE were even slightly dependent on the value of  $\sigma$ , all other KIE being essentially independent of this parameter. Accordingly, it was apparent that these calculations would serve equally well for comparison with available experimental KIE for substituted (2-phenylethyl)trimethylammonium ions.

For the parent compound ( $\sigma = 0.0$ ), there are then two independent transition-state structural parameters:  $n_{\alpha-N}$  and  $n_{\beta-H'}$ . For each transition-state model, the net negative charge developed at carbon,  $q_f$ , is given by eq 23. The calculated  $\beta$ -deuterium and

$$q_f = q^- - q^+ = n_{\beta-H'} - n_{\alpha-N} \quad (23)$$

nitrogen-15 KIE were plotted as functions of  $n_{\alpha-N}$  for each value of  $q_f$ , which produced two families of KIE curves. Each curve intersects with the corresponding experimental KIE to yield a range of transition-state structures for which the calculated KIE agree with the experimental value within the experimental uncertainty. When plotted on a transition-state map, these transition-state structures define narrow bands for both the  $\beta$ -D<sub>2</sub> and the <sup>15</sup>N KIE. Fortuitously, these bands produced one small region of intersection, as in Figure 6. Only transition-state structures within this region of intersection produce  $\alpha$ -D<sub>2</sub> and <sup>15</sup>N KIE which are simultaneously in agreement with the corresponding experimental values. The transition state defined by  $n_{\alpha-N}$  and  $n_{\beta-H'}$  at the center of this region of intersection was used as the "best" transition-state model for the unsubstituted compound; KIE calculated for this model are given in Table III.

From the data in Table III, it is immediately apparent that there are serious discrepancies between the calculated and experimental values of the secondary deuterium ( $\alpha$ -D<sub>2</sub>)<sup>6,7</sup> and leaving group deuterium [ $N(CD_3)_x(CH_3)_{3-x}$ ,  $x = 1-3$ ]<sup>10</sup> KIE; the calculated secondary deuterium KIE is significantly larger than the measured value, whereas the leaving group deuterium KIE are all  $\sim 2$  orders of magnitude smaller than the experimental values. It is significant that the isotopic isomers for which these discrepancies occur all have substitution by deuterium in fairly close proximity to the charged nitrogen atom. In view of this, the most reasonable explanation for these discrepancies appears to be that the experimental results reflect considerable solvent participation in the reaction, for which no provision is made in the models employed. A differential solvation of reactant and transition state has been proposed<sup>41</sup> and recently confirmed by calculations<sup>35</sup> to account



**Figure 6.** Transition-state map indicating the range of transition-state structures (shaded areas) for which calculated KIE reproduce measured KIE within experimental error.

**Table III.** Calculated KIE for the Hofmann Elimination of (2-Phenylethyl)trimethylammonium Bromide by Ethoxide Ion at 40 °C for the Unsolvated Model<sup>a</sup>

isotopic isomer	KIE <sub>calcd</sub>	KIE <sub>obsd</sub>	ref
$\beta$ -D <sub>2</sub>	3.12	3.12 <sup>b</sup>	44a
$\beta$ - <sup>14</sup> C	1.039		
$\alpha$ -D <sub>2</sub>	1.069	1.03	6
$\alpha$ - <sup>14</sup> C	1.029		
<sup>15</sup> N	1.0132	1.0133 ± 0.0002	9
N(CH <sub>3</sub> ) <sub>2</sub> CD <sub>3</sub>	1.0006	1.05 ± 0.03	10
N(CD <sub>3</sub> ) <sub>2</sub> CH <sub>3</sub>	1.0011	1.10 ± 0.03	10
N(CD <sub>3</sub> ) <sub>3</sub>	1.0017	1.12 ± 0.03	10

<sup>a</sup> Bond orders:  $n_{\beta-H'} = 0.29$ ;  $n_{\alpha-N} = 0.60$ . <sup>b</sup> Calculated from temperature dependence data given.

for the magnitude of chlorine-37 KIE in substitution reactions.

