J. Am. Chem. Soc. **1992**, *114*, 2897-2903

Epimer Distinction and Structural Effects on Gas-Phase Acidities of Alcohols Measured Using the Kinetic Method

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Abstract: Epimers of methylcyclohexanol are distinguished by their relative gas-phase acidities ($\Delta G^\circ_{\text{acid}}$) obtained by a kinetic method which is based on the relative rates of competitive fragmentations of cluster ions. The estimated $\Delta G^\circ_{\text{acid}}$ values for *cis*-2-methylcyclohexanol, *trans*-2-methylcyclohexanol, *cis*-4-methylcyclohexanol, and *trans*-4-methylcyclohexanol are 364.1 ± 0.1, 365.1 ± 0.1, 365.1 ± 0.1, and 366.2 ± 0.1 kcal/mol, respectively. These results illustrate the high sensitivity of the kinetic method to small differences in gas-phase acidity (±0.1 kcal/mol using the triple-quadrupole mass spectrometer) and the fact that it allows the distinction of isomeric compounds. The difference in acidities of the epimers is explained by steric decompression due to hyperconjugation which involves contributions by the hydride–ketone ion/molecule complex. 1,3-Diaxial interactions are relieved in the course of hyperconjugation as the axial alkoxide adopts a quasi-equatorial orientation and so increases the acid strength of the cis alcohols. The greater acidity of the 2-substituted over the 4-substituted alcohols is due to interactions of the oxygen atom with the vicinal methyl group. Changes in the type of alcohol groups involved in hydrogen bonding to the proton have a discernible influence on the relative rates of competitive dissociation of the proton-bound dimers. This is reflected in the susceptibility to dissociation, expressed as an effective temperature, which is largest for metastable dissociations of the proton-bound cluster ion comprising a primary alcohol proton-bound to a secondary alcohol and smallest when two secondary alcohols comprise the cluster ion. These changes are due to differences in the vibrational states of the proton-bound dimers.

Introduction

By establishing an equilibrium involving suitable ions, it is possible to determine thermodynamic quantities, such as gas-phase acidities and basicities, by mass spectrometry. Ion/molecule reaction equilibria were first measured by Kebarle et al.[1] and have been used subsequently by many investigators[2-5] to characterize thermochemical quantities. The position of the equilibrium is measured by sampling the equilibrated mixture or by measuring the rate constants (k_a and k_b) of the forward and reverse reactions. For example, in the case of proton transfer,

$$AH + B^- \underset{k_b}{\overset{k_a}{\rightleftharpoons}} A^- + BH$$

$$K_{eq} = k_a/k_b$$

and the standard free-energy change (ΔG°) for the reaction is given by

$$\Delta G^\circ = -RT \ln K_{eq} = \Delta H^\circ - T\Delta S^\circ$$

The gas-phase-acidity difference $\Delta(\Delta G^\circ_{\text{acid}})$ between species AH and BH is given by the equation

$$\Delta(\Delta G^\circ_{\text{acid}}) = \Delta G^\circ_{\text{acid}}(AH) - \Delta G^\circ_{\text{acid}}(BH) \simeq \Delta H^\circ_{\text{acid}}(AH) - \Delta H^\circ_{\text{acid}}(BH)$$

For proton-transfer reactions, ΔS° is approximately zero and the free-energy change may be equated with the enthalpy change, giving access to the relative proton affinities of the two bases. Note that even if ΔS° for proton transfer is not zero, the difference $\Delta(\Delta S^\circ)$ will often be negligible.

This method has proven extremely valuable, and most of the gas-phase thermochemical information available in the current literature has been obtained in this way.[6,7] For example, McIver et al.[8] measured the acidities of alcohols using ionic equilibria in the gas phase while equilibria involving stronger acids have been measured by Kebarle and co-workers.[9] Some recent applications of the equilibrium method include determination of proton affinities of organic radical anions,[10] α,β-unsaturated acid derivatives,[11] and determination of gas-phase basicities of α,α,α-trifluoroacetophenones.[12] Gas-phase stabilities of phenonium ions have been studied by the equilibrium method by determining relative bromide ion affinities.[13] This method has also been used to study substituent effects on the stability of proton-bound dimers of phenoxide anion and halide anion.[14] The proton affinity of NH_3 has been determined using isobutane as the reference compound,[15] and quantitative investigations of substituent effects in amine cations[16] have also been reported by gas-phase equilibrium studies.

The equilibrium method is not applicable to impure or nonvolatile samples, and in such cases alternative methods are desirable. One such alternative, known as the kinetic method,[17,18] makes extreme assumptions regarding the factors controlling dissociation kinetics. It is a limiting-case procedure, and its use is justified only by the fact that it provides the desired information in cases where alternatives do no exist. The kinetic method

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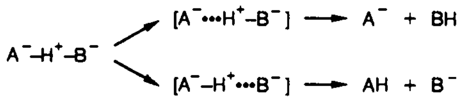
employs competitive dissociations of cluster ions. In the case of particular interest here, a mixed dimer, $(A-H-B)^-$, is formed in a high-pressure ion source, using negative-ion chemical ionization. Relative gas-phase acidities (ΔG°_{acid}) are estimated by the kinetic method by observing competition for the proton during dissociation of the negatively-charged proton-bound dimer (eqs 1 and 2). The



$$A^- -H^+-B^- \rightarrow \begin{cases} [A^-\cdots H^+-B^-] \longrightarrow A^- + BH & (1) \\ [A^- -H^+\cdots B^-] \longrightarrow AH + B^- & (2) \end{cases}$$

ratio of the relative fragment-ion abundances yields the desired thermochemical information by the following arguments. The unimolecular reaction rate constant k_i is given by statistical rate theory[19,20] as

$$k_i = (kT/h)\frac{\Pi_j Q^*_{i,j}}{\Pi_j Q_{i,j}}\exp(-\epsilon^\circ_i/RT) \quad (3)$$

where ϵ°_i is the energy of activation/mole at the absolute temperature T, Q^* and Q are the partition functions for the activated complex and the unactivated species, respectively, k is the Boltzmann constant, h is Planck's constant, and i and j indicate initial and final states, respectively.

