Resolution enhancement by Lorentzian to Gaussian conversion[12] was employed in the F_1 dimension, sacrificing some sensitivity but giving line widths of less than 0.5 Hz. Six long-range couplings are evident in Figure 2, any others being judged to be less than about 0.2 Hz from the absence of broadening on the appropriate carbon-13 resonances. The weak artifacts at $F_1 = 0$ are due to pulse imperfections and the tails of nearby carbon-13 lines. An indication of the complexity of the conventional proton-coupled carbon-13 spectrum is provided by the multiplets from sites d and e (bottom trace).

Although two-dimensional spectra may have somewhat poorer sensitivity than the corresponding one-dimensional spectra acquired in the same total time,[13] this is more than offset in the present experiment by the considerable reduction in the number of times a given carbon-13 resonance is split. However, a single two-dimensional experiment of this kind measures long-range coupling to only one proton site, so the experiment may need to be repeated, and not all proton sites are necessarily accessible. Strong coupling effects are evident in the conventional carbon-13 spectrum (particularly at the methylene sites), but it is expected that the corresponding distortions of the two-dimensional spectrum will be less serious since only one proton is flipped.[14] Nevertheless, care should be exercised in interpreting the observed CH splittings when the protons are strongly coupled.

The proposed technique looks promising for precise measurements of long-range heteronuclear spin–spin coupling constants and for their assignment. The key factor is the simplicity of the multiplets (doublets, triplets, quartets) since each long-range coupling is displayed separately. Sensitivity can be higher than the conventional proton-coupled spectrum.

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Registry No. Carvone, 99-49-0.

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Bridging the Gap between the Gas Phase and Solution: Transition in the Kinetics of Acid–Base Reactions

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Recent gas-phase investigations of ion–molecule reactions have provided an important new dimension to the acid–base chemistry of anions in solution; it has become possible to execute solution acid–base reactions of type 1 in the complete absence of solvent

$$B^- + AH \rightleftarrows A^- + BH \qquad (1)$$

and to scrutinize the influence of solvent as a function of stepwise solvation with studies of reactions of type 2. Equilibrium constant

$$B^-\cdot S_n + AH \rightleftarrows A^-\cdot S_n + BH \qquad (2)$$

measurements for reactions of type 1 have allowed the determination of relative intrinsic acidities of molecules[1] whereas similar measurements for reactions of type 2 have provided a means to follow changes in relative acidities with added solvent.[2] Here we report the first attempt to follow systematically the transition in the *rate* of acid–base reactions which ensues from the stepwise solvation of B^-. Hydrated hydroxide ions and methoxide ions solvated with methanol were chosen for study because of their importance as bases in solution. Their gas-phase reactivities are followed from the total absence of solvent to solvation with up to three molecules of solvent. The acids chosen as substrates have allowed us to establish trends in reactivity when relative acidity is preserved and to observe the abrupt change in rate which accompanies a reversal in relative acidity upon solvation.

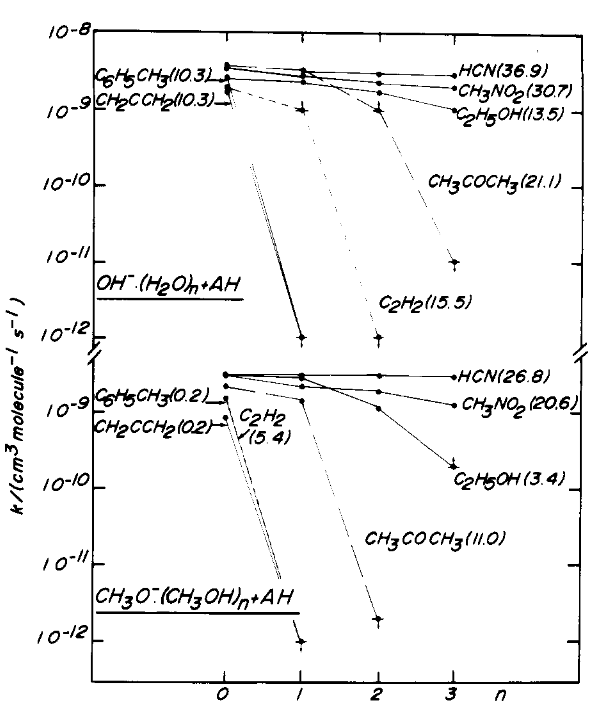

Figure 1. Observed variations in the rate constants at 298 K for acid–base reactions in the gas phase between the acids AH = allene, toluene, ethanol, acetylene, acetone, nitromethane, and hydrogen cyanide and hydrated hydroxide ions (top) and methoxide ions solvated with methanol (bottom). The reactions with acetone and hydrogen cyanide in the upper graph involve $OD^-\cdot(D_2O)_n$. The accuracy of the rate constants is better than ±50%. The values indicated in parentheses correspond to the relative intrinsic acidities, in kcal mol^{-1}, i.e., $-\Delta G^\circ$ for the solvent-free reactions at 298 K. For all of the reactions with $k \geq 10^{-10}$ cm^3 molecule^{-1} s^{-1}, formation of product ions of the type $A^-\cdot S_n$ was observed concomitant with the disappearance of the reactant ions $OH^-\cdot(H_2O)_n$ or $CH_3O^-\cdot(CH_3OH)_n$.

