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AM1 Studies of E2 Reactions. 2. Regioselectivity, Stereochemistry, Kinetic Isotope Effects, and Competition with S_N2 Reactions

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Abstract: The regioselectivity and stereochemistry of bimolecular elimination (E2) reactions have been studied by use of the AM1 model. Calculations are first carried out for reactions of compounds of the type H–CHR–CHS–X, where X is the leaving group while R and S are H, CH_3, C_2H_5, or phenyl. In the first series, X is neutral (halogen) and the base anionic (methoxide ion), while in the second, X is cationic ('onium ion) and the base neutral (ammonia). The results account for the different regioselectivities shown by the two types of elimination, as embodied in the Saytzeff and Hoffmann rules. Our calculated kinetic isotope effects also agree with experiment and support our formulation of the two types of elimination (in the gas phase) as E2/E1cB and E2, respectively. Calculations for reactions of methoxide ion with cyclic bromides show that anti (axial–axial) elimination is favored in all cases. In derivatives of cyclohexane, equatorial–equatorial gauche elimination is predicted to be more facile than axial–equatorial. Calculations for parallel E2 and S_N2 reactions predict the E2 reactions of methoxide ion with alkyl halides to be preferred. Substitution becomes more competitive in the reactions of ammonia with 'onium ions.

The previous paper[1] (part 1) described initial AM1[2] studies of a number of simple E2 elimination reactions, designed to study the mechanisms and effects of different leaving groups. Here we report further work designed to investigate the regioselectivity, stereochemistry, and the factors determining the choice between alternative E2 and S_N2 reaction paths. The notation used here follows that of part 1.

The first problem concerns the effects of substituents, in particular for cases where elimination can take place in more than one way. Reactions of this kind, involving alkyl derivatives of ethylene, are interesting because of their erratic regioselectivity. Two conflicting rules have been formulated to systematize the situation. Saytzeff's rule[3] states that the preferred product is the olefin with the *greatest* number of substituents attached to the double bond, while Hoffmann's rule[4] states that the preferred product is the olefin with the *least* number of such substituents. While different examples of each specific type of E2 reaction usually follow the same rule and while the rule followed in each specific case is usually known, the basic factors responsible remain uncertain except when steric effects control the orientation. We hoped that calculations for a number of reactions of this kind might clarify the situation.

The second problem concerns the choice of stereochemistry in E2 reactions where attack on different protons can lead to products with different geometries. Simple considerations of orbital overlap indicate that the most stable form of an E2 transition state (TS) should be one in which the base, the two carbon atoms involved in olefin formation, and the leaving group are coplanar. This condition is, however, satisfied equally well by the TSs for both syn (cis) and anti (trans) eliminations and the choice between them is less clear. The experimental results[5,6] indicate that anti elimination is usually preferred for a strong base and the formation of a free anionic leaving group, while the syn elimination is preferred for a weak base. E2 reactions, overall, cover the whole spectrum from all anti to all syn.

Previous calculations correctly predicted anti elimination to be preferred in E2 reactions of simple ethane derivatives.[1] Additionally, syn TSs of higher energy were found in certain cases for gauche attack. Any systematic comparison of the three possible modes of elimination (syn, anti, and gauche) was precluded by the ease with which ethane derivatives underwent conformational isomerization by rotation about the C–C bond. Here, we addressed this question by carrying out calculations for a number of E2 reactions involving cyclic substrates where conformational isomerization is ruled out by the presence of rigid rings.

The third problem, one of practical importance in synthesis, concerns the choice between alternative elimination (E2) and nucleophilic substitution (S_N2) reactions. In the first case the base (nucleophile) abstracts a proton, while in the other it displaces the leaving group. We have approached this problem by comparing the rates of the E2 and S_N2 reactions of a given nucleophile (base) with a number of alkane derivatives.

Procedure

The procedure used has been described in part 1.[1] The only new feature was the calculation of kinetic isotope effects (KIE). These were determined by using the rigid-rotor-harmonic-oscillator approximation and neglecting tunneling effects.[7] The calculations were carried out using a locally developed computer program,[8] based on vibrational frequencies given by AMPAC.[9] These frequencies were also used to calculate molecular entropies and entropies of activation.[10] Options for all these procedures are included in AMPAC.

Results and Discussion

As indicated above, our first concern was the choice between the Saytzeff and Hoffmann rules in cases where alternative products can be formed in an elimination. The reactions examined were of the type

$$B + H{-}CHR{-}CHS{-}X \rightarrow BH^+ + RCH{=}CHS + X^- \quad (1)$$

where X is the group lost in the reaction and R and S are hydrogen, methyl, ethyl, or phenyl. For reasons indicated in part 1,[1] calculations were carried out for reactions of methoxide ion as the base with neutral substrates (X = halogen), and of ammonia as the base with 'onium ion (X = OH_2^+).

A. Regioselectivity in the Reactions of Methoxide Ion with Alkyl Halides. The first series of reactions studied were those of methoxide ion with substituted ethyl halides, X in eq 1 being

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[1] Dewar, M. J. S.; Yate-Ching Yuan, *J. Am. Chem. Soc.*, preceding article in this issue.

[2] Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem Soc.* **1985**, *107*, 3902.

[3] Saytzeff, A. *Justus Liebigs Ann. Chem.* **1875**, *179*, 296.

[4] Hoffmann, A. W. *Justus Liebigs Ann. Chem.* **1851**, *78*, 253; *79*, 11.

[5] de Koning, L. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1987**, *109*, 1715.

[6] Angelini, G.; Lilla, G.; Speranza, M. *J. Am. Chem. Soc.* **1989**, *111*, 7393.

[7] Sicher, J.; Svoboda, M.; et al. *Collect. Czech. Chem. Commun.* **1971**, *36*, 3633.

[8] Dewar, M. J. S.; Kuhn, D. R.; Healy, E. F. To be submitted.

[9] Available from the Quantum Chemistry Program Exchange (QCPE) program No. 506.

[10] Dewar, M. J. S.; Yamaguchi, Y.; Suck, S. H. *Chem. Phys.* **1979**, *43*, 145.

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Table I. Heats of Formation for Relevant Stationary Points, and Activation Energies ($\Delta H^{\ddagger}$) for E2 Reactions Starting from the Initial CD Complexes, for E2 Reactions of Methoxide Ion with Substituted Ethyl Chlorides

	substituents		heat of formation, kcal/mol					
rxn	β	α	reactant	STCD[a]	TS[b]	PTCD[c]	PDT[d]	$\Delta H^{\ddagger}$
1a	H	H	-64.7	-74.8	-68.6	-84.2	-78.2	6.2
2a	CH_3	H	-71.1	-81.5	-76.6	-98.0	-88.1	4.9
3a	C_2H_5	H	-76.5	-87.0	-80.2	-112.5	-93.8	6.8
6a	Ph	H	-37.6	-50.1	-48.2	-76.2	-56.0	1.9
5a → 8	CH_3	CH_3	-75.3	-87.5	-80.7	-107.3	-97.0	6.8
5a → 9	CH_3	CH_3	-75.3	-88.5	-81.6	-108.9	-98.0	6.9
4a	H	CH_3	-69.8	-82.0	-73.7	-98.9	-88.1	8.3
5a → 10	H	C_2H_5	-75.3	-87.5	-79.0	-105.8	-93.8	8.5
7a	H	Ph	-35.6	-49.6	-39.0	-75.0	-56.0	10.6

[a] CD complex formed by the reactants. [b] Transition state. [c] CD complex formed by the products. [d] Products.

Table II. Heats of Formation for Relevant Stationary Points, and Activation Energies ($\Delta H^{\ddagger}$) for E2 Reactions Starting from the Initial CD Complexes, for E2 Reactions of Methoxide Ion with Substituted Ethyl Bromides

	substituents		heat of formation,[a] kcal/mol					
rxn	β	α	reactant	STCD	TS	PTCD	PDT	$\Delta H^{\ddagger}$
1b	H	H	51.6	-61.5	-56.6	-76.2	-61.0	4.9
2b	CH_3	H	-58.0	-68.7	-64.5	-80.8	-70.9	4.2
3b	C_2H_5	H	-61.7	-75.6	-71.7	-94.3	-76.6	3.9
6b	Ph	H	-24.8	-39.5	-35.8	-59.2	-38.7	3.7
5b → 8	CH_3	CH_3	-61.8	-74.4	-68.4	-95.3	-79.7	6.0
5b → 9	CH_3	CH_3	-61.8	-75.3	-69.3	-96.6	-80.8	6.0
4b	H	CH_3	-56.4	-68.8	-61.4	-70.9	-70.9	7.4
5b → 10	H	C_2H_5	-61.8	-75.4	-67.4	-93.4	-76.6	8.0
7b	H	Ph	-22.7	-35.4	-27.6	-58.3	-38.7	7.8

[a] For notation, see Table 1.

Table III. Heats of Formation for Relevant Stationary Points, and Energies of Activation ($\Delta H^{\ddagger}$) for E2 Reactions Starting from the Initial CD Complexes, for E2 Reactions of Methoxide Ion with Substituted Ethyl Iodides

	substituents		heat of formation,[a] kcal/mol					
rxn	β	α	reactant	STCD	TS	PTCD	PDT	$\Delta H^{\ddagger}$
1c	H	H	-39.6	-49.1	-44.0	-56.5	-42.8	5.1
2c	CH_3	H	-45.7	-55.5	-51.8	-66.2	-52.7	3.7
3c	C_2H_5	H	-47.4	-61.3	-57.3	-73.5	-58.4	4.0
6c	Ph	H	-12.6	-27.6	-22.6	-36.4	-20.5	5.0
5c → 8	CH_3	CH_3	-49.3	-61.3	-55.5	-75.9	-61.5	5.8
5c → 9	CH_3	CH_3	-49.3	-62.3	-56.4	-76.7	-62.6	5.9
4c	H	CH_3	-44.2	-53.9	-48.4	-66.8	-52.7	5.5
5c → 10	H	C_2H_5	-49.3	-62.3	-54.3	-73.4	-58.4	8.0
7c	H	Ph	-10.8	-25.3	-15.6	-36.7	-20.5	9.7

[a] For notation, see Table I.

chlorine, bromine, or iodine. The compounds studied were ethyl chloride (**1a**), ethyl bromide (**1b**), ethyl iodide (**1c**), and the corresponding 1-propyl (**2a–c**), 1-butyl (**3a–c**), 2-propyl (**4a–c**), 2-butyl (**5a–c**), 1-phenylethyl (**6a–c**), and 2-phenylethyl (**7a–c**) halides. Figure 1 shows the calculated geometries and formal charge distributions calculated for the haloalkanes. Here, and subsequently, the structures shown in the figures were computer drawn from the calculated atomic coordinates.

