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On the Mechanism of Base-Induced Gas-Phase Elimination Reactions of Ethers

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Abstract: For the base-induced gas-phase elimination reactions of diethyl ether and *cis-* and *trans-*1-*tert*-butyl-4-methoxycyclohexane the kinetic isotope and leaving group effects have been determined as functions of the base strength using the method of Fourier transform ion cyclotron resonance mass spectrometry. The results are interpreted in terms of a variable E2 transition-state structure. Increasing the base strength causes the transition state to shift toward the carbanion or E1cb region of the E2 spectrum, which is also a general phenomenon in the condensed phase. Moreover, it appears that the elimination reactions most readily proceed via a transition state in which the β hydrogen and leaving group are periplanar. If the substrate does not easily allow such a relationship, the transition state is found to shift toward the carbenium ion or E1 region of the E2 spectrum where the geometric restrictions of the substrate are less perceptible. The concept of syn/anti dichotomy is used to explain the formation of free and solvated alkoxide anions in the reactions induced by OH^-. Anti elimination is believed to result in the formation of free alkoxide. Syn elimination, which takes advantage of the electrostatic interaction between the base and leaving group, is held responsible for the formation of solvated alkoxide. The importance of base/leaving group association in the transition state of the syn elimination is demonstrated by the low yield of solvated alkoxide in the reaction of OH^-, solvated by a dimethylamine molecule, with diethyl ether. Finally, it seems that the selectivity of gas-phase elimination reactions is determined by not only the relative heights of the intrinsic reaction barriers, but also the relative stabilities of the ion/molecule complexes preceding the reaction barriers.

From the time Ingold[1,2] introduced the concept of base-promoted olefin-forming elimination reactions, many research groups have been involved in the investigation of this class of reactions.

$$H_3C^{\beta}\text{-}C^{\alpha}H_2X + B^- \rightarrow HB + C_2H_4 + X^- \qquad (1)$$

This has led to a profound documentation of the effects of variation of the attacking bases, the leaving groups and the substituents on the rates, product distribution, and stereochemistry.[3]

Concerted mechanisms do not necessarily involve synchronous cleavage of the C_β–H and C_α–X bonds as was first recognized by Cram et al.[4] and later by Bunnett,[5] who introduced the concept of the variable E2H transition state. In this model the structure of the transition state can vary from paenecarbenium (E1-like) via paeneolefinic (central) to paenecarbanion (E1cb-like). To explain the efficient promotion of elimination reactions by some strong C nucleophiles with low basicity, Winstein and Parker favored their E2H–E2C spectrum having regions where B- -C_α loose covalent interaction is important.[6] Indeed, theoretical justification of this E2H–E2C model has been derived from valence-bond calculations.[7] McLennan[8] has suggested adding a transition-state structure to the E2H and E2H–E2C spectra to account for some experimental observations, which could not be explained by the above-mentioned models. This structure appears to couple the E2H and E2H–E2C spectra.

Experimental justification of the proposed spectra has been derived from a large number of mechanistic studies in which Hammett correlations,[9,10] stereoelectronic control,[11] and element effects[12] have been interpreted in terms of variable E2 transition-state structures. On the other hand, however, it seems as if the mechanism of elimination reactions in some cases still is a subject of controversy. The confusion mainly derives from the dichotomy of stereochemistry and of base species, as it is not always clear what the influence is of solvent molecule and/or counterion association on the mechanism of polar elimination reactions.[3,13] In order to tackle this problem, some research groups have studied polar elimination reactions in the gas phase where participation of solvent molecules and counterions is avoided. These studies, therefore, reflect the intrinsic properties of isolated reaction systems.

The energy profiles of gas-phase reactions, however, differ from those in the condensed phase in this respect in that encounter of reactants, due to electrostatic interactions, results in the formation of an excited complex, which via one or more intrinsic reaction barriers is converted into a second excited complex, which dissociates into products. This model, first suggested by Olmstead and Brauman for S_N2 reactions,[14] has been well-reproduced by ab initio calculations[15,16] and is now accepted by most gas-phase chemists.

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Table I. Overall Kinetic Isotope Effect Associated with the Reaction between B^- and Diethyl Ether

B^-	$PA(B^-)$[a] (kcal/mol)	k_1/k_2	$(CD_3CH_2OC_2H_5)$[b] k_{1H}/k_{1D}	$(CD_3CH_2OC_2H_5)$[b] k_{2H}/k_{2D}	$(CD_3CD_2OC_2H_5)$[c] k_{1H}/k_{1D}	$(CD_3CD_2OC_2H_5)$[c] k_{2H}/k_{2D}	$(C_4H_{10}O/C_4D_{10}O)$[c] k_{1H}/k_{1D}	$(C_4H_{10}O/C_4D_{10}O)$[c] k_{2H}/k_{2D}
NH_2^-	404	∞	5.60 ± 0.04		5.62 ± 0.03		5.62 ± 0.03	
CH_3NH^-	403	∞	4.03 ± 0.06		3.93 ± 0.08			
$C_2H_5NH^-$	399	∞	3.50 ± 0.05		3.41 ± 0.07			
OH^-	391	0.45	2.20 ± 0.03	1.55 ± 0.03	2.09 ± 0.03	1.40 ± 0.04	2.31 ± 0.03	1.71 ± 0.05

[a] Proton affinity data taken from ref 59. [b] Given error is the standard deviation over four experiments. [c] Given error is the standard deviation over five experiments.

From the published gas-phase results[17-20] it follows that the base-induced elimination reactions are feasible and as a rule strongly dominate over S_N2 reactions, contrary to what is common in the condensed phase. Minato and Yamabe[16] have shown by ab initio calculations that for the gas-phase reaction of F^- with FCH_2CH_3 the activation entropy, $\Delta S°$, of the net E2 reaction is larger than that of the net S_N2 reaction. The entropy change is more favorable for the E2 reaction, which means that an increase in temperature increases the E2 proportion. Furthermore, Minato and Yamabe showed that the approach of the β hydrogen, leading to E2 elimination, results in an ion/molecule complex which is more stable than the ion/molecule complex resulting from the approach of the α carbon, leading to S_N2 substitution.

They concluded that in the condensed phase interaction of the solvent molecules with the β hydrogen would block the formation of the complex leading to E2 elimination and therefore would promote S_N2 substitution. This idea fits with the experimental tendency that in solution the proportion of elimination strongly depends on the polarity of the solvent and the strength of the attacking base.

The present study, for which the Fourier transform ion cyclotron resonance (FT-ICR)[21] method is employed, is concerned with the mechanism of the base-induced gas-phase elimination reaction of simple ethers. The approach in this work is to estimate the extent and type of bond changes in proceeding from reactants to the activated complex by relating measured kinetic isotope and leaving group effects with the kinetic isotope effect model calculations of base-induced elimination reaction systems, performed by Saunders.[22-24]

Experimental Section

Experiments were performed with our home-made Fourier transform ion cyclotron resonance spectrometer.[25] The total pressure was normally kept below 10^{-4} Pa with a background better than 3×10^{-6} Pa. Partial sample pressures were measured with an ionization gauge placed in a side arm of the main pumping line. When absolute pressures were required, the sample-dependent response of the ionization gauge was calibrated against a MKS Baratron (Type 170 M, head Type 94 AH-1).

