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pearance energy (AE_0) of Me_3Si^+ from HMDS and the heats of formation of Me_3Si^+ and HMDS. Unfortunately, the least accurately known term in the equation for BE(Si–Si) is AE_0, which is multiplied by 2 thereby doubling the uncertainty.

In order to improve on the accuracy of the Si–Si bond energy, we are in need of additional information. The most important and probably easiest method of obtaining this is through the ionization potential of Me_3Si. The Si–Si bond energy is related to the Me_3Si IP and well-known heats of formation via the relation

$$\mathrm{BE(Si{-}Si)} = 2\Delta H_f{}^\circ{}_0(\mathrm{Me_3Si^+}) - 2\mathrm{IP(Me_3Si)} - \Delta H_f{}^\circ{}_0(\mathrm{HMDS})$$

The Me_3Si IP is most often quoted or assumed to be about 7 eV. Our BE and AE_0 values yield an IP of 7.03 eV, while the Davidson and Stephenson BE implies an IP of 6.7 eV. Both are reasonable numbers in that they are lower than the measured IP of Me_3C of 7.4 eV.

It is interesting to compare the Si–Si bond energy in HMDS with the C–C bond energy in hexamethylethane. The latter, determined from thermochemical[20] and photoelectron spectroscopic data,[35] is 295.9 kJ/mol. It is thus evident that the Si–Si bond is somewhat weaker than the C–C bond. CNDO/2 calculations show that the $4a_{1g}$ orbital of these compounds has an $\gg$M–M$\ll$ character (localized bonding) which contributes 48.8% to the bonding in Me_3C–CMe_3 and 65.7% in Me_3Si–$SiMe_3$.[15] The higher degree of delocalization of the C–C bond is one of the factors that causes the C–C bond to be stronger than the Si–Si bond.

One of the major aims of this study was to investigate the applicability of the statistical theory to the dissociation of organometallic ions. Our data reveal no inconsistencies with the statistical theory. On the other hand, one might not expect to find nonstatistical energy flow in a molecule such as HMDS whose bond energy is only about 10% weaker than the corresponding C–C analogue. We plan on extending this study to the more metallic tin and germanium analogues in which the metal-to-metal bond energies are considerably less strong, and in which the presence of the heavy atoms may inhibit the free flow of vibrational energy.[36]

Acknowledgment. L. Szepes thanks the CIES for a Fulbright Grant and the University of North Carolina for its hospitality. This work was supported by a grant from the National Science Foundation.

Registry No. Me_6Si_2, 1450-14-2; Me_4Si, 75-76-3; Me_3SiCl, 75-77-4; Me_3SiBr, 2857-97-8; Me_3SiI, 16029-98-4; Me_2SiCl^+, 43641-60-7; Me_2SiBr^+, 43641-30-1; $Me_5Si_2^+$, 87862-42-8; Me_3Si^+, 28927-31-3; $Me_3Si\cdot$, 16571-41-8.

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(36) Lopez, V.; Marcus, R. A. *Chem. Phys. Lett.* **1982**, *93*, 232.

The Ionic Hydrogen Bond. 4. Intramolecular and Multiple Bonds. Protonation and Complexes of Amides and Amino Acid Derivatives

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Contribution from the Chemical Thermodynamics Division, Center for Chemical Physics, National Bureau of Standards, Washington, DC 20234. *Received August 29, 1983*

Abstract: The thermochemistry of protonation and ion-neutral interactions of $CH_3CON(CH_3)_2$ (DMA) and of the peptide-like alanine derivative $CH_3CONHCH(CH_3)COOCH_3$ (**1**) are models for ionic interactions in proteins. High proton affinity and negative entropy of protonation of **1** vs. DMA indicate intramolecular hydrogen bonding in $\mathbf{1}H^+$. The intermolecular bond in $\mathbf{1}H^+$, i.e., in

$$CH_3CO\overset{\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots}{H^+NHCH(CH_3)CO}OCH_3$$

stabilizes this ion by 7 kcal mol^{-1}. However, the internal hydrogen bond decreases the availability of the proton for external hydrogen bonding. Thus, the attachment energy of H_2O to $\mathbf{1}H^+$, 13.0 kcal mol^{-1}, is lower than that to $DMAH^+$, 16.5 kcal mol^{-1}. The thermochemistry of the $\mathbf{1}H^+\cdot H_2O$ complex suggests a T-shaped structure, or one where H_2O bridges between the two carbonyl groups. In other complexes **1** can serve as a neutral ligand. In such a complex, $CH_3NH_3{}^+\cdot\mathbf{1}$, the unusually large experimental enthalpy of complexation, −40.1 kcal mol^{-1}, suggests multiple hydrogen bonding. These results, combined with the thermochemistry of protonated amide dimers, suggest that intramolecular and multiple ionic hydrogen bonds can contribute significantly to the stabilities of ionic intermediates in protein and enzyme environments. Such contributions can range, per single hydrogen bond, from 5 kcal mol^{-1} for strained and distorted bonds to 30 kcal mol^{-1} for geometrically optimized bonds.

Many organic and enzymic reactions proceed through protonated intermediates. The proton affinities of complex molecules and the interactions of the protonated species with polar ligands therefore can be important in bioenergetics.[1] This paper examines the proton affinities and ionic hydrogen bonding of some amides and of the N-acetylated amino acid derivative $CH_3CONHCH(CH_3)COOCH_3$, (CH_3CO-Ala-OCH_3, also denoted here as compound **1**). The thermochemistry of these species can serve as a model for the energetics of protonated intermediates in acid hydrolysis of amides and the energetics of protonated amide groups in proteins.