The measurements were carried out with the flowing afterglow technique.[3] Hydroxide (or OD^-) ions and methoxide ions were generated by electron impact on H_2O (or D_2O) and CH_3OH upstream in a flowing He or H_2 plasma at total pressures of ca. 0.4 torr. The ions were solvated by reactions of type 3 and

$$B^-\cdot S_n + S + He(H_2) \rightarrow B^-\cdot S_{n+1} + He(H_2) \qquad (3)$$

thermalized by collisions with the buffer molecules prior to the reaction region. Partial pressures of added solvent were in the range 0.005–2 mtorr. The decays of the $B^-\cdot S_n$ ions and the formation of the $A^-\cdot S_n$ ions were monitored as a function of the additon of AH (in order of increasing intrinsic acidity): allene, toluene, ethanol, acetylene, acetone, nitromethane, and hydrogen cyanide. Rate constants were derived in the usual manner from the observed decays of $B^-\cdot S_n$.[4] The results are indicated in Figure 1.

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(4) The initial relative population of the cluster ions, $B^-\cdot S_n$, was dependent on the amount of added solvent vapor. Complications which arose due to the depletion of the precurser ions, $B^-\cdot S_{n-1}$, were taken into account in the analysis of the decay of $B^-\cdot S_n$. Also contributions to the measured ion signals due to the presence of the impurity ions $^{35}Cl^-\cdot(H_2O)_{n-1}$ were taken into account in the measurements of $OH^-\cdot(H_2O)_n$; the $^{37}Cl^-\cdot(H_2O)_{n-1}$ signals were measured concomitantly.

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The proton-transfer reactions of the solvent-free hydroxide and methoxide ions were all observed to proceed rapidly with rate constants $\gtrsim 10^{-9}$ cm^3 molecule^{-1} s^{-1}.[5] Solvation of the bare ions was observed to result either in a slight or a dramatic reduction in the rate of reaction, the latter occurring in some instances already after the addition of just one molecule of solvent. This remarkable divergence in behavior can be accounted for by a careful consideration of the degree of stabilization of the bare ions by solvation.[6] The solvent-free reactions are all exoergic: they span ranges in $-\Delta G°$ (i.e., relative intrinsic acidity) from 10.3 to 36.9 kcal mol^{-1} for the reactions with OH^- and from 0.2 to 26.8 kcal mol^{-1} for the reactions with CH_3O^-.[1,7] The free energies of solvation of the reactant ions act to decrease the reaction exoergicities and can lead to changes in the sign of $\Delta G°$ (reversals in relative acidity) and therefore changes in the preferred direction of reaction unless they are offset by the solvation energies of the conjugate bases produced.[8]

The carbanions produced by the deprotonation of allene and toluene, the acids closest in intrinsic acidity to water and methanol, are expected to have free energies of solvation insufficient to compensate for the high solvation free energies of OH^- and CH_3O^-.[9] The sharp (3 orders of magnitude) drop in the rate of deprotonation observed upon the addition of just one molecule of solvent is therefore a manifestation of a reversal in the relative acidity of these two carbon acids and water or methanol.

The addition of one methanol molecule to CH_3O^- causes an immediate reversal in the relative acidity of methanol and acetylene; reaction 4 was not observed. In contrast, the reversal in

$$CH_3O^- \cdot CH_3OH + C_2H_2 \nrightarrow C_2H^- \cdot CH_3OH + CH_3OH \qquad (4)$$

the relative acidity of water and acetylene is delayed by one solvent molecule; reaction 5 was observed to occur rapidly. Apparently

$$OH^- \cdot H_2O + C_2H_2 \rightarrow C_2H^- \cdot H_2O + H_2O \qquad (5)$$

the lower free energy of hydration by one water molecule expected for C_2H^- is compensated for by the higher relative intrinsic acidity of water and acetylene.[10]

For the deprotonation of acetone by OH^- and CH_3O^-, both reversals also occur, but they are delayed by one additional molecule of solvent; the sharp decline in the rate occurs at n = 3 and 2, respectively.[11]

No reversals are observed for the deprotonation of nitromethane, hydrogen cyanide, and ethanol; reaction 2 remains rapid up to the addition of three solvent molecules.[12] The intrinsic acidities of nitromethane and hydrogen cyanide are sufficiently high to offset the weaker anion–solvent interactions expected for $CH_2NO_2^-$ and CN^-.[13] In comparison, the intrinsic acidity of ethanol is relatively close to that of water and methanol, but in this case the order of acidity is preserved up to the addition of three solvent molecules by the strong solvation of $C_2H_5O^-$.[14]

The trends in the rates of the acid–base reactions of type 2 identified in this study are consistent with rate measurements made in solution[15] and with known solution acidities. Indeed, they provide a vivid confirmation of expectations on the basis of measurements made in solution. The approach which has been developed should be applicable to the investigation of transitions in the relative acidity of other acid pairs and with solvents other than water and methanol. However, a clear pattern has already emerged from the measurements reported here which may well be representative of the general transition in the rates of reactions of type 2 between the gas phase and solution.