Negative ions were generated by electron impact using an electron beam pulse of typically 25-ms duration and an emission current of 700 nA. The ions were trapped in the magnetic field of 1.4 T by applying a small negative voltage (−1.1 V) to the trapping plates of the cubic inch cell.[26]

Secondary electrons and primary formed H^- ions were ejected from the cell by applying radio-frequency (rf) pulses with a variable width and frequencies of about 8 MHz and 160 kHz, respectively, to the trapping plates. The cyclotron motion of the ions was excited by a fast frequency swept rf pulse with a typical sweeping rate of 1 MHz/ms and an amplitude of 10 Vp-p, covering the frequency range of 1600–40 kHz and corresponding to a mass range of m/z 15–500. The image current, induced by the translationally and coherently excited ions, in the receiver plates was monitored, digitized, and stored in a fast buffer. After every experiment a quench pulse followed to remove all ions from the cell before a new chemistry cycle was started. In order to improve the signal-to-noise ratio a number of transient signals was recorded, whereafter the accumulated signal was subjected to Fourier transformation.

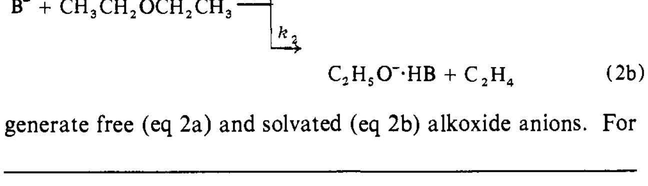
Both OH^- and NH_2^- were formed by dissociative resonant capture of electrons with a kinetic energy of 5 eV by H_2O (OH^- is formed via H^-) and 4.5 eV by NH_3. $^{18}OH^-$ was formed in the absence of water by dissociative capture of 1.1-eV electrons by $N_2{}^{18}O$, generating $^{18}O^{\bullet -}$, followed by hydrogen abstraction from the substrate by $^{18}O^{\bullet -}$. CH_3NH^- and $C_2H_5NH^-$ were formed via proton abstraction from CH_3NH_2 and $C_2H_5NH_2$ by NH_2^-. After generation of the base, all ions except for the base itself were ejected from the cell using the notch ejection technique.[27,28] During the reactions of the amine bases, OH^-, possibly formed by proton abstraction from background water, was continuously ejected. Peak intensities were corrected for "picket fence" errors by weighting the digitized signal[29] and for uneven ion excitation by a deconvolution procedure.[30] Errors in the relative peak intensity measurements are estimated to be smaller than 5%.[31]

The gas-phase acidity difference between CH_3OH and CD_3OH, between C_2H_5OH and CD_3CH_2OH, and between C_2H_5OH and C_2D_5OH were determined from the equilibrium isotopic product distribution of the $OH^-/CH_3OH/CD_3OH$, the $OH^-/C_2H_5OH/CD_3CH_2OH$, and the $OH^-/C_2H_5OH/C_2D_5OH$ reaction systems. The standard deviation over four independent experiments was in all three cases ±0.03 kcal/mol.

Materials. Most of the chemicals used were commercially available. The labeled diethyl ethers were prepared by a Williamson synthesis using NaH as a base and commercially available deuterium-labeled ethyl bromides and ethanols. $N_2{}^{18}O$ (71.5% ^{18}O) was a gift from Professor F. S. Klein of the Weizmann Institute, Israel. The 1-*tert*-butyl-4-methoxycyclohexanes were prepared by a Williamson synthesis using a cis/trans mixture of 4-*tert*-butylcyclohexanol and $ICH_3(CD_3)$. The cis and trans ethers were separated and purified by preparative GC before use (1-*tert*-butyl-4-methoxycyclohexanes: column OV 275, temperature 100 °C; diethyl ethers: column OV 17, temperature 30–40 °C). For all labeled compounds the label content was better than 99% d_3 or 98% d_5.

Results and Discussion

Diethyl Ether. Elimination Reactions. Flowing afterglow (FA)[19] and ion cyclotron resonance (ICR)[18] studies have shown that reaction of a base with simple ethers proceeds by elimination as represented in eq 2. Under FA conditions both NH_2^- and OH^-



$$B^- + CH_3CH_2OCH_2CH_3 \xrightarrow{k_1} C_2H_5O^- + HB + C_2H_4 \quad (2a)$$

$$B^- + CH_3CH_2OCH_2CH_3 \xrightarrow{k_2} C_2H_5O^-{\cdot}HB + C_2H_4 \quad (2b)$$

generate free (eq 2a) and solvated (eq 2b) alkoxide anions. For

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Table II. Kinetic Isotope and Leaving Group Effects Associated with the Reaction between B^- and Diethyl Ether, Calculated from the Data in Table I[a]

B^-	$k_{1H}/k_{1D}(H_\beta)$	$k_{2H}/k_{2D}(H_\beta)$	$k_{1H}/k_{1D}(H_\alpha)^a$	$k_{2H}/k_{2D}(H_\alpha)^a$	$k_l(OC_2H_5)/$ $k_1(OC_2D_5)^a$	$k_2(OC_2H_5)/$ $k_2(OC_2D_5)^a$
NH_2^-	5.60 ± 0.03		1.01 ± 0.01		1.00 ± 0.01	
OH^-	2.20 ± 0.03	1.55 ± 0.03	1.00 ± 0.02	1.00 ± 0.02	1.05 ± 0.02	1.10 ± 0.03

[a] Errors calculated from the standard deviation data in Table I.

the reaction of OH^- with completely deuterated diethyl ether, DePuy and Bierbaum[19] demonstrated that the solvated alkoxide was produced directly in the elimination and not by association of initially formed ethoxide with adventitious water. From the present study it appears that under FT–ICR conditions at pressures lower by a factor of 10^6, only OH^- produces free as well as solvated alkoxide anions in a ratio identical with that for the same reaction under FA conditions (see Table I).

In order to demonstrate that, here, both free and solvated alkoxide are produced in an elimination reaction and not in a S_N2 process, $^{18}OH^-$ was generated in the absence of water (see Experimental Section) and allowed to react with diethyl ether (eq 3). Exclusively two ions appeared at *m/z* 45 and 65. Low-energy

$$^{18}OH^- + C_2H_5OC_2H_5 \xrightarrow{E_2} [H_2{}^{18}O{\cdot}C_2H_4{\cdot}C_2H_5O^-]^* \rightarrow \underset{m/z\ 45}{H_2{}^{18}O + C_2H_5O^-} + C_2H_4 \qquad (3a)$$

$$^{18}OH^- + C_2H_5OC_2H_5 \xrightarrow{E_2} [H_2{}^{18}O{\cdot}C_2H_5O^-{\cdot}C_2H_4]^* \rightarrow \underset{m/z\ 65}{H_2{}^{18}O{\cdot}C_2H_5O^-} + C_2H_4 \qquad (3b)$$

$$^{18}OH^- + C_2H_5OCH_2H_5 \overset{S_N2}{\not\longrightarrow}$$

$$[C_2H_5{}^{18}O{-}{-}H{-}{-}OC_2H_5]^{-*} \begin{cases} \underset{m/z\ 47}{C_2H_5{}^{18}O^-} + C_2H_5OH & (3c) \\ \underset{m/z\ 45}{C_2H_5O^-} + C_2H_5{}^{18}OH & (3d) \end{cases}$$

(~20 eV) collisional induced dissociation (CID)[32,33] of the ion at *m/z* 65 showed loss of $H_2{}^{18}O$, which is indicative for a water-solvated ethoxide structure. No ^{18}O-containing ethoxide was found, eliminating the possibility of a substitution mechanism (eq 3c and 3d). Based on these results it is believed that reaction of a base with diethyl ether in both a FA tube ($p \sim 70$ Pa)[19] and FT–ICR cell ($p < 10^{-4}$ Pa) exclusively proceeds by an E2 mechanism.