The reactions followed the same pattern as before;[1] the reactants first combined to form an electrostatic (charge–dipole; CD) complex (STCD), which then underwent conversion to the CD complex (PTCD) derived from the products. The reactions all involved trans elimination. Figure 2 shows the geometries and distributions calculated for the initial CD complexes (STCD), while Figure 3 provides similar information for the transition states (TS). Tables I–III list calculated heats of formation for all the relevant stationary points involved in the reactions of the chlorides, bromides, and iodides, respectively, together with enthalpies of activation ($\Delta H^{\ddagger}$) starting from the CD complexes. In the case of **5**, elimination can lead to three products, *cis*- (**8**) or *trans*-2-butene (**9**) and 1-butene (**10**). All three reactions were studied.

The reactions of the derivatives of **1** followed the same pattern as that of **1** itself, being concerted but not synchronous. In the TS, the extent of bond breakage was greater for the CH bond as compared to the CX bond. These reactions can again be classified as E2/E1cB, in agreement with conclusions drawn from theoretical calculation.[11]

Comparison of the results for **1** with those for **4**, or with those for (**5** → **10**), shows that an alkyl substituent α to the halogen (X) increases $\Delta H^{\ddagger}$ and thus retards the reaction, while analogous comparisons of **1** with **2**, or **3**, and **5**, show that a β-alkyl substituent accelerates it. Note that here, and subsequently, comments concerning the effects of substituents apply to reactions of all three halides, the pattern of rates being the same for each; cf. the results in Tables I–III.

According to current ideas[12] concerning substituent effects, the strength of a C–alkyl bond should be greater, the larger the s character of the AO used to bind the alkyl substituent. The fact that β-methyl accelerates the reaction indicates that the breaking CH bond has already been significantly weakened in the TS, leading to a corresponding rehybridization of the β-carbon atom. Likewise the lack of acceleration in the case of α-methyl implies that the C–halogen bond is still almost unchanged. These results would of course be expected if the reactions are indeed of E2/E1cB type.

Similar but much larger effects are predicted for the phenyl derivatives, **6** and **7**, the decrease in activation energy brought about by β-phenyl (4.3 kcal/mol) being much greater than that brought about by β-methyl (1.3 kcal/mol) in the case of the chlorides. This is as expected[13] because the difference in bond

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(11) Minato, T.; Yamabe, S. *J. Am. Chem. Soc.* **1988**, *110*, 4586.

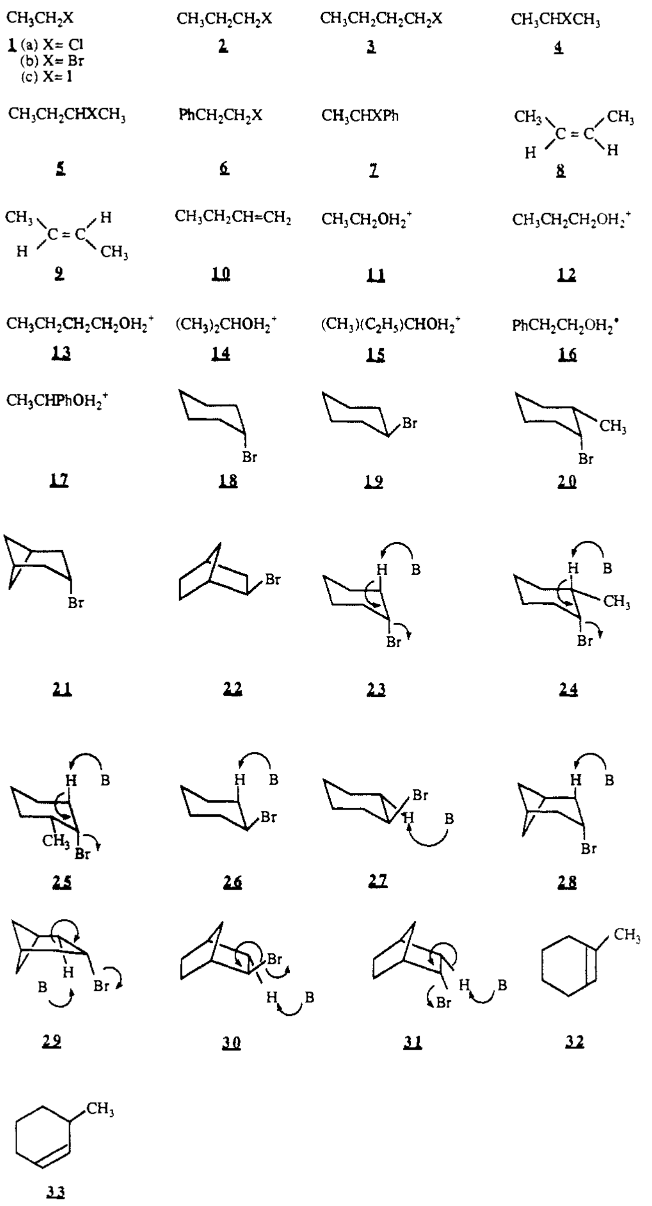
(12) (a) Dewar, M. J. S.; Schmeising, H. N. *Tetrahedron* **1959**, *5*, 166. (b) Dewar, M. J. S. *Hyperconjugation*; Ronald Press: New York, 1962.

Table IV. Heats of Formation for Relevant Stationary Points, and Energies of Activation ($\Delta H^\ddagger$) for E2 Reactions Starting from the Initial CD Complexes, for E2 Reactions of Ammonia with Substituted Ethyloxonium Ions

	substituents		heat of formation,[a] kcal/mol					
rxn	β	α	reactant	STCD	TS	PDTCD	PDT	$\Delta H^\ddagger$
11	H	H	117.6	109.3	118.0	88.5	107.8	8.7
12	CH_3	H	109.6	101.5	110.6	77.0	97.9	9.1
13	C_2H_5	H	102.3	94.3	103.5	69.6	92.2	9.2
16	Ph	H	138.7	131.0	140.9	115.3	130.1	9.9
15 → **8**	CH_3	CH_3	100.7	93.4	98.7	66.8	89.1	5.3
15 → **9**	CH_3	CH_3	100.7	92.8	98.6	65.8	88.0	5.8
14	H	CH_3	107.7	100.2	105.1	76.9	97.9	4.9
15 → **10**	H	C_2H_5	100.7	93.4	98.5	71.4	92.2	5.1
17	H	Ph	136.2	130.0	125.9	105.6	130.1	0

[a] For notation, see Table I.

Chart I



energy between sp^3–sp^3 and sp^3–sp^2 CC bonds is much less than that between sp^3–sp^2 and sp^2–sp^2 bonds.

The predicted retardations by α substituents seem to be due mainly to steric interactions, increasing with the size of the substituent (Me < Et < Ph). Corresponding steric interactions would then be expected to decrease the accelerating effects of β-alkyl substituents. Indeed, Tables I–III show that the accelerating effect of a β-ethyl substituent is less than that of β-methyl.

A further example is provided by comparison of the two modes of elimination from **5**, to form *cis*- (**8**) or *trans*-2-butene (**9**), or 1-butene (**10**). Since the TS for formation of either **8** or **9** contains both α-alkyl and β-alkyl substituents, the corresponding $\Delta H^\ddagger$ is less than that for **1**. The TS for formation of 1-butene, on the other hand, contains only α-alkyl substituents. The corresponding $\Delta H^\ddagger$ is therefore greater than those for formation of 2-butene, the preferred ethylene derivative being the one with the greatest number of alkyl substituents.

Comparison of the results for formation of **8** and **9** provides an indication of the role of steric effects of substituents on both carbon atoms. As Tables I–III show, the heats of formation of the initial CD complex and TS for formation of the trans isomer are lower in each case by 1.0 kcal/mol. Relative to **5**, the TS for elimination is thus lower in energy, in agreement with the fact that **9** is the preferred product.[13]

B. Regioselectivity in Reactions of Ammonia with 'Onium Ions. The second series involved reactions of a neutral base (ammonia) with 'onium ions (**11–17**), B and X in eq 1 being NH_3 and H_2O^+, respectively:

$$H_3N + H—CHR—CHS—OH_2^+ \rightarrow H_4N^+ + RCH{=}CHS + H_2O \quad (2)$$

Figure 4 shows the bond lengths and charge distributions calculated for the free reactants, while Figure 5 shows similar data for the CD complexes and TSs. In the case of **15**, values are shown for both possible modes of elimination leading to **8**, **9**, and **10**. Table IV lists heats of formation for the various stationary points together with $\Delta H^\ddagger$ for reactions starting from the initial STCD.

Comparison of Table IV with Tables I–III shows that the effects of substituents on elimination from the 'onium ions are diametrically opposite to those for the reactions of methoxide ion with alkyl halides. Here α-methyl and α-phenyl lower $\Delta H^\ddagger$ (cf. **11** with **14** or **17**) while β-methyl and β-phenyl raise it; cf. **11** with **12** or **16**. While nearly all experimental regioselectivity studies of elimination from 'onium ions have been carried out in solution using anionic bases, the results certainly confirm the predicted differences between eliminations from neutral and cationic substrates. For reasons indicated earlier,[1] calculations for reactions of 'onium ions with anionic bases in the gas phase would be of little relevance because of their extreme exothermicity. This is largely eliminated in the case of reactions in solution because the solvation energy of the ionic reactants is much greater than that of the neutral products.

C. Hoffmann's vs Saytzeff's Rule. It has been known for many years that an E2 reaction of an alkyl halide tends to give the most alkylated olefin (Saytzeff's rule[3]), whereas a corresponding reaction of an 'onium ion tends to give the least alkylated olefin (Hoffmann's rule[4]). While our calculations reproduce the experimental results, they are not consistent with the explanation commonly given for the difference between the two kinds of elimination.