The ratio of the partition functions ($\Pi_j Q^*_{i,j}/\Pi_j Q_{i,j}$) may be taken as the ratio of the partition functions of internal vibrations,[20] so that

$$k_i = (kT/h)\frac{\Pi_j[1-\exp(-h\nu^*_{i,j}/kT)]^{-1}}{\Pi_j[1-\exp(-h\nu_{i,j}/kT)]^{-1}}\exp(-\epsilon^\circ_i/RT) \quad (4)$$

As for any nonlinear molecule with n atoms, the excited molecule has $3n - 6$ vibrational modes, whereas the activated complex is treated as having $3n - 7$ vibrational modes. Two extreme cases are of interest. First, if $kT \gg h\nu$, i.e., at relatively high temperatures, the $\{1 - \exp(-h\nu_{i,j}/kT)\}^{-1}$ term may be replaced by $kT/h\nu$, leading to

$$k_i = (kT/h)\frac{\Pi_j \nu_{i,j}}{\Pi_j \nu^*_{i,j}}\exp(-\epsilon^\circ_i/RT) \quad (5)$$

Second, if $kT \ll h\nu$, the vibrational partition function is approximately equal to unity and independent of frequency factors; hence,

$$k_i = (kT/h)\exp(-\epsilon^\circ_i/RT) \quad (6)$$

Returning to the general case, for the competing reactions 1 and 2, the ratio of the rate constants is

$$k_1/k_2 = \frac{\Pi_j[1-\exp(-h\nu^*_{1j}/kT)]^{-1}}{\Pi_j[1-\exp(-h\nu^*_{2j}/kT)]^{-1}}\exp[(\epsilon^\circ_2-\epsilon^\circ_1)/RT] \quad (7)$$

Since the two transition states are distinguished principally by the vibrational frequencies of the remaining bonds to the proton, i.e., $\nu^*(B^-\cdots H^+)$ for reaction 1 and $\nu^*(A^-\cdots H^+)$ for reaction 2, we can write

$$k_1/k_2 = \frac{[1-\exp\{-h\nu^*(B^-\cdots H^+)/kT\}]}{[1-\exp\{-h\nu^*(A^-\cdots H^+)/kT\}]}\exp[(\epsilon^\circ_2-\epsilon^\circ_1)/RT] \quad (8)$$

If frequency factors cancel, i.e., $\nu^*(A^-\cdots H^+) = \nu^*(B^-\cdots H^+)$, a situation which is favored when $kT \ll h\nu$ as already noted, the ratio of rate constants becomes directly related to the gas-phase acidities of the species AH and BH, viz.,

$$k_1/k_2 = \exp[(\epsilon^\circ_2-\epsilon^\circ_1)/RT] = \exp\{[\Delta G^\circ_{acid}(BH) - \Delta G^\circ_{acid}(AH)]/RT\} \quad (9)$$

i.e.,

$$\ln(k_1/k_2) = \Delta(\Delta G^\circ_{acid})RT \quad (10)$$

where the substitution $\epsilon^\circ_2 - \epsilon^\circ_1 = \Delta(\Delta G^\circ_{acid})$ follows directly from the definitions, provided the reverse activation energies are negligible or cancel. In the absence of secondary or competitive fragmentations, the ratio of the rate constants can be experimentally determined by measuring the ion abundance ratio, so that

$$\ln(k_1/k_2) = \ln([A^-]/[B^-]) = \Delta(\Delta G^\circ_{acid})/RT \quad (11)$$

or, using the approximations already introduced,

$$\ln(k_1/k_2) \approx (\Delta H^\circ_{acid})/RT \quad (12)$$

It is apparent that the assumptions involved in this approach require that it be used with great care. The derivation is based on a Boltzmann distribution of internal energies which is not representative of isolated ions. In addition, the separability of the frequency factors from the critical (activation) energies is not rigorously possible. Successful applications therefore employ weakly bound cluster ions which undergo simple dissociation kinetics, and it has been shown in detail how this minimizes the consequences of the approximations.[17] In spite of these caveats, a growing number of successful applications of the kinetic method have been reported.[21-30] For example, plots of the product ion abundance ratios for proton-bound dimers of the type AHB^- vs known gas-phase acidities have been used to determine the unknown gas-phase acidities of carboxylic acids and alcohols.[21] Similarly, gas-phase acidities of nucleic acids[22,23] and amino acids[24] have been estimated using this method. Application of the kinetic method has also been extended to the estimation of metal ion affinities[25] and electron affinities,[26] the distinction of isomeric glycosides by utilizing their alkali cation-bound dimers,[27-29] and the estimation of ionization energies of metal clusters.[30]

The influence of the structural environment of an acidic site on the gas-phase acidity has been investigated in the case of alcohols by the kinetic method by Houriet et al.[31] For aliphatic branched alcohols the acidity depends upon the degree of alkyl substitution: ΔH°_{acid}(tertiary) > ΔH°_{acid}(secondary) > ΔH°_{acid}(primary). In addition, the acidity was found to be dependent on the position (α, β, or γ) of methyl substitution, relative to the alcohol functionality. On the other hand, there appears to be no information in the literature on the role played by the stereochemistry of the neighboring groups on the gas-phase acidities of alcohols. Only in the case of isomeric 1,4-cyclohexanediols are stereochemical effects on relative acidity known;[32,33] in this case the cis isomer is 1.2 kcal/mol more acidic than the trans epimer.[32] This result was interpreted as a result of hydrogen-bond stabilization of the deprotonated *cis*-diol, the influence of which on the fragmentation of the $[M - H]^-$ ion was evident in the negative-ion chemical ionization (NICI) mass spectrum.[33]

In the present study, gas-phase acidities of some epimeric methylcyclohexanols are estimated, the effect of the position of

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the methyl group and stereochemistry on acidity are investigated by the kinetic method, and in the course of the investigation, the limits of the method are re-examined.