The present paper continues a series of studies on both the intramolecular and intermolecular hydrogen bonding interactions of polyfunctional ions.[2-4] In those studies, the proton affinities, entropies of protonation, and ionic hydrogen bonding of the polyfunctional species are compared with those of model mono-

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(1) Warshel, A. *Acc. Chem. Res.* **1981**, *14*, 284.

(2) Yamdagni, R.; Kebarle, P. *J. Am. Chem. Soc.* **1973**, *95*, 3504.

(3) Meot-Ner (Mautner), M.; Hamlet, P.; Hunter, E. P.; Field, F. M. *J. Am. Chem. Soc.* **1980**, *102*, 6393.

(4) Meot-Ner (Mautner), M., *J. Am. Chem. Soc.* **1983**, *105*, 4906, 4912.

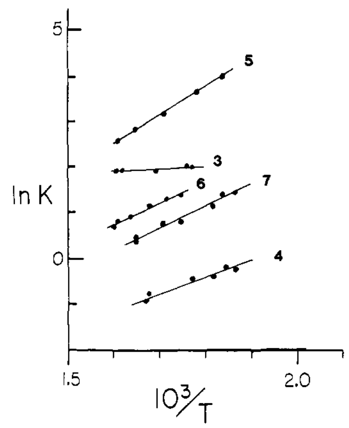

Figure 1. van't Hoff plots for proton-transfer equilibria. Numbers refer to reactions in Table I.

functional molecules. The comparisons show that intramolecular hydrogen bonding can stabilize polyfunctional ions by 5–30 kcal mol^{-1} and lead to negative entropies of protonation as large as −20 cal mol^{-1} K^{-1}. It is also observed that where internal hydrogen bonding occurs, it weakens, hydrogen bonding in external solvents. For example, compared with the hydration of $CH_3CH_2CH_2NH_3^+$, the hydration of

$$\overset{\text{..............................}}{\mathrm{H_2\dot{N}CH_2CH_2CH_2NH_3^+}}$$

by one H_2O molecule is weakened by 3 kcal mol^{-1} due to delocalization by the internal hydrogen bond.[3] On the other hand, when a polyfunctional molecule serves as a ligand to a protonated species, such as in RNH_3^+·polyether and RNH_3^+·crown ether complexes, multiple hydrogen bonding can occur. This can lead to exceptionally strongly bonded complexes, with dissociation energies ($\Delta H°_D$) ranging up to 45 kcal mol^{-1}.

Since the study of these complex systems is biologically motivated, it is pertinent to extend the studies of ionic hydrogen bonds to functional groups and molecules that actually occur in biological systems. Thus, the present study will examine intramolecular hydrogen bonding and its effects on ion solvation in $CH_3COH^+NHCH(CH_3)COOCH_3$ and the interactions of the neutral molecule as a ligand in complexes with ammonium ions. It should be noted that the geometry of the two carbonyl functions here is similar to that of carbonyl functions in two adjacent amide links in a peptide. Therefore this species can serve as a model for some thermochemical properties of ionic hydrogen bonding interactions of amide links in peptides and proteins.

The present studies were carried out in the gas phase, and thus in the absence of bulk solvent effects. These conditions are also pertinent to ionic properties in the interiors of proteins and in enzyme cavities where solvation by bulk water cannot occur.

Experimental

The measurements were carried out on the NBS pulsed high-pressure mass spectrometer.[5] Reaction mixtures included 0.01–1% of the sample in cyclohexane as carrier gas, except for hydration studies where H_2O was used as the carrier gas. Total source pressures were 0.25–0.85 torr. Signal intensities of reactant and product ions were monitored to 2–4 ms after an ionizing pulse of 1 ms. Checks were made to verify that equilibrium constants were independent of pressure within the available range. The chemicals were from commercial sources and were used as purchased. The amides and CH_3CO-Ala-OCH_3 were introduced in cyclohexane or water solution to a heated bulb, and the mixture was flowed to the ion source through heated lines (≈150 °C). CH_3CO-Ala-OCH_3 was sufficiently volatile to be introduced by this method. Unfortunately, analogous derivatives of dipeptides were not sufficiently volatile for similar studies.

Results and Discussion

1. Proton Affinities; Entropies of Protonation; Intramolecular Hydrogen Bonding. The proton affinities (PAs) of amides A were determined by proton-transfer equilibria with reference compounds B:

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

For proton transfer between small molecules which does not involve substantial entropy changes, $\Delta H°_1$ can be obtained from measurement at one temperature by assuming $\Delta H°_1 \approx \Delta G°_1$. The PAs of $HCONH_2$ and $CH_3CONHCH_3$ were determined in this manner. For large flexible polyfunctional molecules, where large entropy changes may be expected, $\Delta H°_1$ and $\Delta S°_1$ are obtained from van't Hoff plots (Figure 1). Table I shows the thermochemistry of proton-transfer equilibria. The consistency of PA values obtained for a given A by measurement vs. several reference bases[6] and the standard deviations of slopes and intercepts of van't Hoff plots suggest error estimates of less than ±1 kcal mol^{-1} for $\Delta H°_1$ and ±2 cal mol^{-1} K^{-1} for $\Delta S°_1$. In addition to the present results, Table I also shows PAs of several amides.[6]

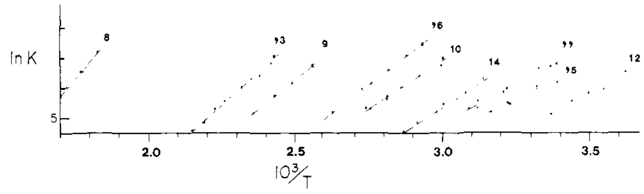

Figure 2. van't Hoff plots for hydration of $HCOH^+NH_2$ (—) and of $CH_3COH^+N(CH_3)_2$ (---). Numbers refer to reactions in Table II.