According to current ideas, elimination reactions of 'onium ions are E2/E1cB reactions, where deprotonation is assisted by the field effect of the adjacent positive charge. Since alkyl groups are usually thought to reduce the acidity of adjacent hydrogens by their inductive effects, the most acidic β-hydrogen should be

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[13] Carey, F. A.; Sunderberg, R. J. *Advanced Organic Chemistry*; Plenum: New York, 1985; Part A, pp 351–356.

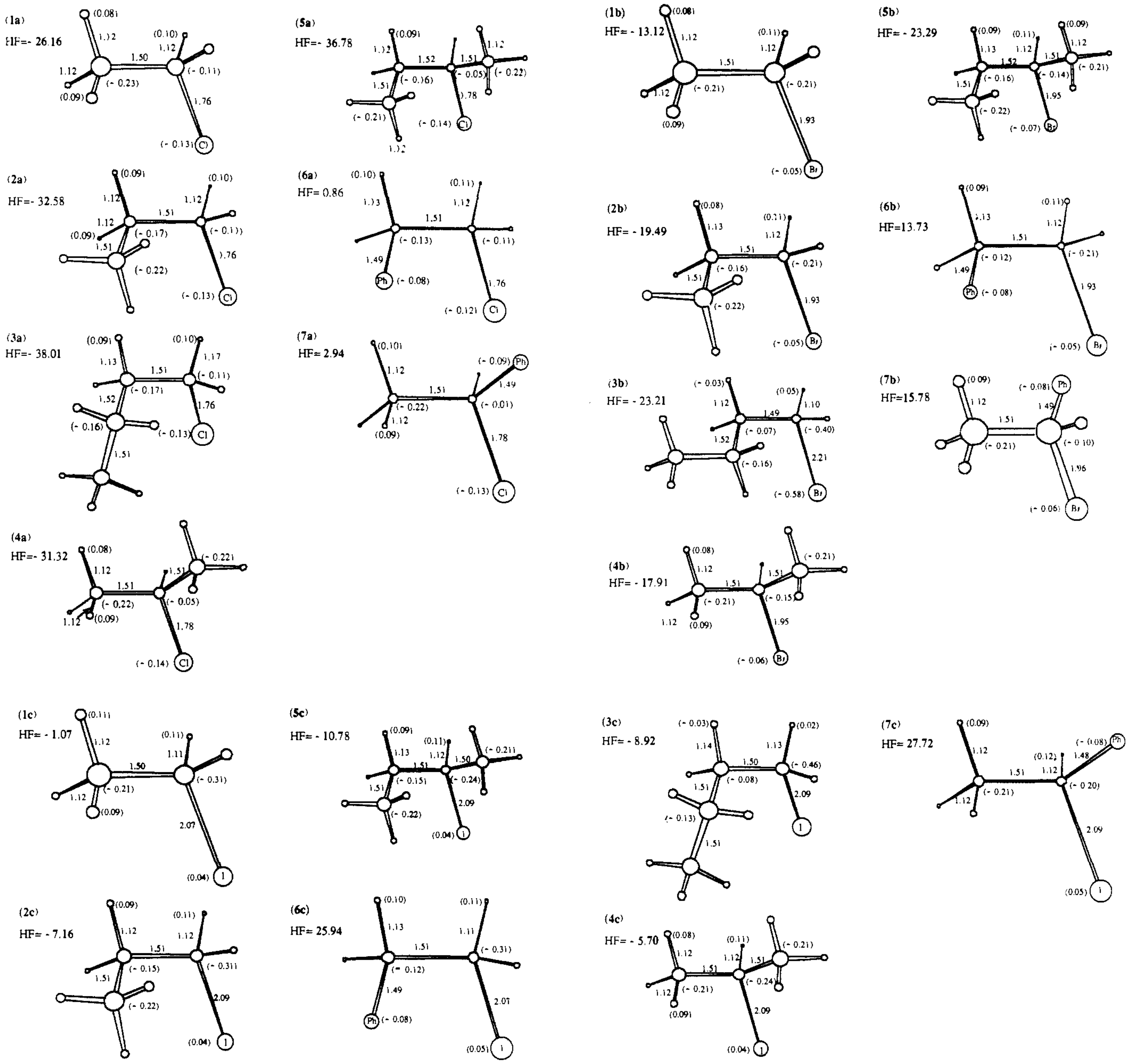

Figure 1. Bond lengths (Å), charge distributions (e), and heats of formation (HF, kcal/mol) in (**1a–c**) haloethanes, (**2a–c**) 1-halopropanes, (**3a–c**) 1-halobutanes, (**4a–c**) 2-halopropanes, (**5a–c**) 2-halobutanes, (**6a–c**) 1-phenyl-2-haloethanes, and (**7a–c**) 2-phenyl-2-haloethanes.

the one with the fewest vicinal alkyl groups. The preferred product should therefore be the olefin with fewest alkyl substituents, as indeed is the case.

Conversely, in an E2 reaction involving a neutral leaving group, deprotonation and ionization of the leaving group are believed to take place more or less simultaneously. Since the α- and β-carbon atoms both undergo a change in hybridization during the reaction from sp^3 to sp^2, both should have intermediate hybridizations in the TS. Bonds formed by sp^2-hybridized carbon atoms are stronger than ones formed by sp^3-hybridized carbon atoms and the difference is greater for CC bonds than for CH ones.[12] The preferred product should therefore be the olefin with the largest number of alkyl substituents.

However, the assumption concerning the effect of alkyl substituents on the strengths of carbon acids is contradicted both by gas-phase experiment[14] and by theoretical calculations.[15] α-Alkyl substituents *stabilize* methyl anion and thus *increase* the strengths of the corresponding carbon acids. The stabilization can be attributed to polarization of the substituent by the adjacent negative charge and/or σ-conjugative[16] interactions between the lone-pair electrons of the anion and the adjacent C–C bond.

Problems also arise in the conventional interpretation of reactions following Saytzeff's rule. If β-alkyl substituents hinder deprotonation, as assumed for reactions obeying Hoffmann's rule, it is not clear why they should not also hinder a synchronous E2 reaction where the β-carbon atom is expected to change its hybridization significantly in the TS.

According to our calculations, E2 reactions between methoxide ion and alkyl halides are of E2/E1cB type. Since the CX bond in the TS is only a little weaker than the same bond in the reactant, the CC bond is only a little shorter in the TS than in the reactant. Deprotonation, on the other hand, has progressed about halfway, the lengths of the forming OH and breaking OH bonds being comparable. Since simple carbanions are pyramidal and since the CC bond has developed little π character, the bond angles at the β-carbon atom are almost the same in the TS as in the

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(14) Bartmess, J. E. *Gas Phase Ion Chemistry*; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2, Chapter 11.

(15) Dewar, M. J. S.; Dieter, K. M. *J. Am. Chem. Soc.* **1986**, *108*, 8075.

(16) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 669.

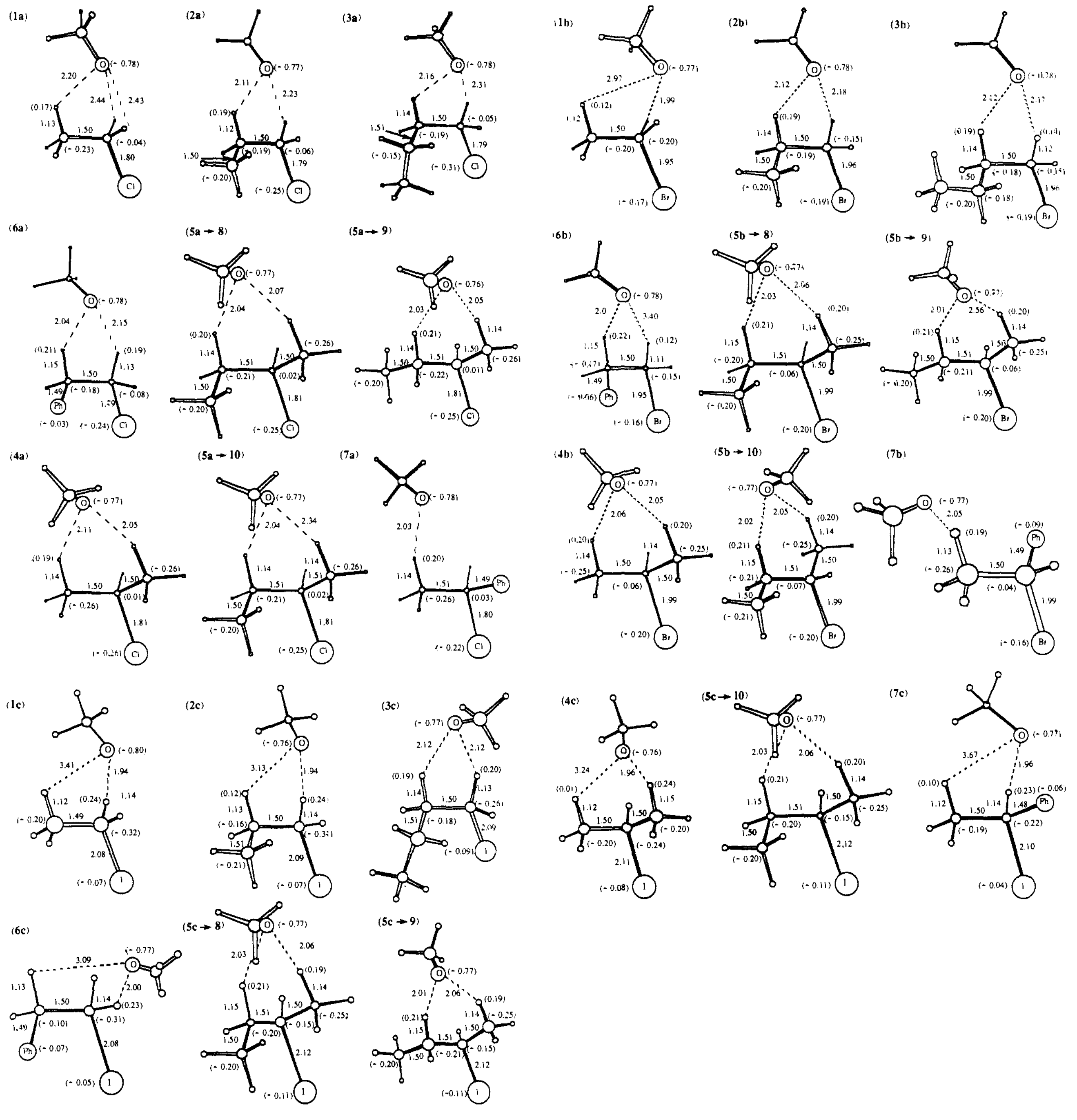

Figure 2. Bond lengths (Å) and charge distributions (e) in the initial CD complexes for E2 reactions of methoxide ion with (**1a–c**) haloethanes, (**2a–c**) 1-halopropanes, (**3a–c**) 1-halobutanes, (**4a–c**) 2-halopropanes, (**5a–c**) 2-halobutanes to form *cis*-butene (**8**), *trans*-butene (**9**), or 1-butene (**10**), (**6a–c**) 1-phenyl-2-haloethanes, and (**7a–c**) 2-phenyl-2-haloethanes.

reactant. The effect of β substituents on the rate should therefore be similar to the effect on the acidity of adjacent hydrogen atoms in a paraffin. As indicated above, this correctly implies that β-alkyl substituents should accelerate such eliminations.