Experimental Section

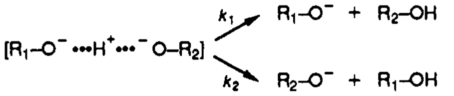
All experiments were performed using a Finnigan TSQ 4500 mass spectrometer. The ions were formed using ammonia as the chemical-ionization reagent. The negatively-charged proton-bound cluster ions of interest were mass selected using the first quadrupole mass analyzer and allowed to collide with argon in the second quadrupole to effect collision-induced dissociation (CID). When metastable-ion decompositions were to be studied, collision gas was not added. The fragment ions resulting from metastable or collision-induced dissociation were mass analyzed using the third quadrupole to record MS/MS product spectra of the proton-bound dimers. Only alkoxide anions were observed during these measurements; no products of further dissociation occurred.

The background pressure in the mass spectrometer was 3×10^{-8} Torr, the partial pressure of the mixture of alcohols (R_1OH and R_2OH) in the ion source was 3.6×10^{-6} Torr, and the source temperature was 190 °C. The pressure of ammonia gas in the ion source was 0,5 Torr. All measured pressures were read using ion gauges and are nominal and uncorrected. For CID experiments, the pressure of argon gas in the second quadrupole (Q2) was approximately 5×10^{-6} Torr, yielding a decrease in parent-ion abundance of approximately 10%, and the collision energy, as measured by the voltage difference between the source and Q2, was 5 eV. These conditions yield predominantly single collisions and correspond to 0.7–0.9-eV relative collision energies in the center of mass frame, depending on the mass of the particular proton-bound dimer.

Additional experiments were performed using a Nermag R-30-10 triple-quadrupole instrument. The background pressure in the collision cell was ca. 2×10^{-7} Torr. Source conditions were similar to those with the TSQ 4500. The argon pressure used for collision-induced dissociation was 4×10^{-6} Torr, and the laboratory collision energy was 5 eV.

Results and Discussion

Proton bound dimer ions can be positively or negatively charged. For example, ketones yield positively-charged proton-bound dimers because two neutral molecules are bound to a proton through hydrogen-bonding interactions as in $(R)_2C{=}O\cdots H^+\cdots O{=}C(R')_2$. While alcohols can yield positively-charged proton-bound dimers, the species studied here are the negatively-charged clusters formed when two alkoxide anions are hydrogen bonded through a proton $[R_1{-}O^-\cdots H^+\cdots {}^-O{-}R_2]^-$. These proton-bound dimers of alcohols were generated by negative-ion chemical ionization with ammonia (e.g., $R_1OH + NH_2^- \rightarrow R_1O^- + NH_3$ and $R_1O^- + R_2OH \rightarrow R_1O^-\cdots H^+\cdots {}^-OR_2$) and dissociate through metastable or collision-induced processes to produce negatively-charged alkoxide ions with the simultaneous loss of alcohol molecules as neutrals. The more acidic alcohol (lower ΔG°_{acid} value) is expected to release the proton more easily, forming the higher abundance alkoxide anion.



$$[R_1{-}O^-\cdots H^+\cdots {}^-O{-}R_2] \xrightarrow{k_1} R_1{-}O^- + R_2{-}OH \quad (13)$$

$$[R_1{-}O^-\cdots H^+\cdots {}^-O{-}R_2] \xrightarrow{k_2} R_2{-}O^- + R_1{-}OH \quad (14)$$

Table I shows MS/MS product spectra of proton-bound dimers formed from 3-pentanol, which is used as the reference acid, and in separate experiments, each of four isomers of methylcyclohexanol. In each case the metastable proton-bound dimer dissociates to give just two fragment ions, the 3-pentoxide ion, *m/z* 87, and the (methylcyclohexyl)oxy ion, *m/z* 113. The abundance of the alkoxide anion of 3-pentanol is much lower than that of the anion of *cis*-2-methylcyclohexanol, comparable in the cases of *trans*-2-methylcyclohexanol and *cis*-4-methylcyclohexanol, and significantly more abundant than the anion generated from *trans*-4-methylcyclohexanol (Table I). The abundances evidently reflect different gas-phase acidities of the four isomers of methylcyclohexanol. Comparison of the ratios of relative abundances of the alkoxide anions given in Table I reveals that the ratio for *trans*-2-methylcyclohexanol, referenced to 3-pentanol, is identical, within experimental error, to that of *cis*-4-methylcyclohexanol referenced to the same compound. Therefore, the gas-phase acidities of these two positional isomers of methylcyclohexanol must be identical or very similar to each other.

Table I. Abundance of Isomeric (Methylcyclohexyl)oxy Ions ($C_7H_{13}O^-$) Relative to 3-Pentoxide Measured in CID Spectra of Proton-Bound Dimers Composed of Diastereomeric Alcohols

	2-methylcyclohexanol		4-methylcyclohexanol	
	cis	trans	cis	trans
$[C_7H_{13}O^-]/[C_5H_{11}O^-]$	5.32	1.11	1.08	0.19

Table II. Gas-Phase Acidity Values of Alcohols[a]

alcohol	ΔG°_{acid}	alcohol	ΔG°_{acid}
1-propanol	368.1	3-pentanol	365.2
1-butanol	367.1	2-methyl-3-pentanol	364.2
1-pentanol	366.2	2,4-dimethyl-3-pentanol	363.6
1-hexanol	365.6	*tert*-butyl alcohol	366.6
1-octanol	364.5	2-methyl-2-butanol	365.4
2-propanol	367.7	3-methyl-3-pentanol	364.6
2-butanol	366.3	3-ethyl-3-pentanol	363.7

[a] In kcal/mol from ref 28.