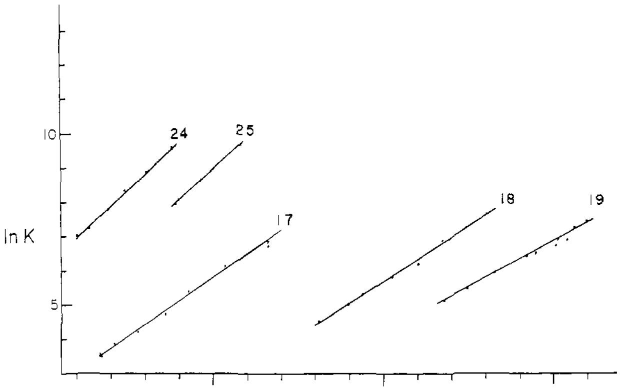

Figure 3. van't Hoff plots for hydration and clustering of CH_3COH^+-Ala-OCH_3 and $CH_3COHN(CH_3)_2$. Numbers refer to reactions in Table II.

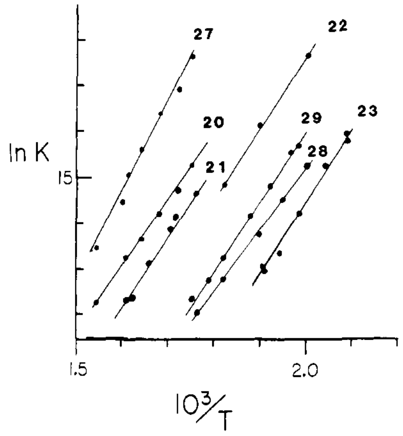

Figure 4. van't Hoff plots for association reactions. Numbers refer to reactions in Table II.

The PA of the alanine derivative $CH_3CONHCH(CH_3)COOCH_3$, which is a polyfunctional secondary amide, is substantially

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[5] Meot-Ner (Mautner), M.; Sieck, L. W. *J. Am. Chem. Soc.* **1983**, *105*, 2956.

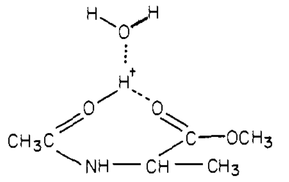
[6] Proton affinities relative to PA(NH_3) = 204 kcal mol^{-1}. PAs of reference compounds are recommended values from Lias: Lias, S. G. *J. Phys. Chem. Ref. Data*, to be published.

Table I. Thermochemistry[a] of Proton-Transfer Equilibria BH^+ + Amide $\rightleftarrows$ AmideH$^+$ + B and Proton Affinities of Amides

reaction no.	BH^+	A	$\Delta H°$	$\Delta S°$	$\Delta G°$ (T)	PA(A)[b]
1	c-$C_5H_{10}OH^+$	$HCONH_2$			+0.7 (600)	199.0[c]
2	$(CH_3)_2COH^+$	$HCONH_2$			−1.9 (600)	198.6[c]
		$HCONH_2$				198.8[d]
		$HCONHCH_3$				204.8[b]
		HCONHn-C_3H_7				210.0[b]
		$HCON(CH_3)_2$				211.4[b]
		CH_3CONH_2				206.3[b]
		$C_6H_5CON(CH_3)_2$				222[e]
3	2-FpyridineH$^+$	$CH_3CONHCH_3$	−2.0	+0.5		212.7[c]
		$CH_3CON(CH_3)_2$				216.8[b]
4	2-FpyridineH$^+$	CH_3CO-Gly-OCH_3	−7.0	−13.4		217.7[c]
	pyrimidineH$^+$	CH_3CO-Gly-OCH_3	−5.7	−11.4		216.7[c]
		CH_3CO-Gly-OCH_3				217.2[d]
5	2-FpyridineH$^+$	CH_3CO-Ala-OCH_3	−12.3	−14.7		223.0[c]
6	$CH_3NH_3^+$	CH_3CO-Ala-OCH_3	−10.2	−14.9		224.3[c]
7	3-FpyridineH$^+$	CH_3CO-Ala-OCH_3	−9.6	−15.7		223.9[c]
		CH_3CO-Ala-OCH_3				223.7[d]

[a] $\Delta H°$ and $\Delta G°$ in kcal mol^{-1}, $\Delta S°$ in cal mol^{-1} K^{-1}; T in K. Error estimates: $\Delta H°$, ±1 kcal mol^{-1}; $\Delta S°$, ±2 cal mol^{-1} K^{-1}. Proton affinities (PA) relative to PA(NH_3) = 204 kcal mol^{-1}. [b] PAs of reference compounds A and of amides where reaction is not given are selected values from PA tabulation by Lias: Lias, S. G. *J. Phys. Chem. Ref. Data*, to be published. [c] PA from this measurement. [d] Average PA from present measurements. [e] R. Taft, private communication.

higher than the PAs of other secondary amides (Table I). By analogy with protonated diamines, diethers, and diketones[2-4] it may be assumed that the increased PA results from the stabilization of the ion by a hydrogen bond between the two carbonyl functions (ion **1H$^+$**). The large negative entropy change associated with the protonation of this molecule (as well as that of $CH_3CONHCH_2COOCH_3$) is also consistent with the formation of the constrained structure **1H$^+$**.