Our calculated TSs for the 'onium eliminations (Figure 5) imply that breaking of the bond to the leaving group, and formation of the C=C double bond, have both progressed much further than in the corresponding TSs for the halide eliminations. The structures of the 'onium TSs also vary more with substitution. Thus, while the reactions of the parent ethyloxonium ion (**11**) and its β-substituted derivatives are predicted to be essentially synchronous, the α substituents increase the extent of ionization of leaving group in the TS, indicating mechanisms of E2/E1 type. The CC bonds remain short in the TS, however, implying that they still have extensive double-bond character. These conclusions are supported by the greater planarity of both carbon atoms in the TSs for the 'onium eliminations, which is apparent from comparisons of the computer-drawn structures in Figures 3 and 5.

These differences in structure imply a change in hybridization of each carbon atom from sp^3 toward sp^2. This in turn should lead to strengthening of bonds to adjacent alkyl or aryl substituents. Substituents at the α-carbon atom should therefore selectively stabilize the TS and increase the rate of elimination. Our calculated activation energies support this conclusion, the effects of such substituents being greater for eliminations from 'onium ions than from alkyl halides. Indeed, the activation energy for elimination from **17** is predicted to be negative, the reaction leading directly to the PTCD.

The same argument should apply to β substituents; yet these are predicted and observed to retard elimination from 'onium ions. The change in the C=C bond must therefore have some additional

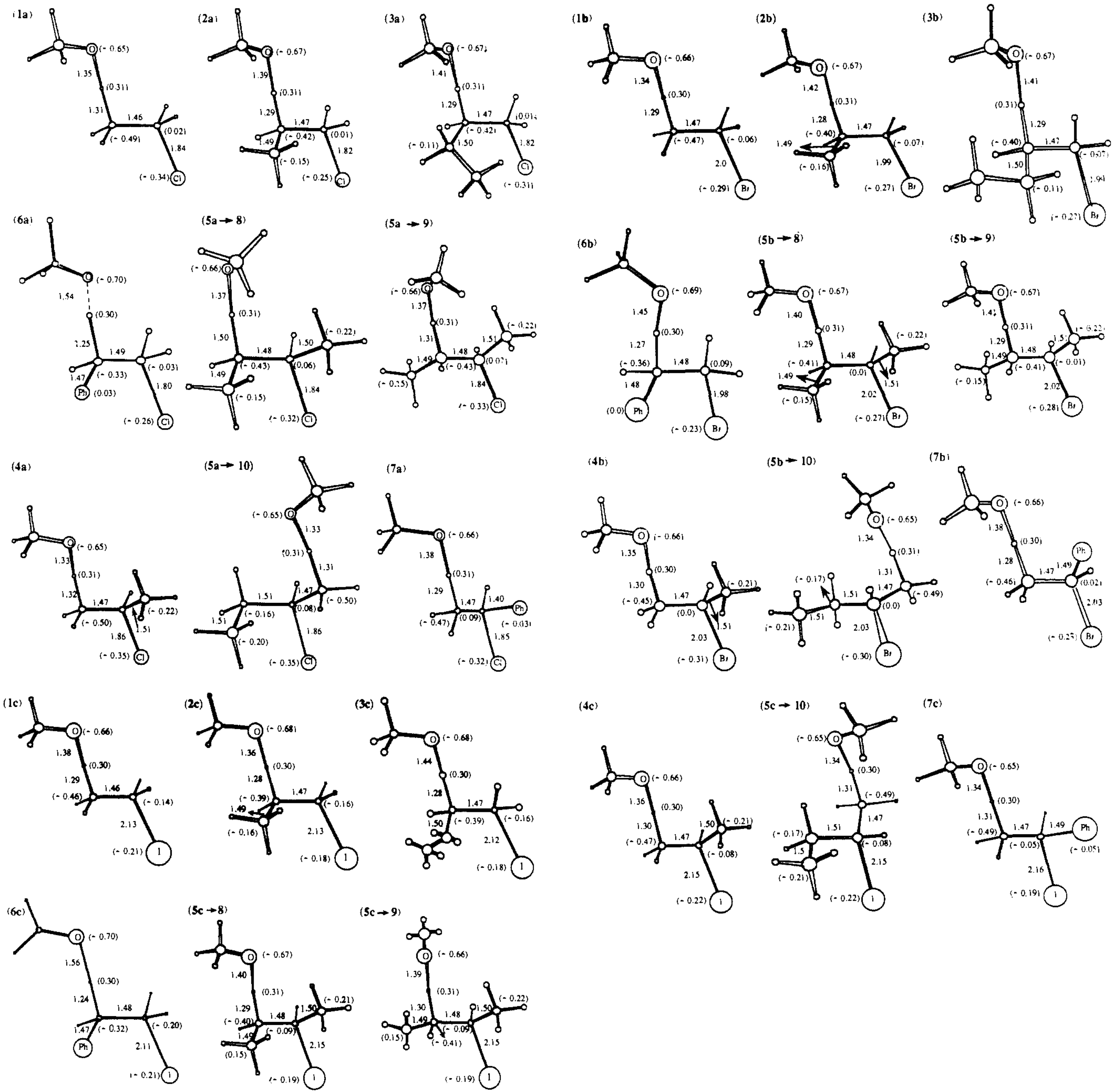

Figure 3. Bond lengths (Å) and charge distributions (e) in the transition states for E2 reactions of methoxide ion with (**1a–c**) haloethanes, (**2a–c**) 1-halopropanes, (**3a–c**) 1-halobutanes, (**4a–c**) 2-halopropanes, (**5a–c**) 2-halobutanes to form *cis*-butene (**8**), *trans*-butene (**9**), or 1-butene (**10**), (**6a–c**) 1-phenyl-2-haloethanes, and (**7a–c**) 2-phenyl-2-haloethanes.

effect at the β-carbon that does not operate in the case of α substituents or in eliminations from alkyl halides.

Steric repulsion between the approaching base and a β substituent seems a good candidate. Analogous steric repulsions seem to play a significant role in the addition of radicals to olefins,[17] and repulsions of this kind should be greater the more nearly planar the carbon atom bearing the substituent. At noted above, our calculations predict just such a difference between the geometries of the β-carbon atoms in the TSs for elimination from 'onium ions and those for elimination from halides.

Since our calculations refer to the gas phase, it is of course possible that reactions in solution follow a different course. As noted in part 1,[1] a polar solvent may lead to modifications of the TSs, corresponding to changes in the timing of bond breaking and deprotonation. However, the arguments presented here suggest that if solvation led in fact to a change in mechanism of the 'onium eliminations to E2/E1cB, it would lead to a corresponding change in regioselectivity, which is not observed.

D. Deuterium Kinetic Isotope Effects. Conclusions concerning the structures of TSs can often be drawn from studies of kinetic isotope effects (KIE), in particular of primary (PDKIE) and secondary (SDKIE) deuterium kinetic isotope effects. Values for these have indeed been reported[18-20] for several E2 reactions and we ourselves have calculated them for some of the reactions studied here.

Table V summarizes our calculated PDKIEs and SDKIEs for the E2 reactions of methoxide ion with ethyl chloride, propyl chloride, isopropyl chloride, and 2-butyl chloride. The PDKIEs

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(17) See: Dewar, M. J. S.; Olivella, S. *J. Am. Chem. Soc.* **1978**, *100*, 5290.

(18) Bierbaum, V. M.; Filley, J.; Depuy, C. H. *J. Am. Chem. Soc.* **1985**, *107*, 2818.

(19) Cockerill, A. F.; Saunders, W. H., Jr. *Mechanisms of Elimination Reactions*; Wiley: New York, 1973; Chapter II.

(20) See, e.g.: McLennan, D. J.; Wong, R. J. *J. Chem. Soc., Perkin Trans. 2* **1974**, 526.

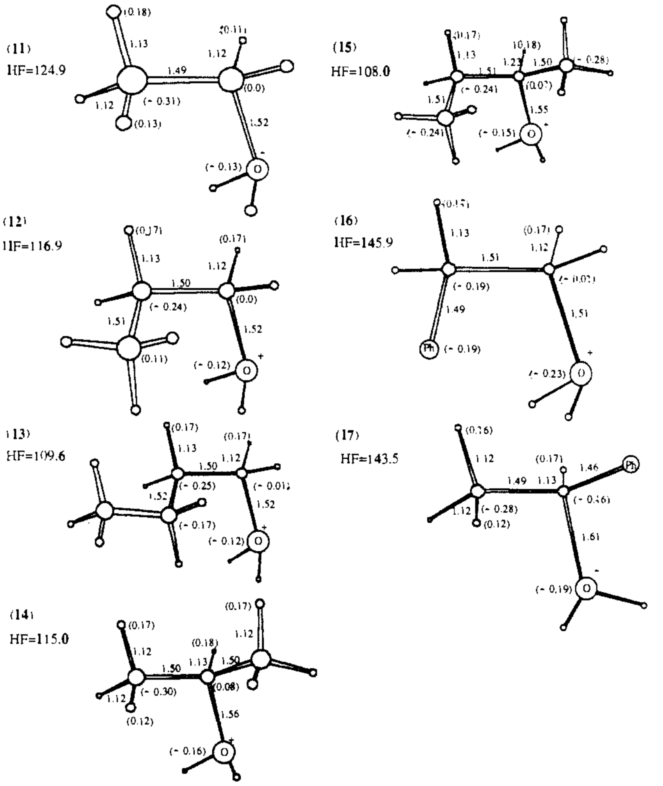

Figure 4. Bond lengths (Å), charge distributions (e) and heat of formations (HF, kcal/mol) in the (**11**) ethyl 'onium ion, (**12**) 1-propyl 'onium ion, (**13**) 1-butyl 'onium ion, (**14**) 2-propyl 'onium ion, (**15**) 2-butyl 'onium ion, (**16**) 1-phenyl 'onium ion, (**17**) 2-phenyl 'onium ion.