The leaving group, which carries a full positive charge in the reactant, would be expected to desolvate during the course of the reaction due to the decreasing charge on nitrogen. In the reactant, the solvation of the trimethylammonium moiety is probably diffuse, occurring by weak interactions between the solvent and the C-H dipoles induced by the charge on nitrogen; direct solvation of the nitrogen atom is almost certainly precluded by steric hindrance. This diffuse solvation sheath should therefore reflect the local C<sub>3v</sub> symmetry presented by the methyl hydrogen atoms, thus allowing representation in the calculations by a single "effective" interaction along the axis of each methyl group, as shown in Figure 7. Each interaction was formally represented as being between the oxygen atom of the solvent and the methyl carbon, the net effect being to restrict the bending or deformation modes of the methyl groups due to the small O...C-H bending force constant. The solvation energy of the trimethylammonium moiety in the reactant was assumed to be approximately 10 kcal mol<sup>-1</sup> ( $a$  value of  $\sim 3.5$  kcal per methyl group). This translates, using Johnston's rules,<sup>36</sup> into an effective bond order of  $n_{C-O} = 0.06$ . In order to maintain the tetravalence of the methyl carbons, we assigned each C-H bond an order of 0.98, simulating the induced dipoles in these bonds. The additional force constants required were assigned as for other bonds and angles. The geometry of each methyl group was maintained tetrahedral; since the C...O distance in the reactant corresponds to  $\sim 2.3$  Å, it was envisaged that this interaction would have a negligible perturbing effect on the geometry about the methyl carbons. The solvation sheath should still be present in the transition state and can be represented in the same manner, since

Table IV. Calculated KIE for Solvated Transition-State Models<sup>a</sup> at 40 °C

isotopic isomer	subst			
	4-OCH <sub>3</sub> <sup>b</sup>	4-H <sup>c</sup>	4-Cl <sup>d</sup>	4-CF <sub>3</sub> <sup>e</sup>
$\beta$ -D <sub>2</sub> <sup>f</sup>	2.66 (2.64)	3.12 (3.12) <sup>g</sup>	3.44 (3.48)	4.06 (4.15)
$\beta$ - <sup>14</sup> C	1.041	1.038	1.035	1.029
$\alpha$ -D <sub>2</sub> <sup>f</sup>	1.041	1.041 (1.03)	1.032	1.021
$\alpha$ - <sup>14</sup> C	1.026	1.027	1.026	1.025
<sup>15</sup> N <sup>f</sup>	1.0138 (1.0137)	1.0133 (1.0133)	1.0115 (1.0114)	1.0090 (1.0088)
N(CH <sub>3</sub> ) <sub>2</sub> CD <sub>3</sub> <sup>f,h</sup>	1.037	1.037 (1.05)	1.037	1.037
N(CD <sub>3</sub> ) <sub>2</sub> CH <sub>3</sub> <sup>f,h</sup>	1.076	1.076 (1.10)	1.076	1.076
N(CD <sub>3</sub> ) <sub>3</sub> <sup>f,h</sup>	1.099	1.099 (1.12)	1.099	1.098

<sup>a</sup>  $n_{\beta\text{-Ph}_1} = 1.0 + 0.5(1.0 + \sigma)q^-$ . <sup>b</sup>  $n_{\beta\text{-H}'} = 0.24; n_{\alpha\text{-N}} = 0.59; \sigma = -0.27$ . <sup>c</sup>  $n_{\beta\text{-H}'} = 0.29; n_{\alpha\text{-N}} = 0.60; \sigma = 0$ . <sup>d</sup>  $n_{\beta\text{-H}'} = 0.32; n_{\alpha\text{-H}} = 0.65; \sigma = 0.23$ . <sup>e</sup>  $n_{\beta\text{-H}'} = 0.37; n_{\alpha\text{-N}} = 0.72; \sigma = 0.54$ . <sup>f</sup> Experimental values given in parentheses. <sup>g</sup> Calculated from data in ref 44a. <sup>h</sup> 80 °C.