1H$^+$

For evaluation of the strength of the internal bond the PA of the molecule in the absence of this bond must be estimated. This value should be similar to the PA of a secondary amide with an alkyl side chain similar in polarizability to $-CH(CH_3)COOCH_3$, e.g., $CH_3CONHCH(CH_3)C_3H_9$. Considering trends in the PAs of other amides (Table I and ref 6), as well as those of ketones and amines,[6] the PA of the latter amide should be higher by 4 ± 1 kcal mol^{-1} than the PA of $CH_3CONHCH_3$, i.e., it should be 212.7 + 4 $\approx$ 217 ± 1 kcal mol^{-1}. The difference between this value and the actual PA of CH_3CO-Ala-OCH_3 suggests that ion **1H$^+$** may be stabilized by 7 kcal mol^{-1} due to the internal bond. This value is similar to the strength of the internal hydrogen bond in $CH_3COH^+CH_2CH_2COCH_3$, which was estimated as 6 kcal mol^{-1} by analogous considerations[4] and whose geometry is similar to ion **1H$^+$**.

The internal hydrogen bond in **1H$^+$** is substantially weaker than the maximum of 30 kcal mol^{-1} observed for $-OH^+\cdots O-$bonds in dimer ions.[7] The weakening of the internal bond from its optimal value can be attributed to the constraints imposed on the bond geometry by the molecular structure. Molecular models show an $OH^{\delta+}\cdots O$ bond angle of $\approx$100° in $CH_3COH^+NHCH(CH_3)$-COOH, which is significantly distorted from the optimal 180°.

2. Hydration of Protonated Amides by 1–3 H_2O Molecules. For monoprotonic ions such as protonated amides, the first H_2O solvent molecule constitutes the inner solvation shell, and the second and third H_2O molecules constitute the second solvation shell. The hydration of protonated amides by 1–3 H_2O molecules is of interest as an example of inner-shell hydration of oxonium ions. It is also of interest since in enzyme cavities, where bulk solvation is precluded, ions can be partially hydrated by a few H_2O molecules.

The thermochemistry of hydrogen-bonding interactions in the inner solvent spheres is obtained from the temperature dependence of clustering equilibria 2

$$AH^+\cdot(n-1)H_2O + H_2O \rightleftarrows AH^+\cdot nH_2O \qquad (2)$$

Here we examine the hydration of $HCOH^+NH_2$ and $CH_3COH^+N(CH_3)_2$, and we compare to these processes the hydration of the internally solvated ion **1H$^+$**.

The attachment energy of the first H_2O molecule to $CH_3COH^+N(CH_3)_2$ is smaller than the attachment energy to $H_2COH^+NH_2$ (Table II). The difference results from the higher delocalization of the proton charge in the more polarizable $CH_3COH^+N(CH_3)$. For similar reasons, the attachment energy to $C_6H_5COH^+N(CH_3)_2$ is lower than that to $CH_3COH^+N(CH_3)_2$. The differences are in accordance with an inverse relation between the PA difference, ΔPA = PA(A) − PA(H_2O), and the hydrogen-bond strength in $AH^+\cdot OH_2$.[8] Differences in the same direction, but smaller in magnitude, are also observed in the second and third hydration steps. Since the PA of $CH_3CON(CH_3)_2$ is similar to that of the amide links in CH_3OC-Ala-OCH_3 as estimated above, and presumably to the PAs of amide links in peptides, the hydration of $CH_3COH^+N(CH_3)_2$ can be seen as a model for the hydration thermochemistry of protonated amide links in peptides in the absence of other interactions of the amide group.

Despite the fact that the PA of the amide group in CH_3CO-$NHCH(CH_3)COOCH_3$ is similar to that of the amide group in $CH_3CON(CH_3)$, and lower than the PA of the amide group in $C_6H_5CON(CH_3)_2$, the hydration of the protonated ion **1H$^+$** is weaker than that of the other two protonated amides (Table II). The lowering of the hydration energy of the protonated amino acid derivative can be caused by the internal bond in **1H$^+$** for the following reasons. In ion **1H$^+$**, there is only one proton associated with the carbonyl group. Therefore if the internal bond is not displaced by H_2O, then the hydrated complex must assume the T-shaped geometry (**2**). In this complex the proton charge is delocalized due to the internal hydrogen bond; therefore hydrogen

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(7) Larson, J. W.; McMahon, T. J. *J. Am. Chem. Soc.* **1982**, *104*, 6255.

(8) The least-squares correlation, based on **15**-$OH^+\cdot H_2O$ complexes with ΔPA from 0 to 40 kcal mol^{-1}, is $\Delta H°_D$ = 30.4 − 0.30ΔPA. For $-NH^+\cdots O-$bonds an analogous linear relation, based on data for 35 dimers, with ΔPA ranging from 0 to 60 kcal mol^{-1}, is $\Delta H°_D$ = 28.5 − 0.23ΔPA. Meot-Ner (Mautner), M. *J. Am. Chem. Soc.*, in press.

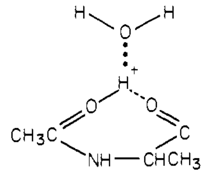
(9) Hirao, K.; Sano. M.; Yamabe, S. *Chem. Phys. Lett.* **1982**, *87*, 181.