Table V. Primary and Secondary Deuterium Kinetic Isotope Effects (KIE) in the E2 Reactions of CH_3O^- with $R_1C_1R'_1HC_2R_2R'_2Cl$ at 45 °C

R_1	R'_1	R_2	R'_2	KIE (k_h/k_d)
		Primary KIE[a]		
H	H	H	H	4.16
CH_3	H	H	H	4.09
H	H	CH_3	H	4.15
CH_3	H	CH_3	H	4.12
		Secondary KIE[b]		
D	D	H	H	1.08
H	H	D	D	0.99
CH_3	D	H	H	1.04
CH_3	H	D	D	0.97
D	D	CH_3	H	1.03
H	H	CH_3	D	1.00
CH_3	D	CH_3	H	1.02
CH_3	H	CH_3	D	0.96

[a] For elimination of H(D) from the β-carbon. [b] For replacement of the indicated D by H.

are large, implying that the proton transfer to methoxide ion has proceeded roughly halfway, while the SDKIEs for the α-deuterio derivatives are close to unity, implying that little change in bonding has occurred at the α-carbon. This supports our conclusion that these reactions involve E2/E1cB mechanisms.

The results from corresponding calculations for E2 reactions of ammonia with various 'onium ions are shown in Table VI. Here the PDKIEs are smaller and the SDKIEs at the α-carbon are larger than for the reactions of the halides (Table V). This supports our conclusion that these reactions tend more toward the E1 limit than the eliminations from halides.

The only related gas-phase study seems to be one by Bierbaum et al.[18] who examined the E2 reactions of diethyl ether (Et_2O) with H_2N^- or HO^-. The PDKIEs found were 5.5 and 2.1, respectively.

Experimental PDKIEs in solution have been reported only for derivatives of **1a** or **11** carrying substituents that would be expected to modify the results. The reported PDKIEs mostly lie in the range 4-8.[19,20] The only related studies[21] of SDKIEs in solution referred

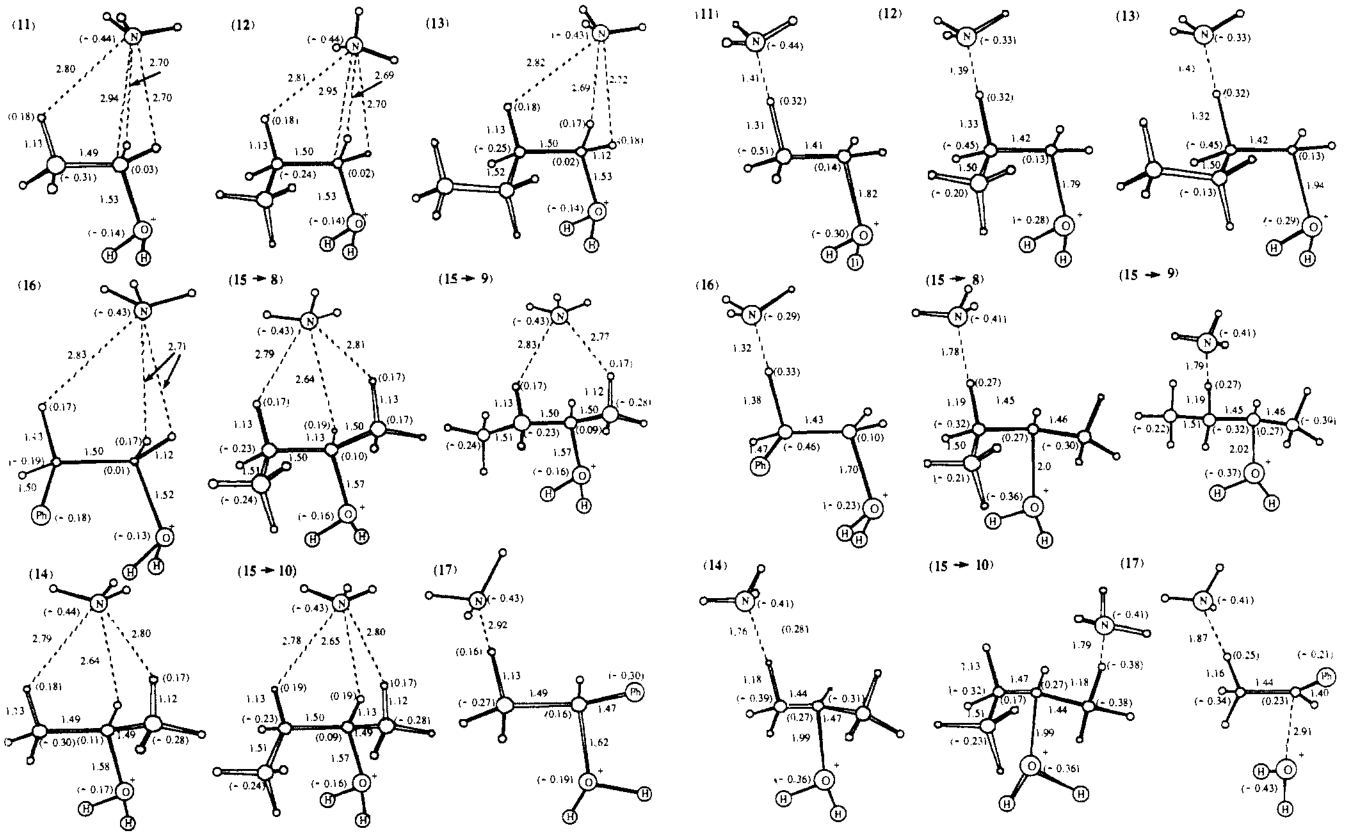

Figure 5. Bond lengths (Å) and charge distributions (e) in the initial CD complexes and transition states for E2 reactions of ammonia with (**11**) ethyl 'onium ion, (**12**) 1-propyl 'onium ion, (**13**) 1-butyl 'onium ion, (**14**) 2-propyl 'onium ion; (**15**) 2-butyl 'onium ion to form *cis*-butene (**8**), *trans*-butene (**9**), or 1-butene (**10**), (**16**) 1-phenyl 'onium ion, and (**17**) 2-phenyl 'onium ion.

Table VI. Primary and Secondary Deuterium Kinetic Isotope Effects (KIE) in the E2 Reactions of Ammonia with $R_1C_1R'_1HC_2R_2R'_2OH_2^+$ at 45 °C

R_1	R'_1	R_2	R'_2	KIE (k_h/k_d)
		Primary KIE[a]		
H	H	H	H	3.65
CH_3	H	H	H	3.88
H	H	CH_3	H	1.64
CH_3	H	CH_3	H	1.63
		Secondary KIE[b]		
D	D	H	H	1.06
H	H	D	D	1.10
CH_3	D	H	H	1.04
CH_3	H	D	D	1.09
D	D	CH_3	H	1.06
H	H	CH_3	D	1.10
CH_3	D	CH_3	H	1.06
CH_3	H	CH_3	D	1.11

[a] For elimination of H(D) from the β-carbon. [b] For replacement of the indicated D by H.

to the E2 reactions of alkoxide ions with 2-phenylethyl halides. The SDKIEs varied, however, with the concentrations of the reactants, implying that the reactions in solution could not have involved simple one-step processes. Dewar and Storch[22] have suggested a possible explanation.

Stereochemistry of Elimination

Nearly all the elimination reactions discussed in part 1[1] and above had TSs in which the departing hydrogen, the leaving group, and the two intervening carbon atoms were coplanar, the hydrogen atom and the leaving group being trans (anti) to one another (antiperiplanar TS). With two exceptions, the corresponding syn structures did not correspond to saddle points on the corresponding potential energy surfaces and the energy of the syn TS was much more positive than that of the corresponding anti one.

Extensive experimental studies have been reported[23] for the stereochemistry of E2 reactions in solution. The results indicate that their course can be profoundly affected by the conditions under which the reactions are carried out, due, e.g., to ion-pairing effects. The results for elimination from open-chain systems are also confused by the possibility of rotation about the CC bond, leading to changes in the dihedral angle between the hydrogen and the leaving group. We therefore confined our attention to elimination from rigid systems with well-defined geometries, e.g., cyclohexane derivatives where the geometry of the ring is locked by a bulky equatorial substituent (**20**) or fusion with another ring; e.g., bicyclo[3.1.1]heptane **21** or norbornane **22**. Axial-axial (ax-ax; **23**) elimination in bromocyclohexane corresponds to a trans orientation of the hydrogen and leaving group while axial-equatorial (ax-eq; **26**) and equatorial-equatorial (eq-eq; **27**) eliminations correspond to gauche eliminations. Genuine syn elimination has been studied by using ring systems where two adjacent carbon atoms are eclipsed; see, e.g., **31**. This also permits study of a fourth possibility where the dihedral angle between the hydrogen atom and the leaving group is 120°; see **30**.

Our approach followed a similar course, involving studies of elimination from (a)- (**23**) and (e)- (**26, 27**) bromocyclohexanone, 1(a)-bromo-2(e)-methylcyclohexane (**24, 25**), 3(a)-bromobicyclo[3.1.1]heptane (**28, 29**), and 2-bromobicyclo[2.2.1]heptane (**30, 31**). Figure 6 shows the calculated bond lengths and distributions of formal charge in the various species studied here, while Figures 7 and 8 provide similar information for the initial CD complexes and TSs, respectively. Table VII shows the activation energies calculated for reactions starting from the CD complexes for the various modes of elimination from each bromide, while Table VIII shows the heats of formation calculated for the relevant stationary points on each minimum energy reaction path (MERP). The structures of the TSs (Figure 8) indicate that these reactions are again of E2/E1cB type, where breaking the C-Br bond occurs to a very limited extent in each TS.