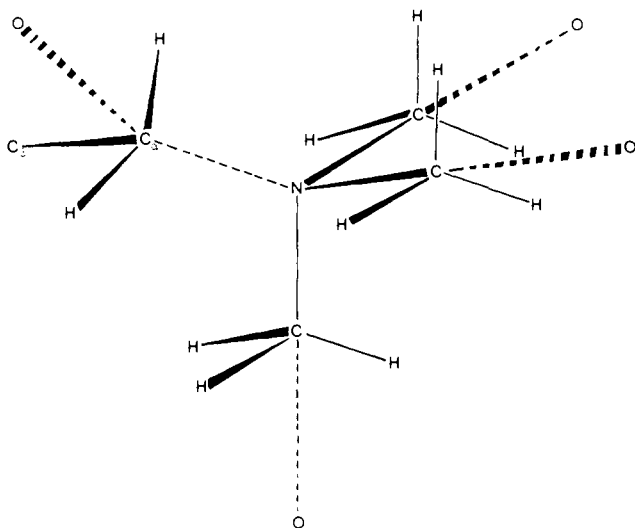


Figure 7. Solvation of the  $\alpha$ -carbon and trimethylammonium leaving group as represented in the calculations.

the bond to nitrogen is still largely intact. The strength of the interaction will be decreased since the product amine is uncharged, and thus the charge at nitrogen decreases as the C-N bond ruptures, leading in turn to smaller C-H dipoles.

By similar reasoning, the C-H bonds at the  $\alpha$ -carbon were assigned bond orders of 0.98 in the reactant, simulating the formation of the C-H dipoles due to the inductive effect of the charged nitrogen atom. The solvating atom was located along the bisector of the H-C-H angle (the position of minimum steric hindrance) with a bond order to the  $\alpha$ -carbon of 0.04 (corresponding to a solvation energy of  $\sim 2.5$  kcal) in order to preserve the tetravalence of the  $\alpha$ -carbon. In contrast to the leaving group, however, the charge at the  $\alpha$ -carbon atom increases on going from reactant to transition state; increased solvation at this position is therefore expected in the transition state, either at the C-H dipoles or at the  $\alpha$ -carbon directly.

Retaining all other parameters of the "best" transition-state model, we varied the bond orders of the solvating groups and, to preserve the tetravalence of the methyl carbons, of the methyl C-H bonds in the transition state. As the strength of the solvation interaction at the leaving group was reduced in the transition state, the calculated leaving group deuterium KIE increased, whereas the other KIE remained essentially unaffected. The best agreement between the calculated and experimental values of the leaving group deuterium KIE was obtained using a solvation energy of  $\sim 1.8$  kcal per methyl group (equivalent<sup>36</sup> to  $n_{\text{C}\cdots\text{O}} = 0.03$ ) in the transition state. The secondary deuterium ( $\alpha$ -D<sub>2</sub>) KIE decreased as the strength of the solvation interaction at the  $\alpha$ -carbon increased; the best agreement between the calculated and experimental values of this KIE was obtained for a solvation energy of  $\sim 3.0$  kcal mol<sup>-1</sup> ( $n_{\text{C}\cdots\text{O}} = 0.05$ ).

A procedure similar to that used to deduce the structure of the transition state for the unsubstituted compound was followed by using appropriate values of  $\sigma$  to obtain transition-state structures