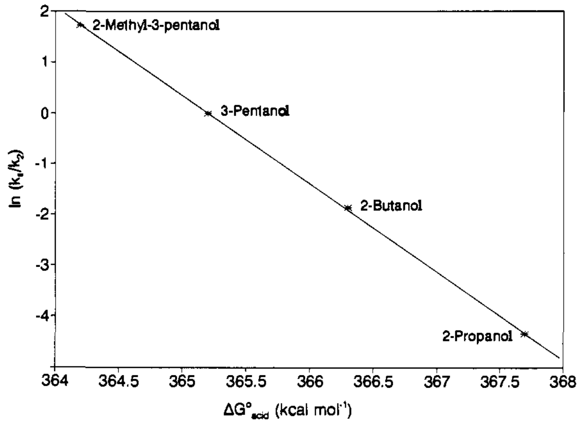


Figure 1. Plot of the logarithm of relative rates of metastable dissociation of proton-bound dimers of a series of secondary alcohols vs gas-phase acidity, using 3-pentanol as the reference acid (T_{eff} = 290 K; r = 0.998).

From Table I is also clear that the ratio of the relative abundance of alkoxide anions of *cis*-2-methylcyclohexanol to 3-pentanol is the reciprocal of the ratio of the relative abundance of the alkoxide anions of *trans*-4-methylcyclohexanol to 3-pentanol. This means that the absolute magnitude of the differences between the acidities of 3-pentanol and the two positional isomers of methylcyclohexanol are very similar, *cis*-2-methylcyclohexanol being a stronger acid and *trans*-4-methylcyclohexanol being a weaker acid than 3-pentanol. On the basis of Figure 1, the four isomers of cyclohexanol can be arranged in order of their gas-phase acidities as *cis*-2-methylcyclohexanol > *trans*-2-methylcyclohexanol, *cis*-4-methylcyclohexanol > *trans*-4-methylcyclohexanol.

The relative abundances $[A^-]/[B^-]$ of the alkoxide ions can often be measured from the MS/MS product spectrum with adequate precision. When this is the case, the ratio $[A^-]/[B^-]$ is measured directly from the MS/MS spectrum of the proton-bound dimer of the compound of interest and a reference compound of known gas-phase basicity as in Table I. A plot of $\ln\{[A^-]/[B^-]\}$ vs. ΔG°_{acid} values[31] (Table II) then provides a reference calibration line with slope $1/RT$ according to eq 10. Such a plot is shown in Figure 1 for a number of proton-bound dimers of secondary alcohols. Linear regression analysis of the plot gives the following equation:

$$\ln(k_{-1}/k_2) = \ln\{[A^-]/[B^-]\} = -1.73\Delta G^\circ_{acid} + 632 \qquad (15)$$

with a correlation coefficient of 0.998. The gas-phase acidity value of a compound of interest can therefore be determined by examining the fragmentation of a cluster ion produced by using a reference acid and then measuring the logarithm of the experimental $k_1/k_2 = [A^-]/[B^-]$ ratio.

This direct method does not work when the ratio $[A^-]/[B^-]$ is large (i.e., the difference in gas-phase acidities of the two species is high). In that case one can utilize an indirect method which

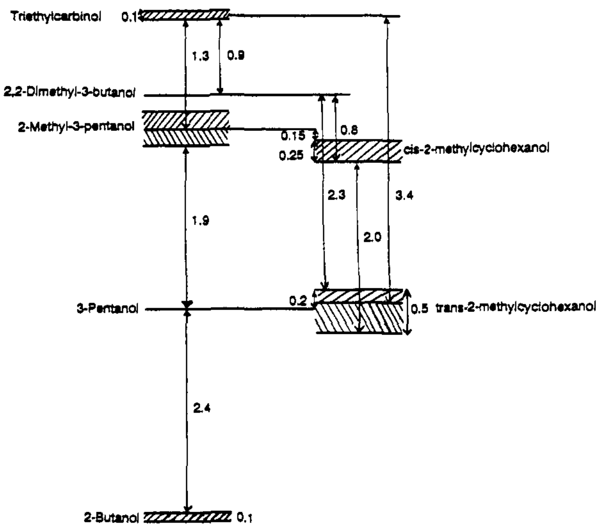
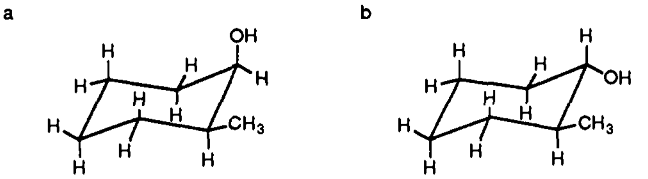


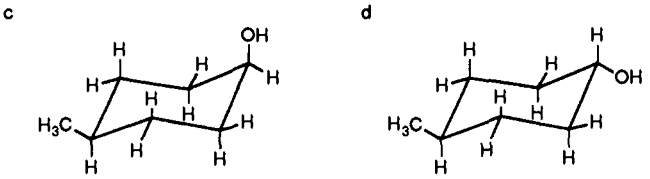
Figure 2. Multiple measurements used to estimate the relative acidities of secondary alcohols by the indirect method.

Scheme I



cis-2-methylcyclohexanol
ΔG°_{acid} = 364.1 ± 0.1 kcal/mol

trans-2-methylcyclohexanol
ΔG°_{acid} = 365.1 ± 0.1 kcal/mol



cis-4-methylcyclohexanol
ΔG°_{acid} = 365.1 ± 0.1 kcal/mol

trans-4-methylcyclohexanol
ΔG°_{acid} = 366.2 ± 0.1 kcal/mol

employs an intermediate compound (C) to measure the ratio $[A^-]/[B^-]$ so that

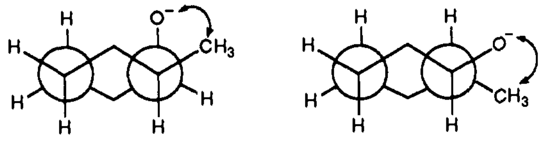
$$[A^-]/[B^-] = ([A^-]/[C^-])([C^-]/[B^-]) \qquad (16)$$

$$\Delta G^\circ_{acid}(BH) - \Delta G^\circ_{acid}(AH) = \Delta G^\circ_{acid}(CH) - \Delta G^\circ_{acid}(AH) + \Delta G^\circ_{acid}(BH) - \Delta G^\circ_{acid}(CH) \qquad (17)$$

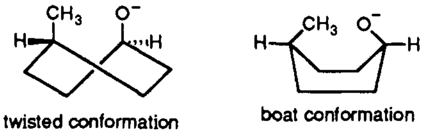
The indirect method is associated with increased uncertainties, since errors accumulate in the individual steps, but it is a way to extend the range of ΔG°_{acid} values accessed. Figure 2 shows the relative gas-phase acidities of several secondary alcohols by using cyclopentanol and cyclohexanol as intermediate reference compounds. For a given alcohol, multiple determinations made using the indirect method show that the reproducibility of the acidity value varied from ±0.1 to ±0.5 kcal/mol, as indicated by the shaded area of Figure 2. The following discussion is divided into two parts for convenience.