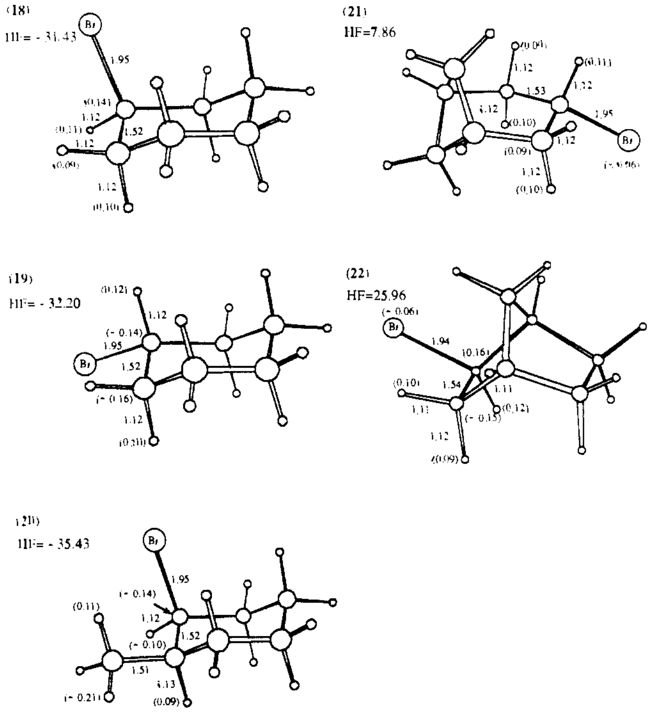

Figure 6. Bond lengths (Å), charge distributions (e) and heats of formation (HF, kcal/mol) in (**18**) (a)-bromocyclohexane, (**19**) (e)-bromocyclohexane, (**20**) 1(a)-bromo-2(e)-methylcyclohexane, (**21**) 3-bromobicyclo[3.1.1]heptane, and (**22**) 2-bromobicyclo[2.2.1]heptane.

Table VII. Activation Energies (kcal/mol) and Stereochemistries of E2 Reactions of Methoxide Ion with Cyclic Bromoalkanes

rxn	reactant	H elim	ΔH^*	stereochem
(**23**)	(a)-bromocyclohexane	C2	6.3	anti (ax-ax)
(**26**)	(e)-bromocyclohexane	C2	9.9	gauche-cis (ax-eq)
(**27**)	(e)-bromocyclohexane	C2	12.3	gauche-trans (eq-eq)
(**24**)	1(a)-bromo-2(e)-methylcyclohexane	C2	4.8	anti (ax-ax)
(**25**)	1(a)-bromo-2(e)-methylcyclohexane	C6	6.7	anti (ax-ax)
(**28**)	3-bromobicyclo[3.1.1]heptane	C2	7.6	anti (ax-ax)
(**29**)	3-bromobicyclo[3.1.1]heptane	C2	14.2	gauche-syn
(**30**)	2-bromobicyclo[2.2.1]heptane	C3	12.6	anti
(**31**)	2-bromobicyclo[2.2.1]heptane	C3	9.5	syn

Table VIII. Heats of Formation (kcal/mol) for the MERP Stationary Points of Elimination Reactions of CH_3O^- with Substituted Cyclic and Bicyclic Bromoalkanes

	heat of formation, kcal/mol				
rxn	reactant	STCD	TS	PTCD	product
(**23**)	-69.9	-82.7	-76.4	-98.9	-87.5
(**26**)	-73.9	-80.8	-70.9	-103.5	-95.3
(**27**)	-73.9	-82.8	-70.5	-105.2	-92.3
(**24**)	-70.8	-87.1	-82.3	-106.6	-87.5
(**25**)	-70.8	-87.2	-80.5	-104.1	-87.5
(**28**)	-30.6	-43.0	-35.4	-59.0	-46.5
(**29**)	-30.3	-43.2	-29.0	-64.7	-46.5
(**30**)	-46.7	-58.9	-46.3	-56.5	-51.5
(**31**)	-46.7	-54.8	-45.3	-67.8	-51.5

In the case of the axial cyclohexyl bromides, **18** and **20**, the activation energy calculated for anti elimination (ax-ax) is in each

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(21) (a) Waszczylo, Z.; Westaway, K. C. *Tetrahedron Lett.* **1985**, *26*, 25. (b) Smith, P. J.; Rangappa, K. S.; Westaway, K. C. *Can. J. Chem.* **1984**, *62*, 100.

(22) Dewar, M. J. S.; Storch, D. M. *J. Chem. Soc., Perkin Trans. 2* **1989**, 877.

(23) (a) Saunders, W. H., Jr.; Cockerill, A. F. *Mechanism of Elimination Reactions*; Wiley-Interscience: New York, 1973; Chapter III. (b) Bartsch, R. A.; Zavada, J. *Chem. Rev.* **1980**, *80*, 453.

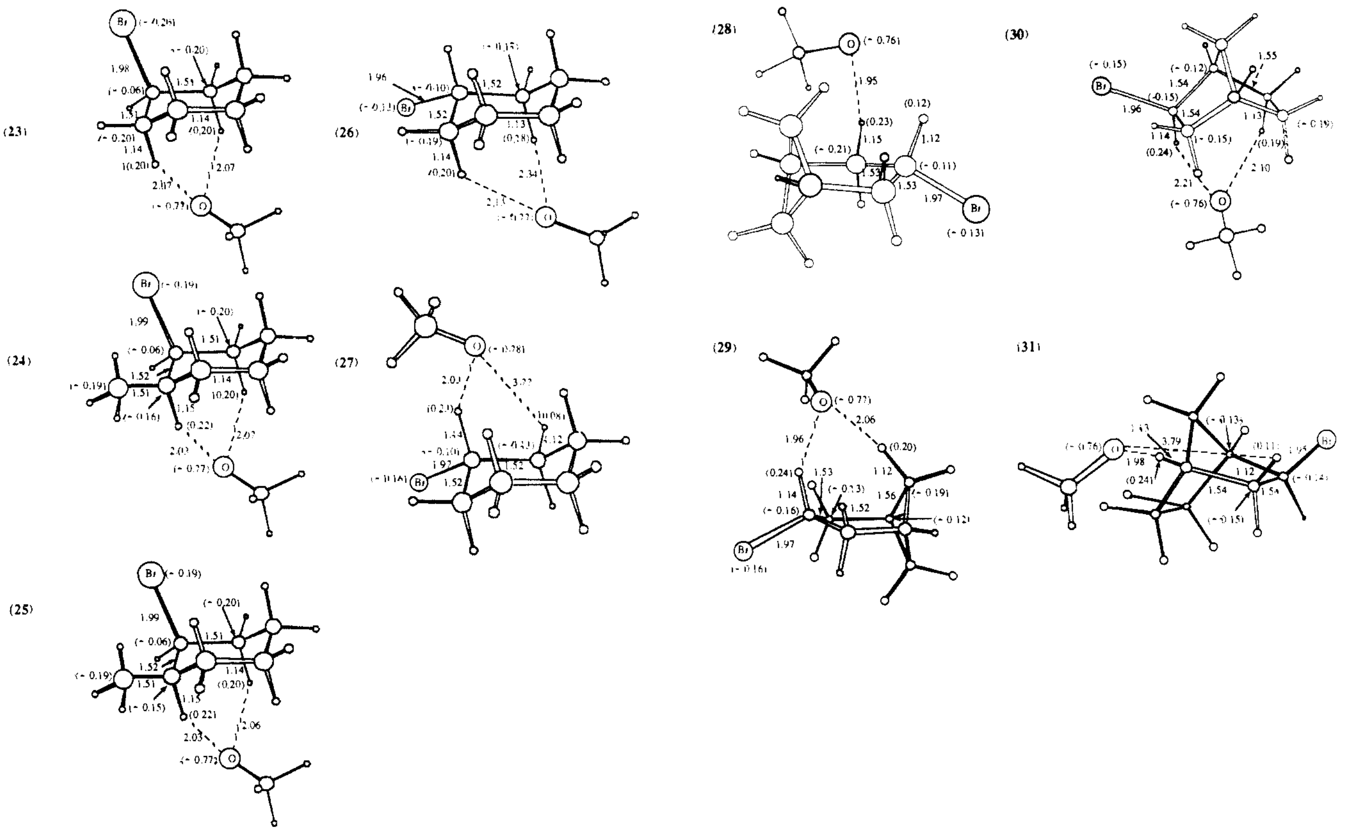

Figure 7. Bond lengths (Å) and charge distributions (e) in the initial CD complexes for E2 reactions of methoxide ion with (**23**) (a)-bromocyclohexane, (**24**) 1(a)-bromo-2(e)-methylcyclohexane to form 1-bromo-2-methyl-1-cyclohexene, (**25**) 1(a)-bromo-2(e)-methylcyclohexane to form 1-bromo-2-methyl-6-cyclohexene, (**26**) (e)-bromocyclohexane by ax-hydrogen abstracting to form bromohexene, (**27**) (e)-bromocyclohexane by eq-hydrogen abstracting to form bromohexene, (**28**) 3(a)-bromobicyclo[3.1.1]heptane by abstracting ax-hydrogen to form 2-bicyclo[3.1.1]heptene, (**29**) 3(a)-bromobicyclo[3.1.1]heptane by abstracting eq-hydrogen to form 2-bicyclo[3.1.1]heptene, (**30**) 2(e)-bromobicyclo[2.2.1]heptane by abstracting ax-hydrogen to form 2-bicyclo[2.2.1]heptene, and (**31**) 2(e)-bromobicyclo[2.2.1]heptane by abstracting eq-hydrogen to form 2-bicyclo[2.2.1]heptene.

case less than that for gauche elimination (ax–eq) by ca. 6 kcal/mol; see Table VII. In practice ax–ax elimination is strongly favored. This indeed has proved to be the case generally for E2 reactions involving elimination from cyclohexane rings.[23] Exceptions arise only when special factors (e.g., steric effects) hinder anti elimination.