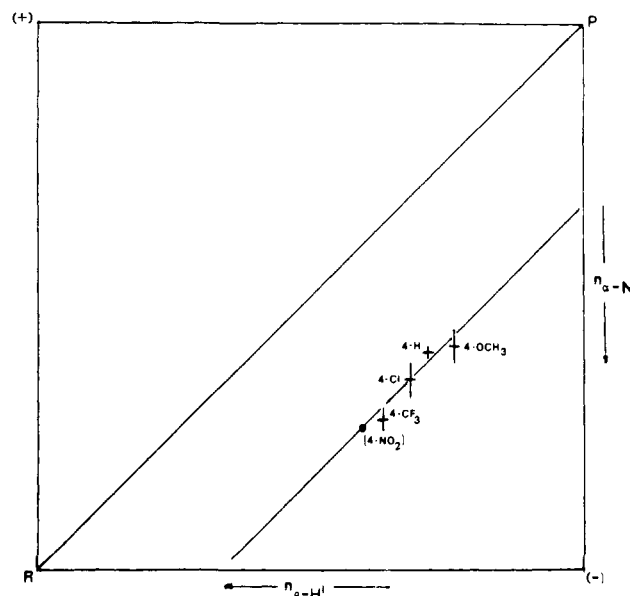


Figure 8. Transition-state map indicating transition-state structures for the Hofmann elimination of para-substituted (2-phenylethyl)trimethylammonium ions. Solid circle for 4-NO<sub>2</sub> derivative is obtained by extrapolation from Figure 9.

Table V. Tritium KIE for the Hofmann Elimination of (2-(4-Nitrophenyl)ethyl)trimethylammonium Bromide by Methoxide Ion at 22 °C<sup>a</sup>

isotopic isomer	KIE <sub>obsd</sub> <sup>b</sup>	KIE <sub>calcd(I)</sub> <sup>c</sup>	KIE <sub>calcd(II)</sub> <sup>d</sup>
primary $\beta$ -T	13.5 $\pm$ 4	10.12	10.43
secondary $\beta$ -T	1.18 $\pm$ 0.10	1.022	1.044

<sup>a</sup>  $n_{\beta\text{-H}'} = 0.41; n_{\alpha\text{-N}} = 0.74; \sigma = 0.78$ . <sup>b</sup> Reference 12.

<sup>c</sup> Calculated using eq 8. <sup>d</sup> Calculated using eq 8'.

for the 4-methoxy-, 4-chloro-, and 4-trifluoromethyl- derivatives of I, for which experimental  $\beta$ -deuterium and nitrogen-15 KIE are also available.<sup>9b</sup> The solvation of the leaving group and of the  $\alpha$ -carbon was assumed in each of these cases to be the same as for the unsubstituted compound since no information on solvation of substituted analogues of I exists. KIE were then calculated for all fully solvated models, and the results are summarized in Table IV. In Figure 8, the transition-state structures determined in this manner for all substituents are indicated on a transition-state map; the error bars indicate the allowable variations in the appropriate bond orders as deduced from the dimensions of the regions of intersection for  $\beta$ -D<sub>2</sub> and <sup>15</sup>N KIE, when plotted as in Figure 6. As can be seen, the transition states are related by a shift parallel to the central E2 diagonal, as predicted by Thornton's force rules.<sup>11,15</sup> Such a shift corresponds to developing a constant partial negative charge  $q_f \approx 0.33$  e at the  $\beta$ -carbon (some of which can be delocalized into the aromatic ring) in the transition state, regardless of the substituent carried by the ring. Stated alternatively, these results suggest that the

Table VI. Final KIE for Solvated Transition-State Models at 40 °C<sup>a</sup>

isotopic isomer	subst			
	4-OCH <sub>3</sub> <sup>b</sup>	4-H <sup>c</sup>	4-Cl <sup>d</sup>	4-CF <sub>3</sub> <sup>e</sup>
β-D <sub>2</sub> <sup>f</sup>	2.63 (2.64)	3.12 (3.12) <sup>g,h</sup>	3.47 (3.48)	4.15 (4.15)
β- <sup>14</sup> C	1.036	1.038	1.039	1.038
α-D <sub>2</sub> <sup>f</sup>	1.042	1.041 (1.03)	1.032	1.020
α- <sup>14</sup> C	1.026	1.027	1.026	1.025
<sup>15</sup> N <sup>f</sup>	1.0138 (1.0137)	1.0133 (1.0133)	1.0115 (1.0114)	1.0091 (1.0088)
N(CH <sub>3</sub> ) <sub>2</sub> CD <sub>3</sub> <sup>f,i</sup>	1.037	1.037 (1.05)	1.037	1.037
N(CD <sub>3</sub> ) <sub>2</sub> CH <sub>3</sub> <sup>f,i</sup>	1.076	1.076 (1.10)	1.076	1.076
N(CD <sub>3</sub> ) <sub>3</sub> <sup>f,i</sup>	1.099	1.099 (1.12)	1.099	1.098