Gas-Phase Acidities of Epimers. ΔG°_{acid} values of four isomers a–d of methyl-substituted cyclohexanol are estimated in this study using the direct method with 3-pentanol as the reference compound (Figure 1). The structures and the measured ΔG°_{acid} values are shown in Scheme I. It is assumed that the greater steric bulk of the methyl group forces it to occupy the equatorial position in the chair conformation. Hence the hydroxyl group is axial in the cis isomer and equatorial in the trans isomer. Increased stabilization of the negative charge on the oxygen atom of the alkoxide anion is expected to be the leading factor for increasing the strength of an acid (i.e., lowering ΔG°_{acid} values). Comparing the ΔG°_{acid} values for the two sets of epimers, a vs b and c vs d, it is clear that in both cases the cis isomer is a stronger acid, by approximately 1 kcal/mol, than the corresponding trans isomer.

Scheme II



Scheme III



twisted conformation

boat conformation

By examining Dreiding models and Newman representations (Scheme II), it is clear that gauche O^-/CH_3 steric interactions occur for the cis a and trans b isomeric alkoxides. However, since identical distances characterize the $H_3C\cdots O^-$ neighboring groups for both diastereoisomeric anions, comparable polarization of the methyl group at C_2 takes place and results in similar stabilization of the alkoxide site, viz., the effect is independent of stereochemistry. Similar stabilization cannot occur for the cis/trans pair of (4-methylcyclohexyl)oxy ions (c and d, in chair conformations) because the CH_3 and O^- groups are too far apart. Note that, for the 1,4-methyl alkoxide c, the $H_3C\cdots O^-$ distance decreases significantly for more coiled conformations (i.e., less stable conformations such as the twist and boat forms, Scheme III). Nevertheless, the methyl groups is not directly responsible for the differences in acidity of the *epimeric* pairs since similar increases in acidity characterize both cis isomeric ions (from a and c) independently of the $H_3C\cdots O^-$ distance.

The stereochemical effect might be due to stabilization by the 1,3-diaxial interactions with the hydrogen atoms in positions 3 and 5 of the six-membered ring. However, such through-space solvation is not likely to make a large contribution to stabilization of cis a and trans b isomeric alkoxides because of the large $O^-\cdots H$ distances and because these are not acidic hydrogens and so cannot participate effectively in hydrogen bonding. Another stereochemical effect influencing the rate constants of competitive dissociations of the proton-bound dimers is the lower stability of the $O^-_{axial}\cdots H^+$ bond (resulting from steric effects) relative to the $O^-_{equatorial}\cdots H^+$ bond in the proton-bound dimer. This will enhance the rate constant for the $O^-_{axial}\cdots H^+$ bond dissociation. However, we suggest that the main reason for the enhanced acidity of the axial alcohols (a and c) is *hyperconjugative stabilization* in the alkoxides as has been proposed by DeFrees et al.[34] to explain the lower acidity of CD_3OH relative to that of CH_3OH. This results in a resonance form which is formally analogous to an ion/molecule complex:

$$R_1R_2CH\text{-}O^- \leftrightarrow [R_1R_2C{=}O,H^-]$$

In the case of cyclic axial alkoxides, 1,3-diaxial interactions (with the CH_3 group occupying the equatorial position) yield a greater steric effect than in the corresponding equatorial alkoxides. Consequently, a greater steric decompression of the axial alkoxide is allowed by the proposed hyperconjugative effect, since the ion/dipole complex contains a carbonyl group in a quasi-equatorial orientation (Scheme IV). Such a steric effect is weaker when the alkoxide is in the equatorial conformation and the resonance contribution of the ion/dipole complex occurs to a smaller extent. A related argument was used by Schwarz et al.[35] to rationalize the absence of stereochemical effects during HD elimination from deprotonated *endo*- and *exo*-3-deuterioborneols. This is because

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(34) DeFrees, D. J.; Bartmess, J. E.; Kim, J. K.; McIver, R. T. Jr.; Hehre, W. J. *J. Am. Chem. Soc.* **1977**, *99*, 6451.

(35) Sülzle, D.; Schwarz, H. *Helv. Chim. Acta* **1989**, *72*, 320.

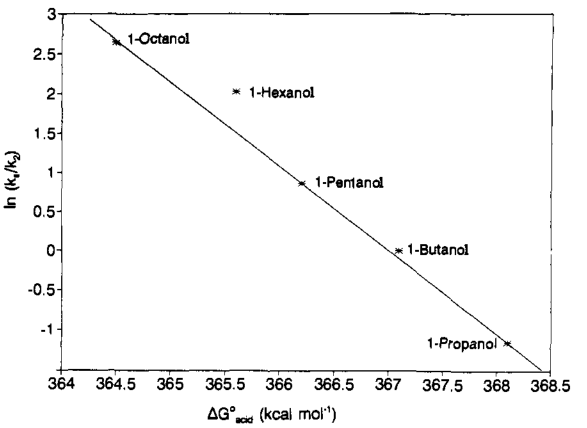
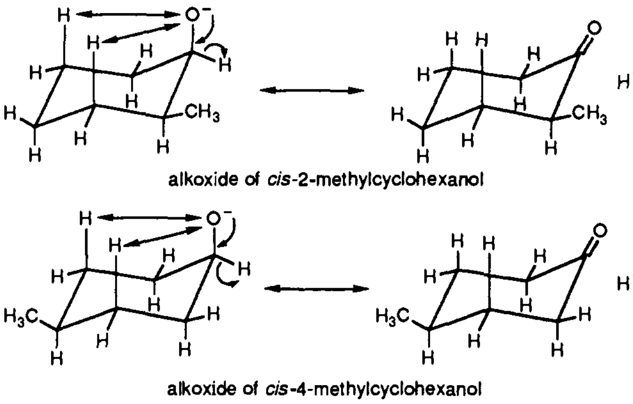


Figure 3. Calibration curve consisting of the logarithm of relative rates of metastable dissociation of proton-bound dimers of a series of primary alcohols vs gas-phase acidity. 1-Butanol is used as the reference compound (T_{eff} = 480 K; r = 0.978).