Isotope and Leaving Group Effects. For the reaction of a number of bases with isotopic isomers of diethyl ether the kinetic isotope effects have been measured. The results of these measurements are listed in Table I. Intramolecular isotope effects were determined from the ratio of the products in the reaction of a base with either $CD_3CH_2OCH_2CH_3$ or $CD_3CD_2OCH_2CH_3$, and intermolecular isotope effects were determined from the ratio of the products in the reaction of a base with an 1:1 mixture of $C_2H_5OC_2H_5$ and $C_2D_5OC_2D_5$. Contributions to the overall isotope effects from primary and secondary deuterium isotope and leaving group effects could be evaluated making use of eq 4a–c, where

$$k_H/k_D(CD_3CH_2OEt) = \frac{[k_H/k_D(\text{prim}H_\beta)][k_H/k_D(\text{sec}H_\beta)]}{k(OCH_2CH_3)/k(OCH_2CD_3)} \qquad (4a)$$

$$k_H/k_D(CD_3CD_2OEt) = \frac{[k_H/k_D(\text{prim}H_\beta)][k_H/k_D(\text{sec}H_\beta)][k_H/k_D(\text{sec}H_\alpha)]}{k(OCH_2CH_3)/k(OCD_2CD_3)} \qquad (4b)$$

$$k_H/k_D(C_4H_{10}O/C_4D_{10}O) = [k_H/k_D(\text{prim}H_\beta)] \times [k_H/k_D(\text{sec}H_\beta)][k_H/k_D(\text{sec}H_\alpha)][k(OCH_2CH_3)/k(OCD_2CD_3)] \qquad (4c)$$

$k_H/k_D(\text{prim}H_\beta)$ refers to the rates of βH vs. βD abstraction, $k_H/k_D(\text{sec}H_\beta)$ is the ratio of reaction rates upon substitution of the two remaining βH's by D, $k_H/k_D(\text{sec}H_\alpha)$ corresponds to the difference in reaction rates if both α H's are substituted by D, and $k(OCH_2CH_3)/k(OCH_2CD_3)$, etc., corresponds to the kinetic effect which arises from replacing H's by D's in the leaving ethoxy group. $k(OCH_2CH_3)/k(OCH_2CD_3)$ was neglected (taken to be unity) since no significant gas-phase acidity difference between CD_3CH_2OH and CH_3CH_2OH could be determined from equilibrium measurements (see also ref 34).

From the data presented in Table I the individual contributions of $k_H/k_D(\text{prim}H_\beta)$ and $k_H/k_D(\text{sec}H_\beta)$ cannot be established and therefore only the overall $k_H/k_D(H_\beta)$ together with $k_H/k_D(\text{sec}H_\alpha)$ and $k(OCH_2CH_3)/k(OCD_2CD_3)$ for the reactions with either NH_2^- and OH^- are listed in Table II. The results show that $k_H/k_D(H_\beta)$ is a smooth function of the base strength and spans a scale from 2.2 for OH^- up to 5.6 for the strongest base used, NH_2^-. A striking result is the very significant difference in $k_H/k_D(H_\beta)$ for the production of free and solvated alkoxide anions in the reaction with OH^-, indicating that possibly two elimination mechanisms are operative. For all bases used no significant $k_H/k_D(\text{sec}H_\alpha)$ was found (within experimental error) other than unity. On the other hand, for the reaction with OH^- a significant contribution to the different overall isotope effects could be assigned to a leaving group effect. This leaving group effect may arise from the difference in leaving abilities of $-OC_2H_5$ and $-OC_2D_5$, as indicated by the acidity difference $\delta\Delta H_{\text{acid}}$ of HOC_2H_5 and HOC_2D_5 of 0.28 kcal/mol which followed from equilibrium measurements.

Variation of Energy. As mentioned before, an encounter of reactants under the low-pressure conditions in the FT–ICR cell results in an excited and thermally isolated ion/molecule complex, the temperature of which cannot be measured. As a consequence, the Arrhenius behavior and the temperature dependences of the isotope effects of the elimination reactions cannot be determined. Alternatively, the effect of variation of the energy of the reactants on the reaction rate and isotope effects has been studied qualitatively. For that purpose, OH^- was produced from different precursor ions. Low-energy OH^- was produced by proton abstraction from water by H^-, generated by dissociative electron attachment to water. This reaction is about 9 kcal/mol exothermic.

High-energy OH^- was produced by hydrogen abstraction from diethyl ether by $O^{\bullet-}$, generated by dissociative electron attachment to N_2O. This reaction is about 20 kcal/mol exothermic, whereas the initially formed $O^{\bullet-}$ may already have an excess energy of about 9.5 kcal/mol.[35] OH^- produced in this way was found to abstract a proton from methylamine, a reaction which is 12 kcal/mol endothermic. The hydroxide ions, generated both from H_2O and N_2O/diethyl ether, were isolated from the reaction mixtures by means of a notch ejection pulse[27,28] and reacted with diethyl ether.

The reaction progress was monitored and analyzed following the next procedure. (1) The decay of OH^- as function of the time was recorded. (2) The ion abundance data were sectioned in time intervals of 100 ms. (3) For every section the data were fitted with a single exponential function, using the method of McLachlan,[36] to obtain the time constant τ per section. (4) For every section the pseudo-first-order reaction rate constant k_{OH^-} was

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Table III. Reaction Rate Constant and Combined Kinetic Primary and Secondary β-Deuterium Isotope Effects as a Function of the Trapping Time of OH^-, Generated from N_2O

$t_{trap\ OH^-}$ (ms)^a	k_{OH^-}^{b}	k_1/k_2	k_{1H}/k_{1D}- $(H_\beta)^{a,c}$	k_{2H}/k_{2D}- $(H_\beta)^{a,c}$
0–100	1.75	1.33	2.18	1.57
100–200	4.10	0.74	2.16	1.56
200–300	5.25	0.57	2.20	1.54
300–400	5.90	0.49	2.19	1.54
400–600	6.10	0.45	2.18	1.55
600–1200	6.10	0.45	2.20	1.54

^{a}See text. ^{b}In units of 10^{-10} cm^3 mol^{-1} s^{-1}. Temperature is assumed to be 298 K. ^{c}Intramolecular isotope effect in the reaction of $CD_3CH_2OC_2H_5$.

calculated (see Table III). (5) The product distribution k_1/k_2 (see eq 2) for every section was determined after 100 ms, ejecting all ions except for OH^- from the FT–ICR cell at the beginning of a time interval (see Table III). (6) In the same way $k_{1H}/k_{1D}(H_\beta)$ and $k_{2H}/k_{2D}(H_\beta)$ were determined from the isotopic product distribution in the reaction of OH^- with $CD_3CH_2OCH_2CH_3$ (see Table III).