<sup>a</sup>  $n_{\beta\text{-Ph}_1} = 1.0 + 0.5q^-$ . <sup>b</sup> See footnote b, Table IV. <sup>c</sup> See footnote c, Table IV. <sup>d</sup> See footnote d, Table IV. <sup>e</sup> See footnote e, Table IV. <sup>f</sup> See footnote f, Table IV. <sup>g</sup> See footnote g, Table IV. <sup>h</sup>  $(E_{\text{aD}} - E_{\text{aH}})_{\text{calcd}} = 0.702 \text{ kcal mol}^{-1}$ ,  $(A_{\text{H}}/A_{\text{D}})_{\text{calcd}} = 1.009$ ; experimental values<sup>44a</sup>:  $(E_{\text{aD}} - E_{\text{aH}}) = 0.92 \pm 0.19 \text{ kcal mol}^{-1}$ ,  $(A_{\text{H}}/A_{\text{D}}) = 0.71 \pm 0.21$ . <sup>i</sup> 80 °C.

amount of charge accumulated at the β-carbon in the transition state is primarily a function of the leaving group, and not of the ring substituent, provided that all other experimental variables (base, solvent, etc.) are kept constant. It therefore follows that for a different leaving group, the transition-state structures should lie along a different line parallel to the E2 diagonal; this is also implied by Thornton's force rules,<sup>11,15</sup> which predict that for a better leaving group, the E1cB character of the transition state should decrease.

All of these results were obtained by using the same reaction coordinate, which was dominated by proton transfer. Since all the transition states lie along a line parallel to the central E2 diagonal, there is no a priori reason to expect much change in the relative importance of heavy-atom motion, as would be expected if the relative E1cB character of the transition states were changing; since good agreement between calculated and experimental KIE is obtained by using a hydrogen-transfer reaction coordinate motion for all KIE considered, it appears that this reaction coordinate motion is at least a reasonable first approximation. The results are, however, relatively insensitive to the magnitudes of the proportionality constants *B* and *C* (provided only that they are substantially smaller than *A*), with the exception of the α- and β-carbon-14 KIE. Until these definitive isotope effects are determined, the relative importance of heavy-atom motion cannot be accurately assessed.

In Figure 9, the bond orders  $n_{\alpha\text{-N}}$  and  $n_{\beta\text{-H}}$  of the transition states are plotted vs.  $\sigma$ . Both plots are reasonably linear with the electron-withdrawing ability of the substituent, allowing for the first time the prediction of transition-state structures for the Hofmann elimination of other substituted (2-phenylethyl)trimethylammonium ions. For example, the bond orders  $n_{\alpha\text{-N}}$  and  $n_{\beta\text{-H}}$  expected for the transition state in the elimination of the 4-nitro-compound were determined by extrapolation to  $\sigma = 0.78$ ; the resulting transition state is indicated by the solid circles in Figures 8 and 9. The primary and secondary β-tritium KIE were calculated for this transition state model and are presented in Table V. Although the calculated primary isotope effect for this model was in satisfactory agreement with the reported value,<sup>12</sup> the secondary KIE calculated was outside the rather large error limits reported for the experimental value. The calculated secondary KIE could be brought into agreement with experiment by reducing all bending force constants about *C*<sub>β</sub> by about 10–15%. There is, however, little evidence to suggest that a lowering of force constants occurs in anionic species without concomitant bond order or geometry changes. It is possible, of course, that eq 8 overestimates the value of  $n_{\beta\text{-Ph}_1}$  for electron-withdrawing substituents. Although the necessary experimental data for carbanions are not available to test eq 8, electron densities for substituted benzylic cations are available in the literature. In these cases, it has been suggested<sup>42</sup> that the electron densities of substituted benzylic cations are very similar to those of the parent cation. On the