The equatorial cyclohexyl bromide (**19**) can undergo gauche elimination in two different ways, **26** and **27**, depending on whether the relevant hydrogen atom is cis (eq–ax) or trans (eq–eq) to the bromine. The results in Table VII imply that eq–ax elimination should occur more readily, the corresponding activation energy being halfway between those for ax–ax and eq–eq elimination. Eq–ax elimination would be expected to be easier because the eq–ax isomer can relax directly to the TS for a syn elimination. The eq–eq isomer, on the other hand, cannot relax likewise to the TS for anti elimination because this would lead to a trans cyclohexene. The methylene groups have to rotate the other way, passing through a configuration where they are orthogonal, to reach the necessary syn TS.

A similar situation exists in the case of norbornane **22**, where the choice is between syn elimination and elimination via a TS where the dihedral angle between the relevant groups is 120°. The latter reaction is analogous to that in eq–eq elimination from **27**. As expected on this basis, syn elimination is predicted to have the lower activation energy, in agreement with experiment.[24]

In the case of **20**, ax–ax elimination can take place in two different ways, one leading to 1-methylcyclohexene (**32**) and the other to 3-methylcyclohexene (**33**). As in the case of the open-chain systems, the more substituted olefin (**32**) is predicted to be favored. E2 elimination does in fact follow Saytzeff's rule.[25]

Table IX. Heats of Formation for the Stationary Points on the MERPs for S_N2 Reactions of Methoxide Ion with Alkyl Chlorides

rxn	alkyl (chloride)	heat of formation, kcal/mol: reactant	STCD	TS	PTCD	product
(**34**)	ethyl	-64.7	-74.8	-63.8	-106.7	-96.4
(**35**)	1-propyl	-71.1	-81.4	-70.4	-113.4	-103.7
(**36**)	1-butyl	-76.5	-89.4	-76.1	-121.7	-109.9
(**37**)	2-propyl	-69.8	-82.0	-64.9	-109.1	-100.5
(**38**)	2-butyl	-75.3	-87.5	-69.8	-114.6	-106.7

Elimination vs Substitution

In E2 reactions, a base (B) induces ionization of the leaving group (X) by deprotonating a β-carbon atom. Alternatively, the base can act as a nucleophile, displacing X directly in an S_N reaction:

$$\text{E2:}\quad B^- + H{-}C{-}C{-}X \rightarrow BH + C{=}C + X^- \qquad (3)$$

$$S_N2\text{:}\quad B^- + H{-}C{-}C{-}X \rightarrow H{-}C{-}C{-}B + X^- \qquad (4)$$

We have examined the competition between elimination and substitution by comparing the reactions of an anionic base (nucleophile) with an alkyl halide, and of a neutral base (nucleophile) with an 'onium ion. As before, the bases chosen were methoxide ion and ammonia, the leaving groups being, respectively, Cl and H_2O^+.

Calculations were carried out for the S_N2 reactions of methoxide ion with ethyl, 1-propyl, 1-butyl, 2-propyl, and 2-butyl chlorides (reactions 34–38) and for the S_N2 reactions of ammonia with the corresponding alkyloxonium ions (reactions 39–43). Bond lengths, charge distributions, and heats of formation have already been reported for the reactants in Figures 1 and 4 and for the intermediate CD complexes and E2 TSs, in Figures 2–4. Figures 9 and 10 provide similar information for the corresponding S_N2 TSs. Tables IX and X list heats of formation for the various stationary

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(24) (a) Cristol, S. J.; Hause, N. L. *J. Am. Chem. Soc.* **1952**, *74*, 2193. (b) Kwart, H.; Liu, K. T.; Nyce, J. L. *J. Am. Chem. Soc.* **1964**, *86*, 4144.

(25) Sicher, J.; Svoboda, M.; et al. *Collect. Czech. Chem. Commun.* **1971**, *36*, 3633.

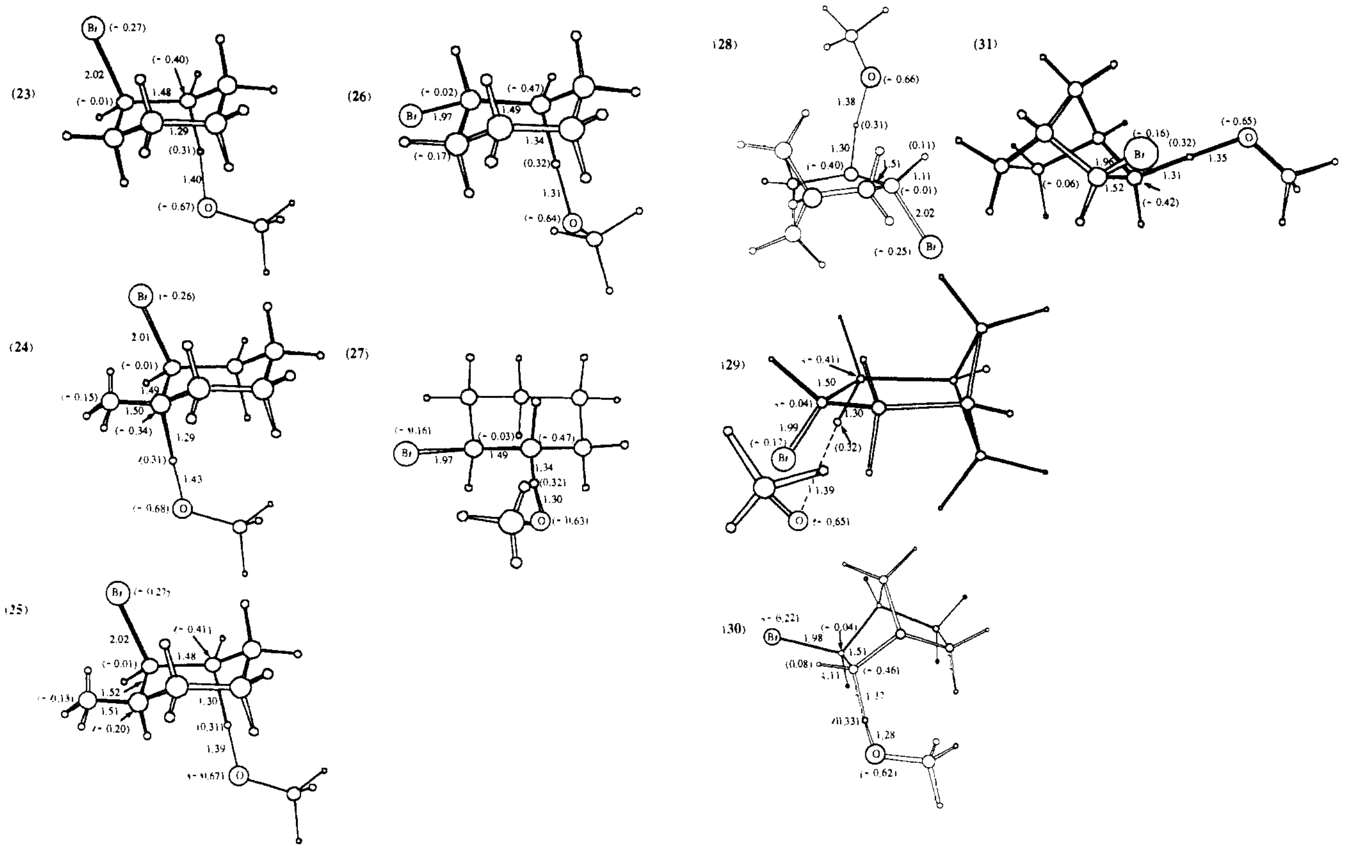

Figure 8. Bond lengths (Å) and charge distributions (e) in the transition states for E2 reactions of methoxide ion with (**23**) (a)-bromocyclohexane, (**24**) 1(a)-bromo-2(e)-methylcyclohexane to form 1-bromo-2-methyl-1-cyclohexene, (**25**) 1(a)-bromo-2(e)-methylcyclohexane to form 1-bromo-2-methyl-6-cyclohexene, (**26**) (e)-bromocyclohexane by ax-hydrogen abstracting to form bromohexene, (**27**) (e)-bromocyclohexane by eq-hydrogen abstracting to form bromohexene, (**28**) 3(a)-bromobicyclo[3.1.1]heptane by abstracting ax-hydrogen to form 2-bicyclo[3.1.1]heptene, (**29**) 3(a)-bromobicyclo[3.1.1]heptane by abstracting eq-hydrogen to form 2-bicyclo[3.1.1]heptene, (**30**) 2(e)-bromobicyclo[2.2.1]heptane by abstracting ax-hydrogen to form 2-bicyclo[2.2.1]heptene, and (**31**) 2(e)-bromobicyclo[2.2.1]heptane by abstracting eq-hydrogen to form 2-bicyclo[2.2.1]heptene.