Scheme IV



in labeled borneols the ion/dipole intermediate leads to loss of stereochemical distinction and consequently HD loss is independent of deuterium stereochemistry.

Both epimers of 2-methylcyclohexanol display lower $\Delta G°_{\mathrm{acid}}$ values compared to the epimers of 4-methylcyclohexanol. The fact that the position of the methyl group in the six-membered ring also affects gas-phase acidity can be explained by interactions with the methyl groups which are only possible in the 2-methyl isomers. In both *cis*-2-methylcyclohexanol a and *trans*-2-methylcyclohexanol b the alkoxide anion is stabilized by a gauche interaction with the methyl hydrogens, as shown in Scheme II. The extent of gauche interaction due to the methyl group is similar in both a and b. In the epimers of 4-methylcyclohexanol, the methyl group is far away from the functional group and hence such interactions are impossible.

The $\Delta G°_{\mathrm{acid}}$ values of the isomeric methylcyclohexanols, shown in Scheme I, demonstrate that the kinetic method can be confidently used to distinguish isomers having small $\Delta G°_{\mathrm{acid}}$ differences.

Structural Effects on Effective Temperature. The term T in eqs 9–12 is an effective temperature rather than an actual temperature when the dissociating proton-bound dimer ions have a non-Boltzmann distribution of internal energies.[17] The magnitude of the effective temperature for a chemical system can be determined from the slope $1/RT$ of the calibration line. The lower the effective temperature, the more sensitive is the ion abundance ratio to differences in gas-phase acidities. For this reason, metastable ions, which have low internal energies, allow small differences in gas-phase acidity to be distinguished. Note that while lower effective temperatures are desirable as a means of increasing sensitivity to differences in gas-phase acidities, the range of values that can be accessed is reduced correspondingly. These effects can be seen by comparing the metastable-ion data with CID data. An increase in effective temperature is observed when the experiment is done under CID conditions compared to that observed under metastable-ion conditions. Figure 4 shows the calibration curve which results from single-collision CID conditions for the same primary alcohols shown in Figure 3. A net increase of 30 K is observed by moving from metastable conditions to the low target pressure (5×10^{-6} Torr) CID conditions for the homogeneous system of primary alcohols. Similar results have been reported[36] for experiments performed at different target pressures and at more elevated collision energies. These increases in effective temperature represent increases in internal energy of the ions as a result of increasing collision pressure or collision energy.

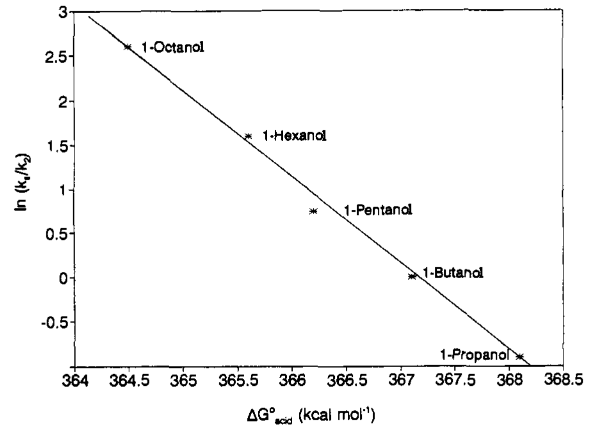


Figure 4. Calibration curve consisting of the logarithm of relative rates of collision-induced dissociation of proton-bound dimers of a series of primary alcohols vs gas-phase acidity. 1-Butanol is used as the reference compound (T_{eff} = 510 K; r = 0.994).

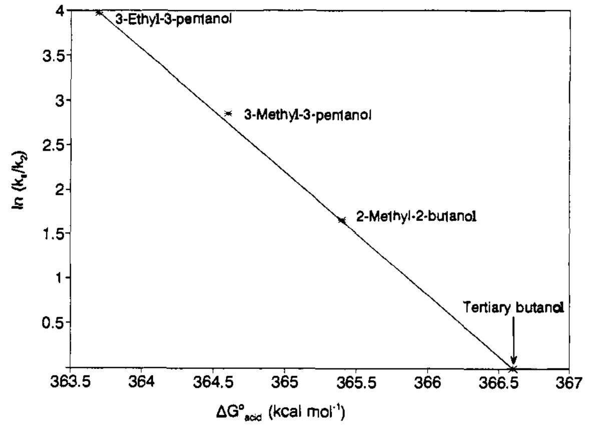


Figure 5. Plot of the logarithm of relative rates of metastable dissociation of proton-bound dimers of a series of tertiary alcohols vs gas-phase acidity, using *tert*-butyl alcohol as the reference compound (T_{eff} = 360 K; r = 0.997).

The calibration line for secondary alcohols (using 3-pentanol as the reference compound) shown in Figure 1 has a correlation coefficient of 0.998 and a slope of −1.73, which gives an effective temperature of 290 K. A least-squares fit of the data for primary alcohols using 1-butanol as the reference compound (Figure 3) also yields a straight line, with a correlation coefficient 0.978 and an effective temperature of 480 K. Thus, metastable decompositions of the proton-bound dimers of two different types of alcohols display different effective temperatures even though the experiments were done under the same experimental conditions. This finding indicates that effective temperatures depend in detail on the structure of the proton-bound species.