Following this procedure, reaction of OH^-, generated from water, resulted in an excellent single exponential fit of the full OH^- decay data set. From this fit the rate constant k_{OH^-} was calculated to be 6.1×10^{-10} cm^3 mol^{-1} s^{-1}, which is in perfect agreement with FA results.[19] Because of this agreement and the observation that k_{OH^-} was found to be independent of the trapping time of OH^-, we must conclude that OH^-, generated from water, is cool. Consequently, the product ratio and isotope effects were also found to be independent of the trapping time of OH^- with $k_1/k_2 = 0.45$, $k_{1H}/k_{1D}(H_\beta) = 2.2$, and $k_{2H}/k_{2D}(H_\beta) = 1.55$ (see also Table II).

For the reaction of diethyl ether with OH^-, generated from N_2O, k_{OH^-} was found to be a function of the trapping time of OH^-, as followed from the results presented in Table III. Up to a trapping time of 400 ms k_{OH^-} gradually increased from 1.7×10^{-10} to 6.1×10^{-10} cm^3 mol^{-1} s^{-1} at which value k_{OH^-} levelled off. This increase of the rate constant is believed to reflect the decrease of the total energy of the reaction system relative to the transition state, as the initially excited OH^- is thermalized slowly under the low-pressures conditions by nonreactive collisions. This phenomenon can be interpreted as a negative temperature dependence which is very common in gas-phase ion/molecule chemistry.[37] Together with the rate constant the branching ratio k_1/k_2 changed from 1.33 to the end value of 0.45, obviously as a result of the different temperature dependences of the two reaction channels. In spite of the fact that the rate constant and the product ratio were found to be very sensitive with respect to the energy of OH^-, $k_{1H}/k_{1D}(H_\beta)$ and $k_{2H}/k_{2D}(H_\beta)$ essentially remained unchanged throughout the trapping time, implying that the isotope effects are relatively insensitive with respect to the energy of the reaction system.

E2 Spectrum. Using a flowing afterglow apparatus Bierbaum et al.[38] have determined overall kinetic isotope effects by measuring the rate constants for the reactions of the amide and hydroxide ions with diethyl ether and diethyl-d_{10} ether. Their values of 5.5 for amide and 2.1 for hydroxide differ slightly from our values, apparently because their results are based on overall reaction rates, disregarding the individual contributions from the free and solvated alkoxide anion formation. In contrast to the present results, they reported that within experimental error no secondary isotope and leaving group effects could be detected. Bierbaum et al. have modelled their data using statistical rate theory[39] where a fit of the data was obtained using a model in which the C–H or C–D symmetric stretch was chosen as the reaction coordinate, but in which other bonds have not changed in the transition state (i.e., an E1cb-like mechanism). This analysis indicated that the transition states for the reactions of amide and hydroxide ions with diethyl ether lie only about 2 and 5 kcal/mol, respectively, below the energy of the reactants. The authors, however, pointed out that the analysis was very sensitive with respect to the choice of frequencies of the newly formed transitional modes in the transition state. A similar analysis has been used by Jasinski and Brauman to rationalize the observed deuterium isotope effects in the gas-phase proton transfer reaction between pyridine bases.[40]

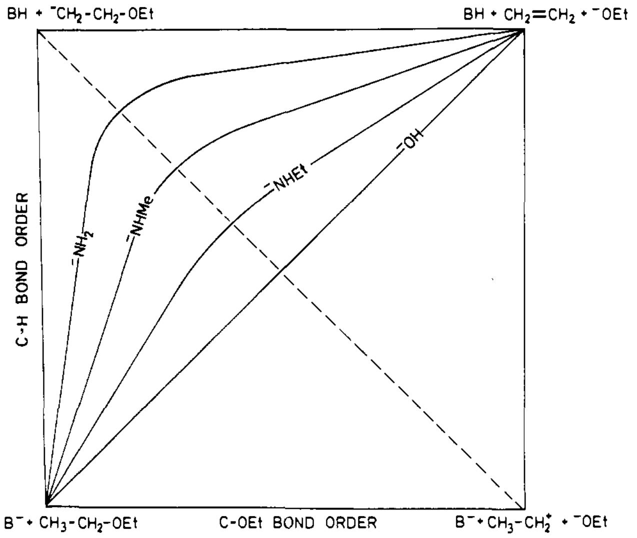

Figure 1. Mechanistic E2 spectrum of diethyl ether, based on observed isotope and leaving group effects; the coordinates of the saddle points for the reactions with the different bases are represented by $^-NH_2$, $^-$NHMe, $^-$NHEt, and $^-$OH.

Indeed, if the structure and frequencies of the transition state are chosen to be independent of the strength of the attacking base, the different kinetic isotope effects would reflect the different energy spacing between reactants and transition state. However, the assumption of a fixed transition-state geometry conflicts with the theory of the variable transition-state structure; this has encouraged us to rationalize our results in terms of an E2 spectrum by fitting our data with kinetic isotope effect model calculations of Saunders.[23,24] These calculations performed for the OH^-/C_2H_5X system describe the relationship between the various isotope effects and the C_β–H and C_α–X bond order in the transition state and include tunnel corrections and temperature dependences.[24] Our data do not include temperature dependences. However, since Saunders predicted normal temperature dependences (decreasing isotope effects with increasing temperature) and since the presently observed isotope effects are found to be relatively insensitive with respect to the energy of the reaction system, at least a qualitative fit of the data presented in Tables I and II with the model calculations of Saunders can be made. This fit results in the E2 spectrum visualized in Figure 1. This More O'Ferrall plot[41] shows an early, reactant-like transition state for the reaction of NH_2^- in which the β hydrogen is situated more or less symmetrically between the β carbon and NH_2^- and in which the C_α–O bond is only minimally stretched (E1cb-like). This model (**1**) is based on the $k_{1H}/k_{1D}(H_\beta)$ of 5.6 and the observation that $k_1(OCH_2CH_3)/k_1(OCD_2CD_3)$ is indistinguishable from unity. The relative large value of 5.6 in theory corresponds only to a symmetric linear arrangement for the base, β hydrogen, and β carbon in the transition state of anti elimination for which

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(37) (a) Sharma, R. B.; Sen Sharma, D. K.; Hiraoka, K.; Kebarle, P. *J. Am. Chem. Soc.* **1985**, *107*, 3747. (b) Meot-Ner, M.; Field, F. H. *J. Chem. Phys.* **1976**, *64*, 277. (c) Meot-Ner, M. *Gas Phase Ion Chemistry*; Bowers, M. T., Ed.; Academic Press: New York, 1979; Chapter 6. (d) Magnera, T. F.; Kebarle, P. *Ionic Processes in the Gas Phase*; Almoster Ferreira, M., Ed.; D. Reidel Publishers: Dordrecht, Holland, 1984; NATO ASI Series, pp 135–157.