Table II. Thermochemistry[a] of Cluster-Dissociation Equilibria $AH^+{\cdot}B \rightarrow AH^+ + B$

reaction no.	AH^+	$\cdot B$	ΔH°_D	ΔS°_D
8	$HCOH^+NH_2$	H_2O	21.3	27.2
9	$HCOH^+NH_2{\cdot}H_2O$	H_2O	14.0	22.7
10	$HCOH^+NH_2{\cdot}2H_2O$	H_2O	11.8	21.0
11	$HCOH^+NH_2{\cdot}3H_2O$	H_2O	9.7	20.2
12	$HCOH^+NH_2{\cdot}4H_2O$	H_2O	9.9	25.6
13	$CH_3COH^+N(CH_3)_2$	H_2O	16.5	26.3
14	$CH_3COH^+N(CH_3)_2{\cdot}H_2O$	H_2O	12.3	26.4
15	$CH_3COH^+N(CH_3)_2{\cdot}2H_2O$	H_2O	9.3	19.2
16	$C_6H_5COH^+N(CH_3)_2$	H_2O	15.1	26.3
17	CH_3CO-Ala-OCH_3H^+	H_2O	13.0	21.2
18	CH_3CO-Ala-$OCH_3H^+{\cdot}H_2O$	H_2O	12.4	26.0
19	CH_3CO-Ala-$OCH_3H^+{\cdot}2H_2O$	H_2O	9.5	21.5
20	CH_3CO-Ala-OCH_3H^+	CH_3NH_2	28.6	19.9
21	$CH_3COH^+NHCH_3$	$CH_3CONHCH_3$	29.8	23.6
22	$CH_3COH^+N(CH_3)_2$	$CH_3CON(CH_3)_2$	31.3	27.4
23	CH_3CO-Ala-OCH_3H^+	CH_3CO-Ala-OCH_3	30.1	31.5
24	$CH_3COH^+N(CH_3)_2$	CH_3COOH	18.4	24.7
25	CH_3CO-Ala-OCH_3H^+	CH_3COOH	18.1	27.2
26	$CH_3NH_3^+$	$HCONH_2$	30.0	33.5
27	$CH_3NH_3^+$	CH_3CO-Ala-OCH_3	40.1	35.1
28	$(CH_3)_3NH^+$	$CH_3CON(CH_3)_2$	27.2	24.1
29	$(CH_3)_3NH^+$	CH_3CO-Ala-OCH_3	29.7	27.6
30	CH_3CO-Gly-OCH_3H^+	pyrimidine	28.6	26.7
31	pyrimidineH^+	CH_3CO-Gly-OCH_3	34.5	38.4

[a] ΔH° in kcal mol^{-1}, ΔS° in cal mol^{-1} K^{-1}. Error estimates are based on the precision of replicate experiments and standard deviations of slopes and intercepts of van't Hoff plots. ΔH°, ±1 kcal mol^{-1}; ΔS°, ±2 cal mol^{-1} K^{-1}.

bonding to H_2O should be weakened. Indeed, ab initio MO calculations showed that



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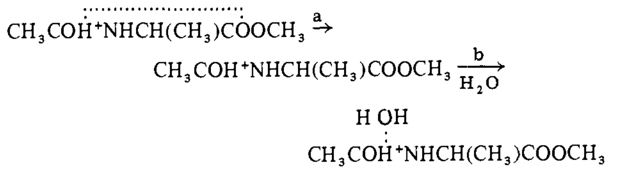
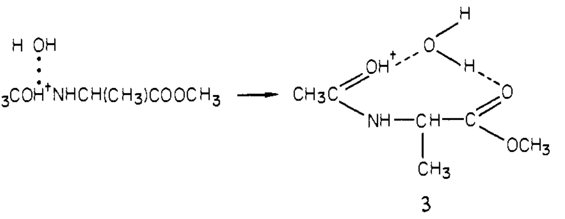
analogous T-shaped structures can yield attachment energies of about 8 kcal mol^{-1} in the trimer $((CH_3)_2O)_3H^+$.[10]

An alternative geometry[a] of the $\mathbf{1}H^+{\cdot}H_2O$ complex may involve the bridged structure **3** (see below). We shall consider the thermochemistry of **3** since similar structures are strongly indicated for the $CH_3CONHCH(CH_3)COOCH_3{\cdot}H^+{\cdot}CH_3NH_2$ complex (below) and also in similar complexes involving polyethers.[4] The formation of **3** consists of the displacement of the internal bond in a sequence of reactions which may be written for thermochemical purposes as eq 3 and 4 (In the actual mechanism, some of these steps may be concerted.)



$$\mathrm{CH_3CO\dot{H}^{+}NHCH(CH_3)C\dot{O}OCH_3} \xrightarrow{a} \mathrm{CH_3COH^{+}NHCH(CH_3)COOCH_3} \xrightarrow[H_2O]{b} \mathrm{CH_3CO\overset{H\,OH}{\overset{\vdots}{H}}{}^{+}NHCH(CH_3)COOCH_3} \quad (3)$$



(4)

3

Using the thermochemistry of the opening of the internal bond (ΔH° = 7 kcal mol^{-1}, ΔS° = 15 cal mol^{-1} K^{-1}) for (3a) and the attachment of H_2O to $CH_3COH^+N(CH_3)_2$ as a model for (3b), ΔH°_3 is estimated as −9.5 kcal mol^{-1} and ΔS°_3 as −11.3 cal mol^{-1} K^{-1}. This sequence predicts the weakening of the attachment energy by the internal bond, but the predicted attachment energy is smaller by 3.5 kcal mol^{-1} than the experimental value. More significantly, the predicted entropy change is smaller by 10 cal mol^{-1} K^{-1} than the experimental value. Reaction 4 would compensate for these differences if ΔH°_4 = −3.5 kcal mol^{-1} and ΔS_4 = −10 cal mol^{-1} K^{-1}. However, these estimated thermochemical values yield $\Delta G^\circ_4(400\ K) = \Delta H^\circ_4 + 400\Delta S^\circ_4 = +1.5$ kcal mol^{-1}. Therefore, the bridged structure[3] may be unstable at the experimental temperatures, and thus the T-shaped structure may be preferred.