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Registry No. Allene, 463-49-0; toluene, 108-88-3; ethanol, 64-17-5; acetylene, 74-86-2; acetone, 67-64-1; nitromethane, 75-52-5; hydrogen cyanide, 74-90-8; hydroxide ion, 14280-30-9; methoxide ion, 3315-60-4.

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(5) These large rate constants correspond to proton transfer at essentially every collision.

(6) The rate of proton transfer can be expected to remain high upon solvation if the reaction remains exoergic. Conversely, a sharp drop in the rate can be anticipated if solvation renders the reaction endoergic.

(7) The intrinsic acidity of allene has been established in our laboratory from a measurement of the equilibrium constant for its deprotonation by CH_3O^-.

(8) Exoergicity will be preserved upon solvation if the free energy of solvation of the conjugate base produced is comparable to or greater than the free energy of solvation of the reactant base or if a lower free energy of solvation of the product base is offset by the exoergicity of the unsolvated reaction.

(9) The free energies of solvation of OH^- by H_2O and CH_3O^- by CH_3OH are approximately 19 and 17 kcal mol^{-1}, respectively. The failure to observe reaction 2 for n = 1 implies free energies of solvation for $C_3H_3^-$ and $C_6H_5CH_2^-$ by H_2O and CH_3OH less than approximately 9 and 17 kcal mol^{-1}, respectively. The free energy of hydration of OH^- was taken from: Kebarle, P. *Annu. Rev. Phys. Chem.* **1977**, *28*, 445. The free energy of solvation of CH_3O^- by CH_3OH was deduced from the results reported in ref 2.

(10) The observation of reaction 5 implies a free energy of hydration for C_2H^- greater than approximately 3.5 kcal mol^{-1}. The equilibrium constant for this reaction appeared to be $\gtrsim 8 \times 10^2$ which raises the lower limit for the hydration free energy to $\sim$7.5 kcal mol^{-1}. Failure to observe the corresponding methanol reaction sets an upper limit of 13 kcal mol^{-1} to the solvation free energy of C_2H^- by CH_3OH.

(11) The decays observed for the $OH^- \cdot (H_2O)_2$ and $OH^- \cdot (H_2O)_3$ ions and their deuterated versions suggest that the reaction with n = 2 may be close to isoergic while the reaction with n = 3 may be only slightly endoergic.

(12) The slight decrease in the rate constants with added solvent observed for the reactions with HCN and CH_3NO_2 corresponds approximately to the decrease in the collision rate constant as calculated from the AADO theory (Su, T.; Su, E.C.F.; Bowers, M. T. *J. Chem. Phys.* **1978**, *69*, 2243). A similar situation exists in the case of ethanol except at the higher values of n where the rate constant appears to drop somewhat faster, presumably because the reactions become nearly isoergic. Our measurements indicate that the equilibrium constant for reaction 2 with $B^- = CH_3OH$, $S = CH_3OH$, and $AH = C_2H_5OH$ diminishes as n increases to a value of $\sim$1 for n = 3.

(13) In fact, the solvent-free reactions are sufficiently exoergic to allow at least the first solvent molecule to be "boiled off".

(14) When the free energies of solvation of the two bases are nearly equal, as is the case here for $OH^-/C_2H_5O^-$ and $CH_3O^-/C_2H_5O^-$, the reversal in relative acidity may be shifted to much higher additions of solvent. The location of these reversals are more accessible to experiments carried out at lower temperatures since solvent binding energies become progressively smaller as n increases.

(15) For example, the reaction between OH^- and HCN is rapid in aqueous solution, $k = 3.7 \times 10^9$ l mol^{-1} s^{-1}, while the reaction with CH_3COCH_3 is much slower, $k = 2.7 \times 10^{-1}$ l mol^{-1} s^{-1} (Eigen, M., *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1).

Stereo- and Regiocontrolled Synthesis of Methyl *N*-Acetyl-α-D-sibirosaminide

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The unique antitumor antibiotic sibiromycin[2] is a glycoside comprising a pyrrolo[1,4]benzodiazapene aglycon, sibiromycinone, and an unusual amino sugar sibirosamine, **8a**. Parker[3] has made significant synthetic advances toward the aglycon, and a synthesis of methyl *N*-acetyl-α-D-sibirosaminide (**8b**) was reported by Dyong and Shulte[4] while our work was in progress. In this communication

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