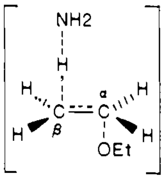
(38) Bierbaum, V. M.; Filley, J.; DePuy, C. H.; Jarrold, M. F.; Bowers, M. T. *J. Am. Chem. Soc.* **1985**, *107*, 2818.

(39) (a) Chesnavich, W. L.; Bowers, M. T. *J. Am. Chem. Soc.* **1976**, *98*, 8301. (b) Chesnavich, W. L.; Bass, L.; Su, T.; Bowers, M. T. *J. Chem. Phys.* **1981**, *74*, 2228. (c) Bowers, M. T.; Jarrold, M. F.; Wagner-Redeker, W.; Kemper, P. R.; Bass, L. *Faraday Discuss. Chem. Soc.* **1983**, *75*, 57.

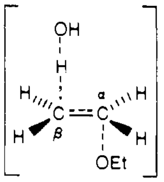
(40) Jasinski, J. M.; Brauman, J. I. *J. Am. Chem. Soc.* **1980**, *102*, 2906.

(41) More O'Ferral, R. A.; *J. Chem. Soc. B* **1970**, 274.

Saunders calculated maximum combined primary and secondary β-deuterium isotope effects[24] of about 9.5 and 5 at temperatures of 5 and 95 °C, respectively. These values were found to drop sharply when going from a symmetrical to an asymmetrical linear proton transfer transition-state structure.



1

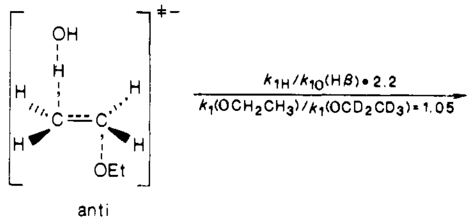


2

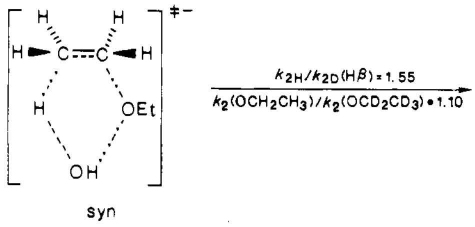
In accordance with the Hammond postulate,[42] reaction of the weakest base used, OH^-, is believed to proceed via a product-like transition state in which the β proton is more than half-transferred and in which the C_α–O bond breaking is substantial (more central E2). This model (**2**) is based on the relative small $k_{1H}/k_{1D}(H_\beta)$ of 2.2 and the significant $k_1(OCH_2CH_3)/k_1(OCD_2CD_3)$ of 1.05. The proposed E2 spectrum nicely harmonizes with the results of a FA study of DePuy and Bierbaum,[19] who have demonstrated that the elimination reactions of mixed dialkyl ethers induced by NH_2^- are proceeding by abstraction of the most acidic hydrogen, in contrast to the elimination reactions induced by OH^-, in the course of which the stability of the leaving group is playing the most important role. In conclusion, it appears that an increase in the base strength enhances the carbanion character of the transition state, which behavior also seems to be a general phenomenon in the condensed phase.[10,43]

Anti vs. Syn Elimination. In previous reports of studies on elimination reactions of ethers,[18-20] it was suggested that the reaction complex of a base B^- and ether is converted via a single reaction barrier into a metastable complex, consisting of loosely bound alkoxide, olefin, and HB. This metastable complex is believed to dissociate to form either free or HB solvated alkoxide anion. In order to stabilize the solvated alkoxide, rearrangement of the complex is necessary as a consequence of which the formation of solvated alkoxide is related to the lifetime of the complex. For this reason the yield of solvated alkoxide was related to the overall exothermicity of the elimination reaction. Indeed, for the reaction of OH^- with diethyl ether it seems very plausible to rationalize the high yield of solvated alkoxide in terms of thermochemistry, since the free alkoxide anion formation is slightly endothermic with $\Delta H = +1.9$ kcal/mol, whereas the free Gibbs energy change $\Delta G = -9.3$ kcal/mol.[19] However, if both free and solvated alkoxide anions are formed via the same reaction barrier, the isotope effects for the two processes are expected to be identical. This is not what we have found. The observed difference in isotope effects may be caused by the difference in stabilities of the solvated alkoxides and the corresponding deuterated solvated alkoxides. However, this explanation is rejected on the basis of the results presented in Table III, from which it appears that the isotope effects are insensitive to variation of the energy of OH^- and thus to the overall exothermicity. Therefore, the large difference, observed in both $k_H/k_D(H_\beta)$ and $k(OCH_2CH_3)/k(OCD_2CD_3)$ for the two reaction channels, is interpreted in terms of two different elimination mechanisms involving different transition states. The production of free alkoxide anions is believed to proceed via an anti elimination pathway, characterized by a staggered transition state in which the β hydrogen and ethoxy group are anti periplanar (eq 5a).

On the other hand, the production of water-solvated ethoxide anions is believed to proceed via a syn elimination pathway, characterized by an eclipsed transition state geometry in which the β hydrogen and ethoxy group are syn periplanar and in which electrostatic interaction between the base and the ethoxy group is essential (eq 5b). Because of this interaction no reorganization of the reaction complex is required in order to stabilize the solvated alkoxide product ion. This is in contrast with the anti elimination mechanism, where solvation of ethoxide can be achieved only after considerable reorganization of the reaction complex.



$$[H_2O\cdot C_2H_4\cdot{}^-OEt]^* \longrightarrow H_2O + C_2H_4 + {}^-OEt \tag{5a}$$



$$[C_2H_4\cdot EtO^- \text{---} HOH]^* \longrightarrow C_2H_4 + EtO^- \text{---} HOH \tag{5b}$$

The relatively small $k_{2H}/k_{2D}(H_\beta)$ of 1.55 and large $k_2(OCH_2CH_3)/k_2(OCD_2CD_3)$ of 1.10 are consistent with a syn elimination transition state, taking advantage of the interaction of the base and the leaving group, for which Saunders calculated a maximum primary isotope effect of only 2.5, associated with a symmetrical, but bent proton transfer at a C_β–H–O bond angle of 120°.[44] Moreover, the syn elimination model is in accordance with the relatively small isotope effects usually observed for syn eliminations in the condensed phase.[12,45] In the condensed phase, syn eliminations are favored as the carbanion character of the transition state increases, e.g., as the strength of the base increases.[10,43,46] However, the present results suggest the opposite. This opposite behavior in the gas phase may be explained by the absence of a solvation mantle as a consequence of which association is possible of the base and the leaving group, resulting in a reduction of the activation enthalpy for the syn elimination. Reaction of a weak base is expected to be favored by a small activation enthalpy, whereas reaction of a strong base is favored by a large activation entropy. Consequently, the elimination reaction induced by the weakest base used, OH^-, is preferred to proceed via the less energetic syn pathway. Analogous arguments have been used to explain the preference for syn elimination of some solvent-phase reaction systems, for which interaction between the base and the leaving group is suggested to proceed through the medium of the metal counterion.[47-49]

In order to test the importance of base/leaving group association in the transition state, $^{18}OH^-\cdot HNMe_2$ was isolated from the reaction mixture of $^{18}OH^-$ and *N*,*N*-dimethylformamide (DMF)[50] and reacted with diethyl ether. The ^{18}O label was introduced to prevent the possible interference of product ions from the reaction with DMF. Although $^{18}OH^-\cdot HNMe_2$ showed an extremely low reactivity toward diethyl ether, it was established beyond any doubt by double resonance experiments that only two primary product ions were formed at *m/z* 45 and 65, corresponding to $C_2H_5O^-$ and $H_2{}^{18}O\cdot C_2H_5O^-$, respectively. Surprisingly, the free ethoxide

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(42) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

(43) (a) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper and Row: New York, 1981; pp 197–210. (b) Winey, D. A.; Thornton, E. R. *J. Am. Chem. Soc.* **1975**, *97*, 3102.