The higher hydration steps of $CH_3COH^+N(CH_3)_2$ and $CH_3COH^+NH(CH_3)COOCH_3$ are comparable, which shows that the effects of internal solvation in the latter are not significant. Possibly, the internal solvation is completely displaced by external solvation. Alternatively, the small difference caused by the identity of the core ion on the first H_2O molecule may not be significant when transmitted to the second shell.

3. Complexes of Protonated Amides with Oxygen and Nitrogen Ligands. Protonated amide groups in solution or in proteins may hydrogen bond to polar functional groups in neighboring molecules or chains, such as neutral amide, ether, carbonyl, or carboxyl groups.

As models for amide$H^+\cdots$ amide and amide$H^+\cdots$ carboxyl interactions we measured ΔH°_D for the symmetric amide dimers and amide$H^+{\cdot}CH_3COOH$ complexes shown in Table II. The bonding energies for $(CH_3CONHCH_3)_2H^+$ and $(CH_3CON(CH_3)_2)_2H^+$ dimers, 29.8 and 31.8 kcal mol^{-1}, respectively, are similar to those found in a large number of various oxonium dimer ions.[7] The bonding energy of 18.4 kcal mol^{-1} for the $CH_3COH^+N(CH_3)_2{\cdot}CH_3COOH$ dimer is normal for an asymmetric oxonium ion dimer where the difference between the proton affinities of the components is 27 kcal mol^{-1}.

Unexpectedly, the analogous dimers of the internally hydrogen bonded ions $(CH_3CONHCH(CH_3)COOH_3)_2H^+$ and $CH_3COH^+NHCH(CH_3)COOCH_3{\cdot}CH_3COOH$ exhibit bonding energies, 30.1 and 18.1 kcal mol^{-1}, similar to those of the simple amides, although their internal hydrogen bonds in the monomer ions would require the occurrence of a sequence similar to (3),

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(10) In the $((CH_3)_2O)_3H^+$ dimer the T-shaped structure is weakened by repulsion by the electron clouds of four methyl groups that covers the proton and results in a large $H^+\cdots O$ distance (3.58 Å).[9] In $CH_3COH^+NHCH(CH_3)COOH$ there are no bulky groups about the proton, and the sharp bond angle also exposes the proton to attack by a neutral ligand.

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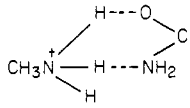
thus presumably lowering the measured value of $\Delta H°_D$ by about 7 kacl mol^{-1}.

The high actual values of $\Delta H°_D$ and $\Delta S°_D$ may suggest that multiple hydrogen bonding in the complexes, analogous to that shown in reaction 4, compensates for the weakening effects of the internal bond. However, it would be fortuitous if a sequence analogous to (3) and (4) resulted in a complexing thermochemistry so similar to that of the simple complexes of $CH_3COH^+N(CH_3)_2$. Nevertheless, the case of the $CH_3CONHCH(CH_3)OCH_3{\cdot}H^+{\cdot}CH_3NH_2$ complex discussed below shows that compensating effects of internal bonding in the monomer and of multiple bonding in the complex can lead to fortuitously straightforward thermochemistry.

4. Complexes of Neutral Amides with Ammonium Ions. While in the above cases the protonated amide is the ionic group, amides can also serve as neutral ligands if protonation occurs on another molecule or functional group of higher proton affinity. In this case simple amides, which have both $-C{=}O$: and $-NR_2$ basic sites, as well as polyfunctional derivatives such $CH_3CONHCH(CH_3)COOCH_3$ can engage in multiple-hydrogen-bonding interactions with the protonated entity.

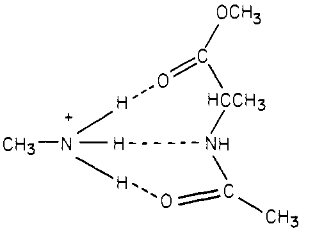
In the present case we examine $CH_3NH_3^+{\cdot}$amide and $(CH_3)_3NH^+{\cdot}$amide complexes. Similar studies on $RNH_3^+{\cdot}$polyether complexes[4] indicated that a second and a third $-NH^+{\cdots}O-$ bond and a further $-CH^{\delta+}{\cdots}O-$ bond can stabilize such complexes by 8, 6, and 3 kcal mol^{-1}, respectively. The total dissociation energies of the multiply bonded complexes were as high as 45 kcal mol^{-1}.

In the complex $CH_3NH_3^+{\cdot}HCONH_2$ formamide is the neutral ligand, and the association energy is 30 kcal mol^{-1}. This complex is significantly more stable than analogous complexes with monofunction oxygen ligands, such as $CH_3NH_3^+{\cdot}CH_3COC_2H_5$, where $\Delta H°_D = 25.2$ kcal mol^{-1}, or $CH_3NH_3^+{\cdot}(CH_3)_2CO$, where $\Delta H°_D = 24.0$ kcal mol^{-1}. The excess stabilization of the amide complex suggests the doubly bonded structure **4**. The entropy change, 33.5 cal mol^{-1} K^{-1}, which is larger than the usual 25 ± 2 cal mol^{-1} K^{-1} for similar complexes, also supports the constrained doubly bonded structure **4**.