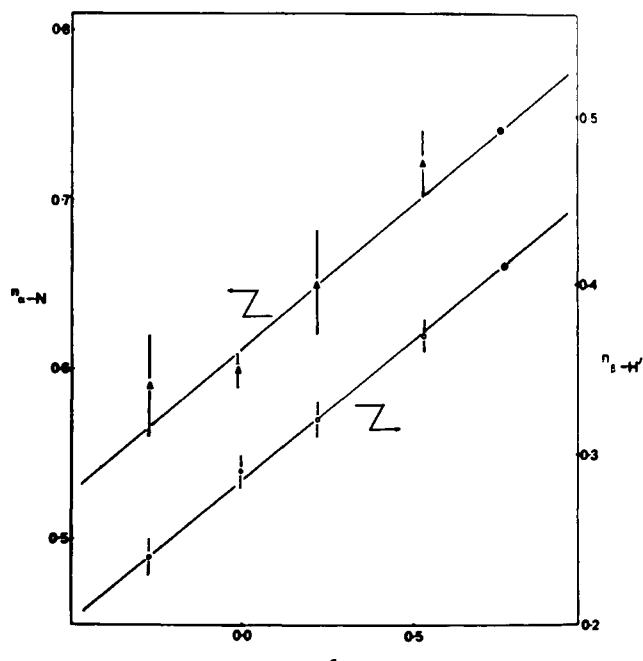


Figure 9. Correlation of bond orders for transition-state structures of Figure 8 with the Hammett  $\sigma$  parameter. Solid circles indicate the values for the 4-NO<sub>2</sub> derivative, obtained by extrapolation to  $\sigma = +0.78$ .

assumption that the behavior of carbanions would be similar to that of carbocations, the calculations of the β-tritium KIE were repeated for the *p*-NO<sub>2</sub> model, allowing the same conjugation of the partial negative charge for all substituents:

$$n_{\beta\text{-Ph}_1} = 1.0 + 0.5q^- \quad (8')$$

As can be seen (Table V), there is slight improvement in the agreement between the calculated and experimental results, but the calculated secondary β-tritium KIE is still considerably smaller than the experimental value. In view of the fact that the secondary KIE is derived from<sup>12</sup> the overall observed effect of tracer labeling with tritium at both β-hydrogens, it is possible that the discrepancy may, in fact, arise from the extraction of the secondary KIE from the experimental measurements. In this case, measurement of the β-carbon KIE would help to resolve this discrepancy.<sup>43</sup>

All KIE for the fully solvated models were calculated for *p*-OCH<sub>3</sub>, *p*-H, *p*-Cl, and *p*-CF<sub>3</sub> transition-state models, using eq 8' to account for delocalization of negative charge accumulated at the β-carbon. The results are tabulated in Table VI; where available, the corresponding experimental data are given in

(42) (a) Streitwieser, A., Jr.; Hammond, H. A.; Jagow, R. H.; Williams R. M.; Jesaitis, R. G.; Chang, C. J.; Wolf, R. *J. Am. Chem. Soc.* **1970**, *92*, 5141. (b) Ray, G. J.; Kurland, R. J.; Colter, A. K. *Tetrahedron* **1971**, *27*, 735. (c) Ray, G. J.; Colter, A. K.; Kurland, R. J. *Chem. Phys. Lett.* **1968**, *2*, 324.

(43) The β-carbon KIE is of particular importance in assessing the contribution of heavy-atom motion to the reaction coordinate; other calculations have shown that the secondary β-hydrogen KIE is also dependent on the reaction coordinate employed, and an increase in β-carbon motion in the reaction coordinate should result in an increase in the calculated KIE.

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parentheses. In almost all cases, the agreement is excellent, although much of the agreement is the result of the method of choosing transition states. Nonetheless, several of the results were obtained without adjustment of parameters, and the overall agreement inspires our confidence in the geometries, bonding parameters, and the reaction coordinate.