(44) Saunders, W. H., Jr. *J. Chem. Soc., Chem. Commun.* **1973**, 850.

(45) Brown, K. C.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 4292..

(46) Bach, R. D.; Badger, R. C.; Lang, T. J. *J. Am. Chem. Soc.* **1979**, *101*, 2845.

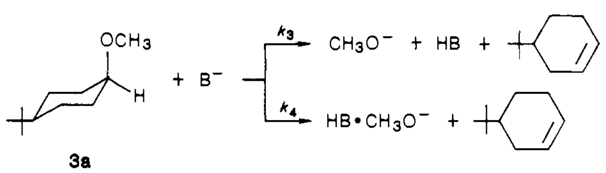
(47) Zāvada, J.; Sicher, J. *Collect. Czech. Chem. Commun.* **1967**, *32*, 3701.

(48) Zāvada, J.; Pánkovā, M.; Sicher, J. *J. Chem. Soc., Chem. Commun.* **1968**, 1145.

(49) Zāvada, J.; Pānkovā, M.; Svoboda, M. *Collect. Czech. Chem. Commun.* **1976**, *41*, 3778.

(50) DePuy, C. H.; Grabowski, J. J.; Bierbaum, V. M.; Ingemann, S.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1985**, *107*, 1093.

Table IV. Leaving Group Effects Associated with the Reaction between B^- and *cis*-1-*tert*-Butyl-4-methoxycyclohexane

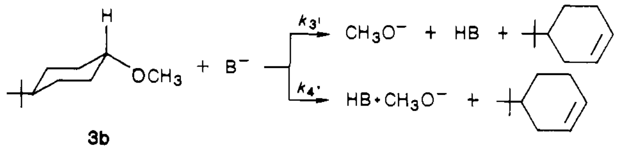


3a

B^-	k_3/k_4	$k_3(OCH_3)/k_3(OCD_3)^a$	$k_4(OCH_3)/k_4(OCD_3)^a$
NH_2^-	∞	1.00 ± 0.02	
OH^-	0.28	1.09 ± 0.03	1.12 ± 0.03

^{a}Given error is the standard deviation over four experiments.

Table V. Leaving Group Effects Associated with the Reaction between B^- and *trans*-1-*tert*-Butyl-4-methoxycyclohexane



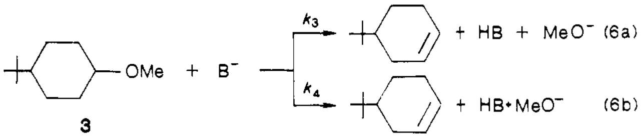
3b

B^-	$k_{3'}/k_{4'}$	$k_{3'}(OCH_3)/k_{3'}(OCD_3)^a$	$k_{4'}(OCH_3)/k_{4'}(OCD_3)^a$
NH_2^-	∞	1.12 ± 0.03	
OH^-	0.82	1.36 ± 0.05	1.45 ± 0.04

^{a}Given error is the standard deviation over four experiments.

was the dominant ion as followed from the product ratio k_1/k_2 of 1.4. Obviously, solvation of OH^- promotes the formation of free ethoxide rather than of solvated ethoxide. This result suggests that the selectivity is likely to be controlled kinetically rather than thermodynamically and is consistent with the idea that association of a solvent molecule reduces the interaction of the base and the leaving group, as a result of which syn elimination is suppressed.

1-*tert*-Butyl-4-methoxycyclohexane. Elimination Reaction. In the previous section it was suggested that elimination reactions of ethers in the gas phase readily proceed via a transition state with a periplanar geometry. This hypothesis, first generally postulated by DePuy et al.[51] and accepted for β-eliminations in the condensed phase, has been tested by studying the stereoelectronic control in the base-induced elimination reaction of 1-*tert*-butyl-4-methoxycyclohexane (**3**). Like diethyl ether, both *cis*- and *trans*-1-*tert*-butyl-4-methoxycyclohexane react with a base exclusively by an E2 mechanism as shown in eq 6. No evidence, whatsoever, was found for a displacement of the *tert*-butylcyclohexyloxy anion by B^-. Instead, MeO^- and $HB{\cdot}MeO^-$ were the only product ions observed in the reaction with either NH_2^- or OH^-. Again, only OH^- generated both free and solvated alkoxide anions, showing a different selectivity in the reaction with the cis and trans substrate (see Tables IV and V).



3
cis and *trans*

Isotope and Conformational Effects. Leaving group effects were determined from the isotopic product ratio in the reaction of NH_2^- and OH^- with a 1:1 mixture of 1-*tert*-butyl-4-methoxycyclohexane and 1-*tert*-butyl-d_3-4-methoxycyclohexane. The results of these measurements for the cis and trans substrates **3a** and **3b** are given in Tables IV and V, respectively.

Conformational effects, indicated by $k_3/k_{3'}$, were analyzed by determining $k_3(OCD_3)/k_{3'}(OCH_3)$ from the isotopic product distribution in the reaction of the base and a 1:1 mixture of *cis*-1-*tert*-butyl-d_3-4-methoxycyclohexane and *trans*-1-*tert*-butyl-4-methoxycyclohexane. Correction for the leaving group effect using eq 7a offered $k_3/k_{3'}$. Identical values for $k_3/k_{3'}$ were obtained by correcting $k_3(OCH_3)/k_{3'}(OCD_3)$, determined in the reaction of base and a 1:1 mixture of *cis*-1-*tert*-butyl-4-methoxycyclohexane and *trans*-1-*tert*-butyl-d_3-4-methoxycyclohexane, for the leaving group effect according to eq 7b:

Table VI. Conformational Effects Associated with the Reaction between B^- and *cis*- and *trans*-1-*tert*-Butyl-4-methoxycyclohexane

B^-	$k_3/k_{3'}$	$k_4/k_{4'}$
NH_2^-	3.7	
OH^-	2.6	4.2

$$\frac{k_3(OCD_3)}{k_{3'}(OCH_3)}\left[\frac{k_3(OCH_3)}{k_3(OCD_3)}\right] = \frac{k_3}{k_{3'}} \tag{7a}$$

$$\frac{k_3(OCH_3)}{k_{3'}(OCD_3)}\Bigg/\left[\frac{k_{3'}(OCH_3)}{k_{3'}(OCD_3)}\right] = \frac{k_3}{k_{3'}} \tag{7b}$$

Finally, $k_4/k_{4'}$ was determined following an analogous procedure (Table VI). Although this procedure seems rather complicated, the introduced errors are limited to a few percent, whereas the errors in $k_3/k_{3'}$ and $k_4/k_{4'}$, directly determined from absolute reaction rate constant measurements, would certainly have exceeded 20%.