4

When the polyfunctional molecule $CH_3CONHCH(CH_3)COOCH_3$, rather than a simple amide, serves as a ligand for $CH_3NH_3^+$, the complex is further stabilized, with $\Delta H°_D = 40.1$ kcal mol^{-1} and $\Delta S°_D = 35.1$ cal mol^{-1} K^{-1}. The unusually high stability and large entropy change suggest multiple ionic hydrogen bonding, i.e., a structure like **5**.



5

The system of CH_3CO-Ala-OCH_3 and CH_3NH_2 represents a special case in that the gas-phase basicities of the two compounds are similar. Therefore, both ions as well as the dimer can be observed, and the three equilibria, reactions 5–7, monitored simultaneously. (The notation on the right-hand side of (6) and (7) indicates the triple hydrogen bond.)

Reaction 5 is a proton-transfer equilibrium. Reaction 6 is an association equilibrium which, as we saw, shows large enthalpy

$$CH_3NH_3^+ + CH_3CONHCH(CH_3)COOCH_3 \rightarrow CH_3COH^+NHCH(CH_3)COOCH_3 + CH_3NH_2 \quad (5)$$

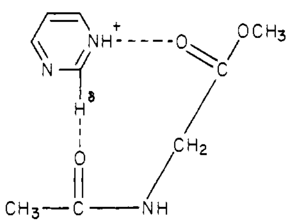
$$CH_3NH_3^+ + CH_3CONHCH(CH_3)COOCH_3 \rightarrow CH_3NH_3^+\vdots CH_3CONHCH(CH_3)COOCH_3 \quad (6)$$

$$CH_3COH^+NHCH(CH_3)COOCH_3 + CH_3NH_2 \rightarrow CH_3NH_3^+\vdots CH_3CONHCH(CH_3)COOCH_3 \quad (7)$$

and entropy changes indicative of the formation of the multiply bonded complex **5**. However, reaction 7, which also yields the same complex **5**, shows an enthalpy change (−28.6 kcal mol^{-1}) and an entropy change (−19.9 kcal mol^{-1}) characteristic of a simple, singly bonded $-NH^+{\cdots}O-$ dimer. The apparently straightforward thermochemistry of reaction 7 is misleading, however, since reaction 7 actually leads from the internally bonded ion **1** to the multiply bonded complex **5**. The combined thermochemistry of (5) and (6) necessarily adds up to that of (7). This is a case where seemingly straightforward complexation thermochemistry results from compensation between the unfavorable effects of intramolecular bonding in the monomer and the stabilizing effect of multiple bonding in the complex.

For the further examination of the significance of multiple bonding in complex **5**, the ammonium ion can be substituted by $(CH_3)_3NH^+$ in which only one proton is available for hydrogen bonding. The complex with CH_3CO-Ala-OCH_3 is significantly less stable than the analogous complex **5**, which again demonstrates the effect of multiple bonding in **5**.

An analysis analogous to reactions 5–7 applies to proton transfer from pyrimidineH^+ to $CH_3CONHCH_2COOCH_3$ (i.e., CH_3CO-Gly-OCH_3) (Table I) and the association reactions in this system (30 and 31, Table II). However, $\Delta H°_D$ for reaction 31 is less exothermic than that for reaction 6, indicating that multiple bonding in complex **6** is not as efficient as that in **5**. This is understandable, since in **6** the second bond is of the weak $-CH^{\delta+}{\cdots}O$ type.[4] The pyrimidine$H^+{\cdot}$ CH_3CO-Gly-OCH_3 complex **6** may be a model for interaction between protonated nucleic bases and peptides.



6

Summary

In continuation of studies of ionic hydrogen bonding in complex molecules, we examined some interactions involving CH_3CO-Ala-OCH_3, a model compound as close to peptides as volatility restrictions permit. Comparison with simple amides shows that intramolecular hydrogen bonding increases the stability of the $CH_3COH^+NHCH(CH_3)COOCH_3$ ion by 7 kcal mol^{-1}. Indeed, intramolecular bonding seems to be quite prevalent in protonated polyfunctional bases.

In longer chains, such as in large polyethers, the strength of the intramolecular $-OH^+{\cdots}O-$ bond can reach up to 30 kcal mol^{-1}. Possibly, this strength also can be approached between nonadjacent amide links in peptides if the ionic hydrogen bond can achieve optimal geometry. The strengths of such optimal ionic hydrogen bonds between functional groups in protonated macromolecules can be estimated on the basis of a linear correlation between hydrogen-bond strength and the relative proton affinities of the functional groups.[4]

We also determined the thermochemistry of partial hydration of portonated amide groups, such as may occur in enzyme cavities, and the weakening effect of intramolecular solvation on ion hy-

dration. Further, in complexes of ammonium ions with polyfunctional ligands such as $CH_3CONHCH(CH_3)COOCH_3$, multiple $-NH^+\cdots O-$, and possibly $-NH^+\cdots N-$, interactions are indicated. The strength of single $-XH^+\cdots Y-$ bonds in complexes involving polyfunctional ligands ranges from 3 to 30 kcal mol^{-1}, and total bonding energies over 40 kcal mol^{-1} in a given complex are observed. The observations suggest that intramolecular and multiple ionic bonds may be significant factors in bioenergetics.