The results support the presumption of an E1cB-like E2 mechanism for the Hofmann elimination from (2-phenylethyl)-trimethylammonium ions; they also support Thornton's predictions

of substituent effects on transition-state structure. The leaving group and  $\alpha$ -D<sub>2</sub> kinetic isotope effects lend strong support to the importance of differential solvation of the reactant and transition state and of the necessity of considering the role of solvent in interpreting leaving group KIE.

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## Ring Strain in Cyclopropane, Cyclopropene, Silacyclopropane, and Silacyclopropene

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**Abstract:** The strain energy in four three-membered rings is calculated by using the appropriate isodesmic reactions. Calculations with and without d functions on the heavy atoms indicate that while these polarization functions tend to reduce ring strain, the addition of d orbitals has little effect on the predicted trends. While introduction of unsaturation drastically increases the strain in the carbon system (cyclopropane  $\rightarrow$  cyclopropene), this is not the case for silicon (silacyclopropane  $\rightarrow$  silacyclopropene). As a result cyclopropane and cyclopropene are predicted to be the least and most strained rings, respectively.

Ring strain is a concept which is frequently used to rationalize instability and reactivity of small cyclic compounds. Recently, a novel quantitative measure of ring strain has been proposed.<sup>1</sup> This method makes use of *isodesmic reactions* in which the number of bonds of each type is formally conserved on going from reactants to products. The use of isodesmic reactions is particularly useful in quantum chemistry since the effect of correlation error is expected to be minimal in such reactions. As a result, one can use Hartree-Fock-level energy differences with some degree of confidence.

In this paper the ring strain in cyclopropane, cyclopropene, silacyclopropane, and silacyclopropene is examined by using ab initio molecular orbital calculations. Cyclopropane and cyclopropene have been studied before<sup>1</sup> and are included here for internal consistency. While semiempirical<sup>2-4</sup> and ab initio<sup>5</sup> calculations have been carried out on the silicon rings, no attempt has been made to evaluate the strain in these rings or, more importantly, their ring strain relative to the hydrocarbon analogues. In view of the apparent stability of the silicon-containing rings,<sup>6</sup> such a comparison is clearly of interest.

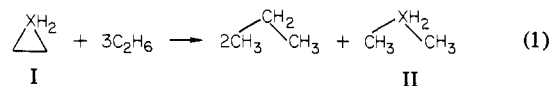
The methodology used in the calculations is summarized in the Methodology section, while the results of the ring strain calculations are presented and discussed in the Results and Discussion section. To aid the latter discussion approximate quadratic force fields have been generated for the four rings, and these are also presented in the Results and Discussion section.

### Methodology

Two separate basis sets have been used in these calculations. All geometry optimizations were performed by using the 3-21G basis set developed recently.<sup>7,8</sup> Because split valence basis sets

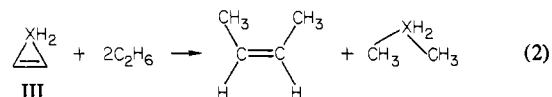
are known<sup>9</sup> to overestimate ring strain, the geometry optimizations were followed by single point 6-31G<sup>9,10</sup> calculations at the final geometries. Addition of polarization functions appears to give a proper accounting of strain.<sup>9</sup> The geometry optimizations and force field calculations were carried out with the use of the HONDO system of programs.<sup>11</sup>

The isodesmic reaction used to measure strain in the saturated rings is

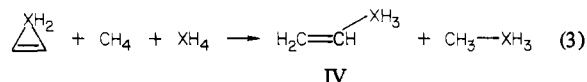


where X may be C or Si. In eq 1 the strained XH<sub>2</sub> and CH<sub>2</sub> groups on the left are replaced by their unstrained counterparts on the right. The addition of ethane provides the appropriate number of methyl groups.

The appropriate reaction for the unsaturated rings is less clear. The analogous reaction to (1) is



in which a strained XH<sub>2</sub> and substituted ethylene are replaced by their unsubstituted analogues. However,<sup>1</sup> the use of eq 2 is somewhat ambiguous since it measures, in addition to ring strain, the stabilization or destabilization effect due to the proximity of the XH<sub>2</sub> and unsaturated moieties. An isodesmic reaction which corrects this problem is



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