Stereoelectronic Control. The leaving group effects found for the reactions of the cis substrate **3a** (Table IV) surprisingly resemble those found for the reactions of diethyl ether (Table II). The slightly larger values observed for the reaction of OH^- may be due to the poorer leaving group ability of CH_3O^- in the gas phase and the larger difference in leaving group abilities between CH_3O^- and CD_3O^-, as indicated by the gas-phase acidity difference $\delta\Delta H_{acid}$ of CH_3OH and CD_3OH of 0.45 kcal/mol, which followed from equilibrium measurements (see also ref 52).

Assuming that the bulky *tert*-butyl group fixes the methoxy group in the axial position,[53] a perfect antiperiplanar relationship exists between the methoxy group and the β hydrogens, as a consequence of which anti elimination is feasible. Since also diethyl ether can fulfil these conformational requirements, no appreciable difference is to be expected in the transition-state structure of the elimination reactions of **3a** and diethyl ether, as may be evident from the leaving group effect data. However, the enormous increase in the leaving group effects, found in going from the cis **3a** to the trans **3b** substrate (Table V), indicates a drastic shift of the transition state toward the carbenium ion or E1 region of the E2 spectrum. This shift is very plausible, if it is accepted that also gas-phase elimination reactions are stereoelectronically controlled. The methoxy group in **3b**, fixed in the equatorial position, has no periplanar relationship with any of the β hydrogens. In order to cope with this unfavorable situation, the C_α–O bond stretch in the transition state has to be increased, so as to develop some positive charge on the α carbon, by which its hybridization becomes more sp^2. As a result of this distortion, the unfavorable nonperiplanarity of the methoxy group and both the equatorial and axial β hydrogens is cancelled to some extent. Moreover, the importance of stereoelectronic control is clearly demonstrated by the relative large conformational effects, expressed by $k_3/k_{3'}$ and $k_4/k_{4'}$ (Table VI). Although these ratios

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(51) DePuy, C. H.; Thurn, R. D.; Morris, G. F. *J. Am. Chem. Soc.* **1962**, *84*, 1314.

(52) Grabowski, J. J. Thesis, University of Colorado, Boulder, 1983.

(53) *tert*-Butylcyclohexanes are believed to exist in a uniformal conformation: (a) Winstein, S.; Holness, N. J. *J. Am. Chem. Soc.* **1955**, *77*, 5562. (b) Cf. Allinger, N. L.; Freiberg, L. A. *Ibid.* **1960**, *82*, 2393. The free energy difference between equatorial and axial *tert*-butyl in an aprotic solvent is estimated to be larger than 5.5 kcal/mol and probably much larger in the gas phase. Besides, interconversion barriers of cyclohexane chair conformations are found to be much higher in the gas phase: Ross, B. D.; True, N. S. *Ibid.* **1983**, *105*, 4871. McKenna discussed the validity of 4-*tert*-butylcyclohexanes as a model for kinetic methods of conformational analyses: Brown, D. R.; Leviston, P. G.; McKenna, J.; McKenna, J. M.; Melia, R. A.; Pratt, J. C.; Hutley, B. G. *J. Chem. Soc., Perkin Trans. 2* **1976**, 838.

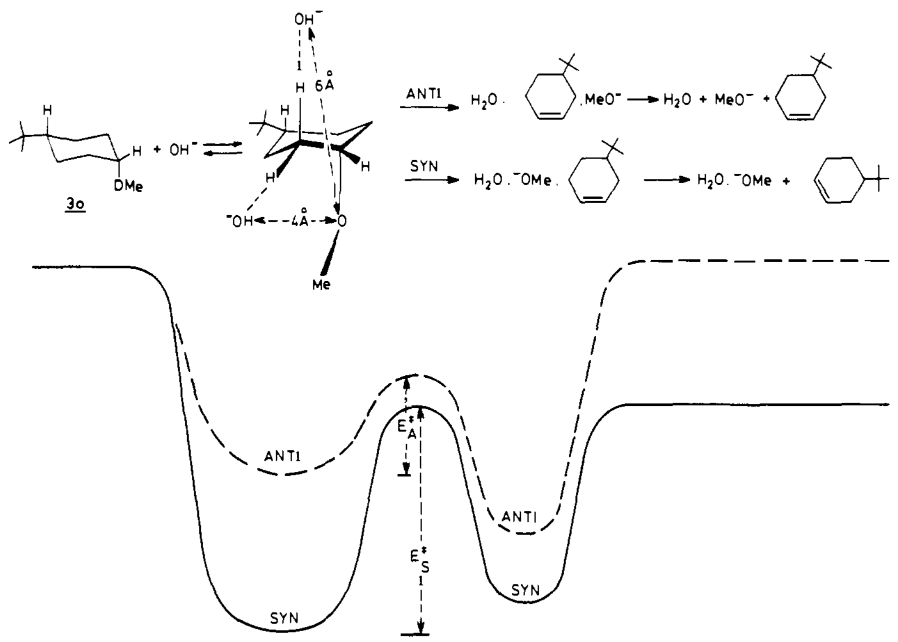

Figure 2. Outline of the energy profile for the reaction between OH⁻ and *cis*-1-*tert*-butyl-4-methoxycyclohexane.

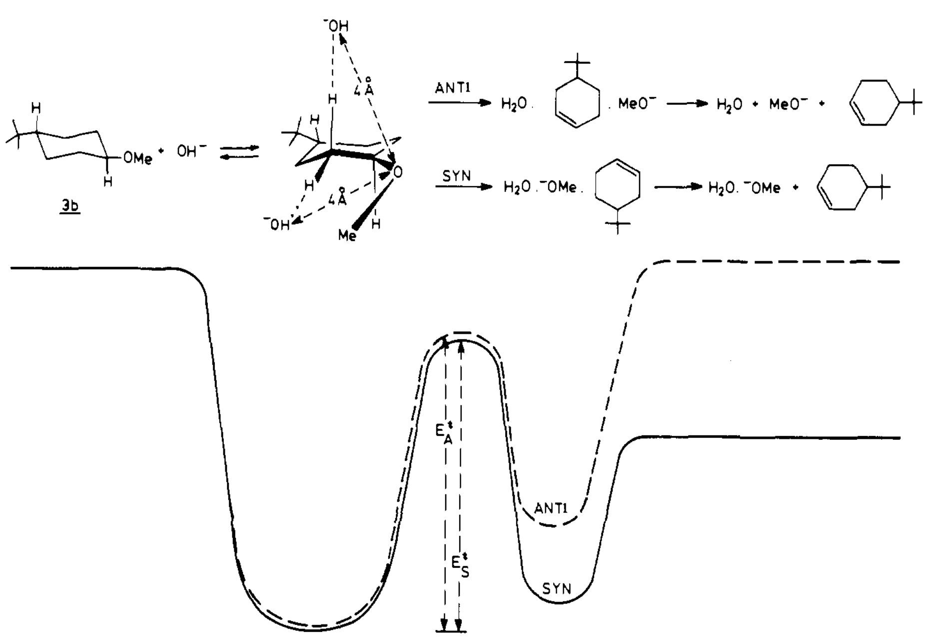

Figure 3. Outline of the energy profile for the reaction between OH⁻ and *trans*-1-*tert*-butyl-4-methoxycyclohexane.