Registry No. c-$C_5H_{10}OH^+$, 88001-03-0; $(CH_3)_2COH^+$, 43022-03-3; $CH_3NH_3^+$, 17000-00-9; $HCONH_2$, 75-12-7; $HCONHCH_3$, 123-39-7; HCONHn-C_3H_7, 6281-94-3; $HCON(CH_3)_2$, 68-12-2; CH_3CONH_2, 60-35-5; $C_6H_5CON(CH_3)_2$, 611-74-5; $CH_3CONHCH_3$, 79-16-3; $CH_3CON(CH_3)_2$, 127-19-5; CH_3CO-Gly-OCH_3, 1117-77-7; CH_3CO-Ala-OCH_3, 3619-02-1; $HCOH^+NH_2$, 50785-80-3; $HCOH^+NH_2{\cdot}H_2O$, 88001-04-1; $HCOH^+NH_2{\cdot}2H_2O$, 88001-05-2; $HCOH^+NH_2{\cdot}3H_2O$, 88001-06-3; $HCOH^+NH_2{\cdot}4H_2O$, 88001-07-4; $CH_3COH^+N(CH_3)_2$, 52754-55-9; $CH_3COH^+N(CH_3)_2{\cdot}H_2O$, 88001-08-5; $CH_3COH^+N(CH_3)_2{\cdot}2H_2O$, 88001-09-6; $C_6H_5COH^+N(CH_3)_2$, 88001-10-9; CH_3CO-Ala-OCH_3H^+, 88001-11-0; CH_3CO-Ala-$OCH_3H^+{\cdot}H_2O$, 88001-12-1; CH_3CO-Ala-$OCH_3H^+{\cdot}2H_2O$, 88001-13-2; $CH_3COH^+NHCH_3$, 34134-26-4; $(CH_3)_3NH^+$, 16962-53-1; CH_3CO-Gly-OCH_3H^+, 88001-14-3; H_2O, 7732-18-5; CH_3NH_2, 74-89-5; CH_3COOH, 64-19-7; 2-FpyridineH$^+$, 59278-66-9; pyrimidineH$^+$, 17009-95-9; 3-FpyridineH$^+$, 59278-67-0; pyrimidine, 289-95-2.

Study of Hydrogen Atom Abstraction Reactions of Triplet Diphenylcarbene in Solution[1]

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Abstract: Excimer laser flash photolysis of diphenyldiazomethane produces triplet diphenylcarbene (DPC) which can be detected in absorption at 314 nm. In cyclohexane triplet DPC reacts via hydrogen atom abstraction to give the diphenylmethyl radical. The growth of the radical can be cleanly and conveniently monitored at 334 nm. The growth kinetics can be fit to an exponential rate law with a time constant of 1.6 μs. The pseudo-first-order rate constants of formation of the diphenylmethyl radical in various solvents at 300 K are 5.7×10^5 (cyclohexane), 4.8×10^5 (toluene), 2.3×10^6 (tetrahydrofuran), 4×10^6 (cyclohexane), and 2.5×10^6 s^{-1} (triethylamine). The following kinetic isotope effects were measured: 2.6 (cyclohexane–cyclohexane-d_{12}), 6.5 (toluene–toluene-d_8), and 1.5 (cyclohexene–cyclohexene-d_{10}). The observed activation energies for hydrogen atom transfer were 3.2 (toluene), 2.5 (cyclohexane), and 2.9 kcal/mol (cyclopentane).

Introduction

Triplet carbenes have radical-like properties which are a consequence of two singly occupied molecular orbitals. As a result, they can participate in typical free-radical reactions, such as hydrogen or halogen abstractions and radical additions to carbon–carbon double bonds. From the point of view of reaction kinetics, the information available is quite limited. At the outset of this work not a single absolute constant for a triplet carbene atom transfer reaction in solution was known. A limited amount of information on hydrogen abstraction is available for fluorenylidene[4] and 1-naphthylcarbene.[5] In these cases, however, analysis of the kinetics are complicated by rapid singlet $\rightleftharpoons$ triplet equilibration and concurrent singlet insertion reactions.

In this study we report the kinetics of hydrogen atom abstraction reactions of triplet diphenylcarbene. These include reactions with solvents, as well as a variety of olefinic quenchers. We have addressed the question of allylic hydrogen abstraction vs. addition to double bonds. Kinetic isotope effects and temperature dependencies are reported for selected examples.

Previous Studies of Diphenylcarbene

1. Chemical Analysis. Diphenylcarbene (DPC) has been studied extensively. The ground state of DPC is known to be the triplet on the basis of low-temperature ESR work.[6] The solution chemistry of DPC reflects the radical-like properties of the triplet state. Kirmse, Horner, and Hoffmann studied the chemistry of DPC in cyclohexane.[7] These workers found that tetraphenylethane (**5**) was the major reaction product. This product was believed to have been formed via hydrogen atom abstraction of triplet DPC from solvent to give radical pair **3**. The triplet pair can diffuse apart whereupon **5** will be formed upon recombination of diphenylmethyl radicals. In principle, singlet DPC can also react with solvent by direct insertion into a carbon hydrogen bond to give **2a**, but it does not seem likely that singlet DPC can be a precursor of the radical dimer **5**.

Kirmse et al. have also studied the chemistry of DPC in toluene and diisopropyl ether and again observed the formation of radical dimer **5**. This was again interpreted on the basis of hydrogen atom abstraction reaction of triplet DPC. Closs has reexamined the DPC–toluene system in considerable detail.[8] He found a statistical mixture of bibenzyl (**4b**), triphenylethane (**2b**), and tetraphenylethane (**5**). This was compelling evidence that the near-

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