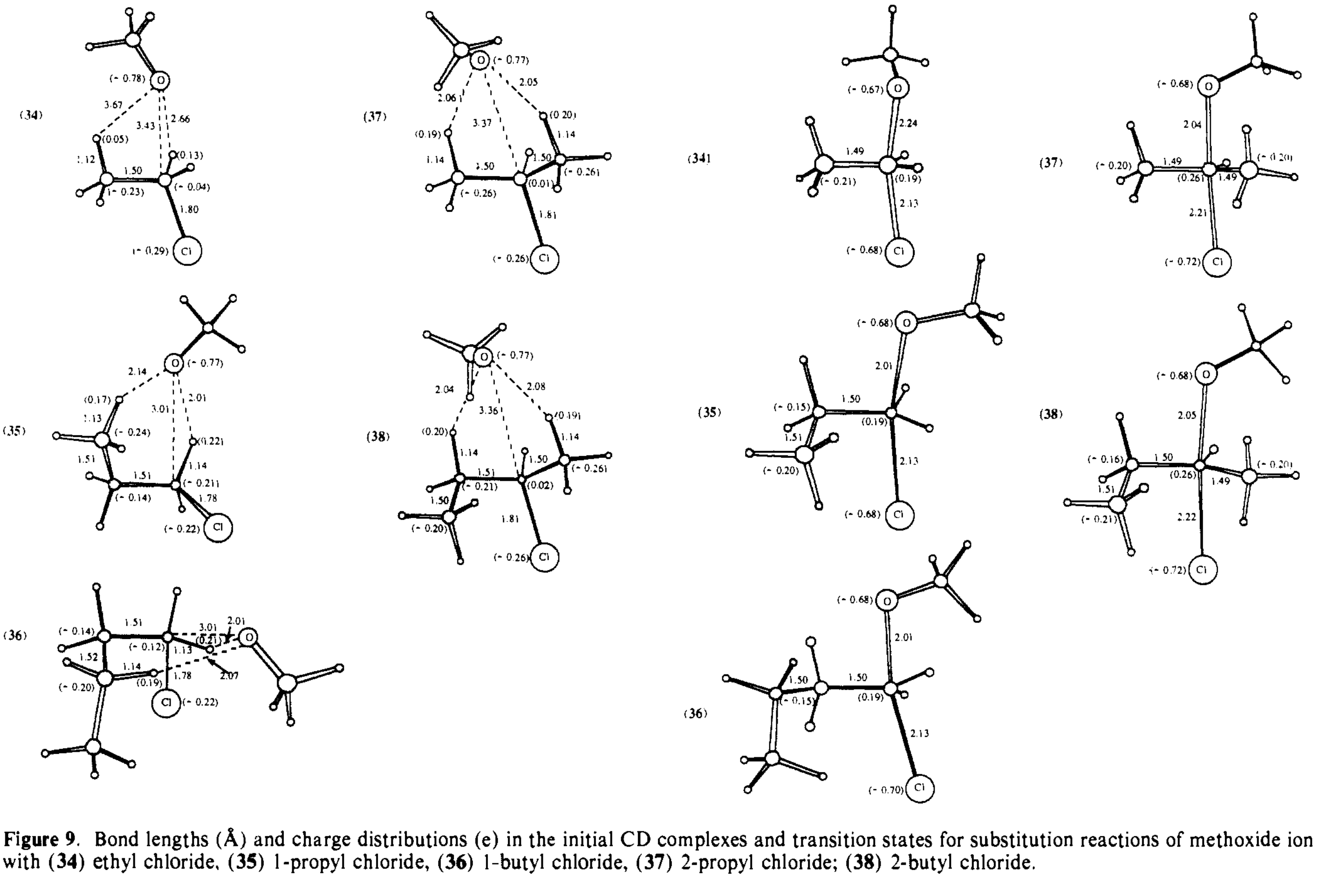

Figure 9. Bond lengths (Å) and charge distributions (e) in the initial CD complexes and transition states for substitution reactions of methoxide ion with (**34**) ethyl chloride, (**35**) 1-propyl chloride, (**36**) 1-butyl chloride, (**37**) 2-propyl chloride; (**38**) 2-butyl chloride.

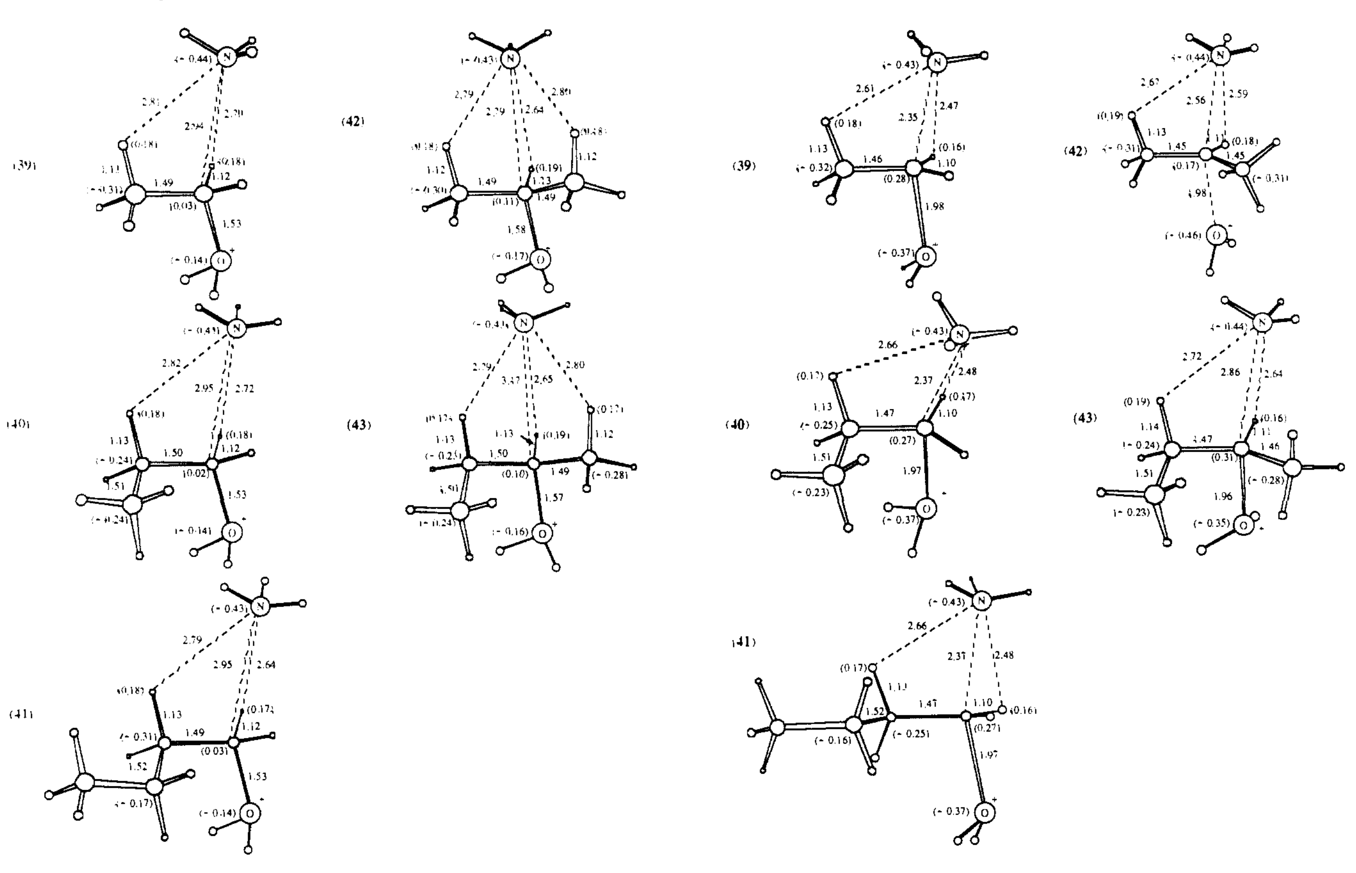

Figure 10. Bond lengths (Å) and atomic charges (e) in the initial CD complexes and transition states for substitution reactions of ammonia with (**39**) ethyl 'onium ion, (**40**) 1-propyl 'onium ion, (**41**) 1-butyl 'onium ion, (**42**) 2-propyl 'onium ion, and (**43**) 2-butyl 'onium ion.

Table X. Heats of Formation for the Stationary Points on the MERPs for S_N2 Reactions of Ammonia with Alkyloxonium Ions

rxn	alkyl ('onium ion)	heat of formation, kcal/mol				
		reactant	STCD	TS	PTCD	product
(**39**)	ethyl	117.6	109.3	117.0	65.5	79.5
(**40**)	1-propyl	109.6	101.5	109.6	58.2	72.1
(**41**)	1-butyl	102.3	94.3	102.2	50.7	64.5
(**42**)	2-propyl	107.7	100.2	104.6	58.2	71.8
(**43**)	2-butyl	100.7	93.4	97.3	51.8	64.5

points. An interesting point is that each chloride formed two distinct CD complexes with methoxide ion, both corresponding to genuine minima on the relevant potential energy surface. Since their energies differed by only a few tenths of a kilocalorie per mole, the differences have been ignored. Similar results were obtained by ab initio calculations of the CD complexes formed by halide ions with ethyl halides.[26]

Table XI compares the enthalpies of activation, starting from the initial CD complexes, for each pair of alternative E2 and S_N2 reactions.

It will be seen that elimination is predicted to be the more facile process in the reactions of each of the alkyl chlorides with methoxide ion. This is contrary to the results from studies of such reactions in solution, substitution being usually preferred. Indeed, in the reaction of ethyl bromide with alcoholic potash, no detectable amount of ethylene is formed.[27] However, recent studies[28] of the reactions of anions with ethyl halides in the gas phase have shown that elimination is indeed the preferred process under these conditions. The predominance of substitution in solution must therefore be attributed to solvent effects.

Table XI. Comparisons of Activation Energies for Substitution and Elimination Reactions of Alkyl Derivatives

alkyl	activation energies, kcal/mol			
	ammonia + 'onium ion		methoxide ion + alkyl chloride	
	S_N2	E2	S_N2	E2
ethyl	7.9	8.7	11.0	6.2
1-propyl	8.1	9.1	11.0	4.9
2-propyl	4.4	4.9	17.1	8.5
1-butyl	7.9	9.2	13.3	6.8
2-butyl	3.9	5.3	17.7	6.8

In the case of the reactions of ammonia with oxonium ions, on the other hand, substitution is predicted to be the more facile process. As noted in part 1,[1] there is a dearth of relevant experimental data for reactions of this kind. The experimental work so far reported has usually referred to reactions of 'onium ions with anionic bases in solution or to the decomposition of solid or molten 'onium salts. Under these conditions elimination is usually preferred. However, it has very recently been reported[29] that ammonia reacts with ethyldimethyloxonium ion ($CH_3CH_2OMe_2^+$) in the gas phase mainly by substitution, the ratio of substitution to elimination being 7:3.

Acknowledgment. This work was supported by the Air Force Office of Scientific Research (Grant AF 89-0179), the Robert A. Welch Foundation (Grant F-126), and the National Science Foundation (CHE 87-12022).

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(26) Minato, T.; Yamabe, S. *J. Am. Chem. Soc.* **1988**, *110*, 4586–4593.

(27) Dhar, M. L.; Hughes, E. D.; Ingold, C. K.; Masterman, S. *J. Chem. Soc.* **1948**, 2055.

(28) (a) Jones, M. E.; Ellison, G. B. *J. Am. Chem. Soc.* **1989**, *111*, 1645. (b) Ridge, D. P.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1974**, *96*, 637, 3595. (c) Sullivan, S. A.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 1160. (d) Depuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1981**, *103*, 5034. (e) King, G. K.; Maricq, G. K.; Bierbaum, V. M.; Depuy, C. H. *J. Am. Chem. Soc.* **1981**, *103*, 7133.

(29) Occhiucci, G.; Speranza, M.; de Koning, L. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1989**, *111*, 7387.