are substantially smaller than those usually observed for analogous systems in the condensed phase, they certainly cannot be neglected, taking into account that the rates of gas-phase ion/molecule reactions, including the elimination reactions, are already very close to the collision rate. Furthermore, it follows from the data in Table VI that the stereoelectronic control in the reaction induced by the stronger base, NH_2^-, is more strict than in the reaction induced by the weaker base, OH^-. This behavior shows that stereoelectronic control is a function of the degree of the carbanion character of the transition state as also suggested by the shifts of the transition state toward the carbenium ion region of the E_2 spectrum when the periplanarity of the transition state becomes more hindered by the geometric restrictions of the substrate (vide supra).

Potential Energy Profile. The different behavior of the cis and trans substrate, as indicated by the leaving group effects and relative rates, is also demonstrated by the selectivity k_3/k_4 and $k_{3'}/k_{4'}$ in the reaction with OH^- (Tables IV and V). The threefold preference for solvated alkoxide formation over free alkoxide formation in the reaction of the cis substrate **3a** contrasts with the very small preference for solvated alkoxide formation in the reaction of the trans substrate **3b**. The nature of this diversity strongly conflicts with the idea that the yield of free alkoxide is thermodynamically controlled (vide supra), since the reaction of **3a** is about 0.7 kcal/mol more exothermic than the reaction of **3b**.[54] At first sight also the syn/anti dichotomy, suggested in a previous section, cannot be responsible for the observed phenomenon: for **3a** anti elimination, resulting in free alkoxide, is preferred stereoelectronically over syn elimination. On the other hand, unusually facile syn eliminations have also been observed in the condensed phase for cyclohexane derivatives, when induced by complex base aggregates. As in the present gas-phase study, it is assumed that these syn eliminations result from a two-side interaction of the β hydrogen and the leaving group with the base, here assisted by its metal counterion.[55,56] Therefore, the syn/anti

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[54] The free energy difference between axial and equatorial methoxide is 0.74 kcal/mol in an aprotic solvent: Noyce, D. S.; Dolby, L. J. *J. Org. Chem.* **1961**, *26*, 3619.

[55] (a) Caubere, P.; Coudert, G. J. *J. Chem. Soc., Chem. Commun.* **1972**, 1289. (b) Guillaumet, G.; Lemmel, V.; Coudert, G.; Caubere, P. *Tetrahedron* **1974**, *30*, 1289.

[56] Lee, J. G.; Bartsch, R. A. *J. Am. Chem. Soc.* **1979**, *101*, 228.

dichotomy may still offer the explanation, if also the stabilities of the ion/molecule complexes, leading to either syn or anti elimination, are taken into account. In principle, these stabilities can be obtained by ab initio calculations.[15,16] However, this is beyond the scope of the present study. Therefore, rough approximations to the bond dissociation energies of the ion/molecule complexes have been obtained by calculating the pure long-range electrostatic interactions between the species,[57] estimating the geometric parameters from the corresponding molecular models. For **3a** these calculations clearly indicate that the formation of the complex leading to syn elimination can be as much as 10 kcal/mol more exothermic than the formation of the complex leading to anti elimination. Thus, in spite of the relatively low intrinsic reaction barrier, associated with the electronically favored anti elimination, the density of states in the transition state of the syn elimination may still be higher relative to the anti elimination. Consequently, solvated alkoxide formation is favored over free alkoxide formation as is visualized by the potential energy profile outlined in Figure 2.

For **3b** the approximations to the bond dissociation energies of the ion/molecule complexes, leading to either syn or anti elimination, suggest equal exothermicity with respect to the formation of both complexes. Since also both intrinsic reaction barriers of syn and anti elimination suffer about equally from the unfavorable geometry of the substrate, the preference for syn elimination, e.g., solvated alkoxide formation, may be lost. This is visualized by the potential energy profile outlined in Figure 3. In the proposed mechanism only a fraction of all the phase space of the ion/molecule complex is associated with the conversion into products. This fraction is related to the structure of the transition state, implying that collision dynamics may play an important role in the product distribution. The importance of collision dynamics in product distribution of gas-phase ion/molecule reactions has been suggested earlier by Minato and Yamabe on the basis of an ab initio study of the reaction of F^- and FC_2H_5 (vide supra).[16]

Still, our model is only based on branching ratios, disregarding the influence of minor changes in reaction energetics and reactant structure on the encounter rate itself, and the rate of nonreactive collisions.[58] We realize that this aspect of the mechanism must be investigated by analyzing the absolute kinetics of the elimination reactions of **3a** and **3b**. Unfortunately, absolute gas-phase rate constant measurements still suffer from large experimental errors, a consequence of which small changes in the absolute rates cannot be detected.

Conclusions

Although the energy profiles of ion/molecule reactions in the gas phase principally differ from those in the condensed phase, it seems that the properties of the transition state of base-induced gas-phase elimination reactions of ethers are very well in line with the theoretical model set up for concerted β-eliminations in the condensed phase. However, where in the condensed phase association of solvent molecules or counterions may play an important role, electrostatic interactions in the gas phase of the base and the substrate itself may partly be responsible for the mechanistic course of the elimination reaction.

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Registry No. 3a, 15875-99-7; **3b**, 15876-31-0; Dz, 7782-39-0; diethyl ether, 60-29-7.

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Ab Initio Study of the Unimolecular Pyrolysis Mechanisms of Formic Acid: Additional Comments Based on Refined Calculations

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Abstract: Refined ab initio calculations on the dehydration and decarboxylation mechanisms of formic acid in the gaseous state above 670 °C are presented, taking into account the effect of electron correlation on both the geometries and energies of the different stationary points. The classical barrier heights of the two processes are much more affected by the quality of the basis set used at the SCF level and by the correlation corrections evaluated in single-point energy calculations than by the reoptimization of the structures of the MP level.

I. Introduction

Results of ab initio calculations have recently been reported[1] on the two unimolecular competing reactions (dehydration and decarboxylation) occurring during the pyrolysis of formic acid. To explain the apparent inconsistency of the exptl. results, i.e., a lowest activation energy value of the decarboxylation process (48.5 kcal mol^{-1}) vs. the dehydration one (62–65 kcal mol^{-1}) and a CO/CO_2 ratio of product yield of 10, a new reaction mechanism was proposed. In particular, if the dehydration constitutes the main channel of formic acid pyrolysis, then some of the produced water molecules could serve as catalysts for the decarboxylation reaction. In this scheme, the calculated activation barriers were relatively close to the experimental values[2,3] and the observed product ratio was therefore explained by the dependence of one

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