In order to check the effects of structural variations of alcohols on effective temperature, primary, secondary, and tertiary alcohols

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[36] McLuckey, S. A.; Cooks, R. G.; Fulford, J. E. *Int. J. Mass Spectrom. Ion Phys.* **1983**, *52*, 165.

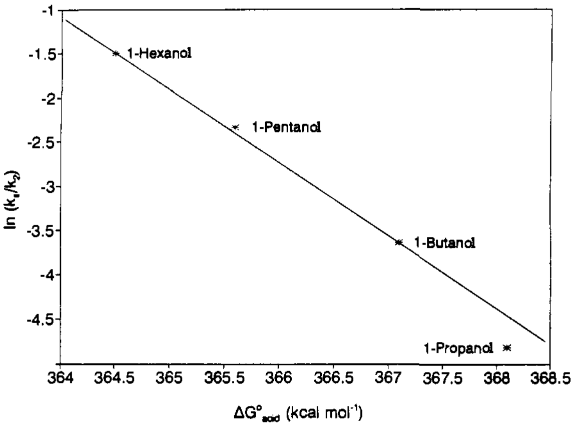

Figure 6. Plot of the logarithm of relative rates of metastable dissociation of mixed proton-bound dimers of primary and secondary alcohols vs gas-phase acidity, using 3-pentanol as the reference compound (T_{eff} = 610 K; r = 0.995).

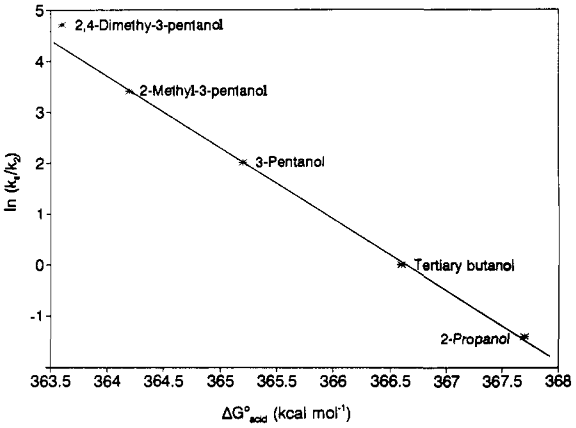

Figure 7. Plot of the logarithm of relative rates of metastable dissociation of mixed proton-bound dimers of secondary and tertiary alcohols vs gas-phase acidity, using *tert*-butyl alcohol as the reference alcohol (T_{eff} = 360 K; r = 0.998).

Table III. Effective Temperatures T Calculated for Proton-Bound Dimer Systems of Different Alcohols

proton-bound alkoxide ions	T (K) TSQ	T (K) Nermag
(primary)·H^+·(primary)	480	420[a]
(secondary)·H^+·(secondary)	290	330[b]
(tertiary)·H^+·(tertiary)	360	320[c]
(primary)·H^+·(secondary)	610	610[d]
(secondary)·H^+·(tertiary)	360	310[e]

[a] 1-Butanol is used as the reference alcohol. [b] 2-Propanol is used as the reference alcohol. [c] *tert*-Butyl alcohol is used as the reference alcohol. [d] 2-Butanol is used as the reference alcohol. [e] *tert*-Butyl alcohol is used as the reference alcohol.

were studied under the same experimental conditions. Metastable dissociations of dimers made up of pairs of tertiary alkoxide anions bound via a proton gave a straight line with a correlation coefficient of 0.997 and an effective temperature of 360 K (Figure 5). Dissociation of the heterogeneous system having primary alkoxide anions proton-bound to secondary alkoxide anions yielded an effective temperature of 610 K (Figure 6), and systems having secondary alkoxide anions proton-bound to tertiary alkoxide anions gave an effective temperature of 360 K (Figure 7). The effective temperatures obtained by metastable decomposition of various proton-bound dimer systems are summarized in Table III. It is evident from Table III that, for homogeneous proton-bound dimers, alkyl substitution at the carbon atom bearing the hydroxyl group has considerable influence on the effective temperature. The effect depends on the number of substituted alkyl groups, the largest effect being observed upon a single alkyl substitution.

These experiments were repeated using a Nermag triple-quadrupole mass spectrometer, and the results are reported in the third column of Table III. The magnitudes of the effective temperatures obtained from the two instruments vary by as much as 60 K for metastable dissociation of the proton-bound dimer of primary alcohols. These differences are not unexpected in view of minor variations in experimental conditions, including the different time scales of the two instruments. The effective temperatures obtained using the Nermag instrument are typically lower than those measured with the Finnigan instrument. Note that this agreement was achieved even though the reference compounds used in the Nermag instrument are 2-propanol in the case of a proton-bound cluster ion of secondary alcohols and 2-butanol in the case of a proton-bound cluster ion of primary and secondary alcohols, whereas 3-pentanol was used in both cases when the Finnigan TSQ instrument was used. In this context it is important to note that the magnitude of the effective temperature is sensitive to experimental conditions as well as to the choice of the reference compound.

In order to explain the variations in effective temperatures with the type of alcohol (primary, secondary, or tertiary) one must recall the assumptions which underlie the kinetic method. In this approximation, the logarithm of the rate constant is given from eq 7 as

$$\ln (k_1/k_2) = \ln [\Pi_j\{1 - \exp(-h\nu^*_{1j}/kT)\}]/[\Pi_j\{1 - \exp(-h\nu^*_{2j}/kT)\}] + \Delta\epsilon^\circ/RT \quad (18)$$

and the application of the method requires separation of the vibrational frequency of the hydrogen bond, ν^*, and the activation energy, ϵ°, of the proton-bound dimer. That is, a direct relationship between ln (k_1/k_2) and the effective temperature T holds only when $\nu^*_{1j} = \nu^*_{2j}$. In the case of proton-bound dimers comprising different types of alcohols, frequency factors will be different and not separable from the activation energy as required by the simplified eq 18. This is clearly the case for dimers comprising different functional groups, and its extension to cases of the same functional group (alcohols) of different types (primary, secondary, and tertiary) is therefore not surprising. A single earlier instance of this behavior has been reported in the case of the formate anions,[37] where the anomalous effects observed were ascribed to entropic effects not possible in the other carboxylates. In order to observe accurate results from the kinetic method, the proton-bound species should be as similar as possible. A dimer involving different types of functional groups bound to the proton is likely to result in different frequency factors in its dissociation.

Conclusion

The gas-phase acidities of the epimers *cis*- and *trans*-2-methylcyclohexanol and *cis*- and *trans*-4-methylcyclohexanol can be distinguished by the kinetic method. In both cases the cis isomers (with axial OH stereochemistry) show lower ΔG°_{acid} values (greater acidity) than the corresponding trans isomers (with equatorial OH stereochemistry), and this is suggested to be a result of extensive hyperconjugative stabilization of the alkoxide anion promoted by steric decompression (relieving 1,3-diaxial interactions) and yielding hyperconjugative resonance structures ($CH-O^- \leftrightarrow C=O, H^-$) with quasi-equatorial stereochemistry. Both epimers of 2-methylcyclohexanol have lower ΔG°_{acid} values than those of 4-methylcyclohexanol. This observation is interpreted as a consequence of stabilization of the alkoxide anion in the former species due to interactions with the methyl group in the 2-position such as reported for branched alcohols.[31]

Results obtained in this study indicate that the kinetic method is very sensitive to small differences in gas-phase acidity. This is consistent with previous results on various systems,[37] and it facilitates the distinction of isomeric compounds. Changes in the type of alcohol geminal substitution cause noticeable effects on the relative rates of competitive dissociation of the cluster ions.

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(37) Wright, L. G.; McLuckey, S. A.; Cooks, R. G.; Wood, K. V. *Int. J. Mass Spectrom. Ion Phys.* **1982**, *42*, 115.

J. Am. Chem. Soc. 1992, 114, 2903-2909

This is seen readily when the effective temperatures from metastable dissociation of proton-bound dimers are considered. The largest effective temperature is observed when the dimer is made up of a primary alcohol proton-bound to a secondary alcohol and the smallest when only secondary alcohols are used. These findings are interpreted as a consequence of different geminal substitution patterns of alcohols affecting the vibrational states of the proton-bound dimer and hence providing an entropic factor which operates together with the enthalpic product stability factor on which the kinetic method is based. As the results show, it is possible to avoid this difficulty and obtain precise gas-phase acidities by using alcohols of the same structural types as reference compounds.

Acknowledgment. This work was supported by the National Science Foundation (Grant CHE 87-21768).

Electronic Structure of the Transition-Metal–Carbene-like Complexes $(CO)_5Mo–M'H_2$ (M' = C, Si, Ge, and Sn). A Theoretical Study Based on ab Initio CASSCF Calculations

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Abstract: A theoretical study of the bond between a transition metal and an element of group 14 is reported. Based on quantum-mechanical calculations carried out at Hartree–Fock SCF and CASSCF levels, the molecular structure of the series $(CO)_5Mo{=}M'H_2$, M' = C, Si, Ge, and Sn, has been determined. The $Mo{=}M'$ double-bond structure corresponds to the well-known sp_σ-donor/p_π-acceptor scheme, which becomes less efficient for the heavier terms of the series. Evolution of geometrical parameters is discussed and found in excellent agreement with experimental trends. In particular, the lowering of the $H–M'–H$ bond angle is well described and appears to be related to the different mix of the M' s and p orbitals. Dissociation energies, potential energy profiles for the dissociation process yielding $(CO)Mo_5$ and $M'H_2$, rotational barriers of the $M'H_2$ ligand around the 4-fold axis of the $(CO)Mo_5$ fragment, and force constants associated to the $Mo{=}M'$ bond stretch are also reported.

Introduction

The nature of the metal–metal bond in heterobi- or heteropolymetallic complexes has been a topic of growing interest in the last few years. The reactivity and potential activity of these compounds in organometallic synthesis are the subject nowadays of considerable work, both experimental and theoretical.[1] From a structural viewpoint, the main interest is constituted by the exciting properties of the metal–metal bond. Among dinuclear compounds, those showing a bond between a transition metal and a metal of group 14 fall into a special category. For instance, transition-metal–tin compounds are in fact heterodinuclear species, but they can be seen as a special type of organometallic complex in which a carbon atom has been replaced by tin. Therefore, it seems reasonable to assume an a priori rationalization of their structural properties on the grounds of their carbon parents.

Since the work of Marks[2,3] in 1971, the chemistry of divalent germanium, tin, and, to a lesser extent, silicon and lead homologues of metal carbenes $L_nM{=}M'XY$, has been the subject of considerable experimental work and has been summarized in excellent review articles.[4] In spite of all this experimental work, the nature of these metal–metal bonds remains somewhat uncertain, in particular as far as the metal–metal double-bond features are concerned.

Metal–carbon double bonding in metallic carbenes has focused the attention of several theoretical works and the notion seems to be well established.[5] Thus, the structure of naked transition-metal carbenes has been carefully analyzed,[6] and experimental data of their thermochemistry are also available.[7] For obvious technical reasons, theoretical calculations on more realistic compounds in which the transition metal has its coordination capabilities fulfilled (typically carbonyl derivatives $(CO)_nM{=}CXY$) are scarce[6a,8] and often based on the approximated Fenske–Hall method.[9] In fact, only a few numbers of Cr, Mo, Ni, and Fe carbonyl carbenes have been examined at an ab initio level of

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(1) For recent reviews, see: (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. (b) Stephan, D. W. *Coord. Chem. Rev.* **1989**, *95*, 41. (c) Adams, R. D. *Chem. Rev.* **1989**, *89*, 1703. (d) *The Chemistry of Heteronuclear Clusters and Multimetallic Catalists*; Adams, R. D., Herrmann, W. A., Eds. *Polyhedron* **1988**, *7*, 2251. (e) Zanello, P. *Coord. Chem. Rev.* **1988**, *87*, 1.

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