

dd, $J = 10$, $J' = 15$ Hz), 6.63 (1 H, dd, $J = 10$, $J' = 15$ Hz), 6.78 (1 H, dd, $J = 10$, $J' = 15$ Hz), 6.94 (1 H, dd, $J = 10$, $J' = 15$ Hz).

Data for **20b**: IR identical with that of **19b** UV (MeOH) λ_{\max} 292, 304, 319 nm; ^1H NMR (400 MHz, acetone- d_6) (the 0–4 ppm range of the spectrum was identical with that of **19b**) δ 4.11 (1 H, m), 4.49 (1 H, m), 4.91 (1 H, dd, $J = J' = 7.5$ Hz), 5.84 (2 H, m), 6.21–6.64 (6 H, m).

The spectral characteristics of **13b** and **14b** were similar to the corresponding 5(*S*),6(*S*) diastereomer.

Conversion of LTA₄ to Lipoxin A Isomers 1a and 1b. The methyl ester of LTA₄ (20 mg, 0.06 mmol) was dissolved in 1,2-dichloroethane (or Me₂SO) (5 mL) containing benzoic acid (7.5 mg, 0.06 mmol). The reaction was heated for 30 min at 60 °C under an inert atmosphere. Removal of the solvent and silica gel chromatography (20% EtOAc/hexane) of the residue produced epimeric benzoates **7a,b** (23 mg, 86% yield). The benzoates **7a,b** were subjected to saponifying conditions (2.5 mL, 4:1 MeOH/2 N NaOH) for 30 min at room temperature to produce vicinal diol acids **8a,b**. The reaction mixture was concentrated in vacuum to remove MeOH, and the remaining solution was diluted in pH 9 borate buffer (1 L). The lipoxidase enzyme (50 mg) was added, and the reaction occurred immediately as determined by monitoring an aliquot by UV spectroscopy (λ_{\max} 273 nm \rightarrow 301 nm). NaBH₄ (20 mg) was added to reduce the resulting hydroperoxides, and after stirring for 10 min at room temperature, the solution was acidified to pH 4–5 by addition of HCl. Extraction with Et₂O, drying (Na₂SO₄), addition of Et₃N, followed by evaporation to dryness produced lipoxin A isomers **1a,b** epimeric at C6 (19 mg, 84% yield). The two isomers were separated by reverse-phase

HPLC (MeOH/H₂O/AcOH, 62:38:0.025) to afford 7.5 mg of the 5(*S*),6(*S*),15(*S*) isomer **1b** and 2.5 mg of the 5(*S*),6(*R*),15(*S*) isomer **1a**.

Data for lipoxin A (5(*S*),6(*S*),15(*S*) isomer **1b) and 6-epi-lipoxin A (5(*S*),6(*R*),15(*S*) isomer **1a**):** 5(*S*),6(*R*),15(*S*) isomer **1a**: ^1H NMR (250 MHz, 5% CD₃OD/D₂O) δ 0.8–0.9 (3 H, brt), 1.2–1.8 (14 H, complex m), 2.1–2.3 (2 H, brt, $J \approx 7.5$ Hz), 3.6–3.7 (1 H, m), 4.05–4.15 (1 H, m), 4.15–4.25 (1 H, q, $J = 6.7$ Hz), 5.7–5.9 (2 H, six lines, 2 overlapping dd), 6.0–6.2 (2 H, five line m), 6.3–6.5 (2 H, complex m), 6.7–6.9 (2 H, complex m); 5(*S*),6(*S*),15(*S*) isomer **1b** (lipoxin A): ^1H NMR (250 MHz, 5% CD₃OD/D₂O) δ 0.8–0.9 (3 H, brt), 1.2–1.8 (14 H, complex m), 2.1–2.3 (2 H, complex m), 3.4–3.6 (1 H, m), 3.95–4.05 (1 H, t, $J = 6.8$ Hz), 4.1–4.2 (1 H, q, $J = 7.1$ Hz), 5.6–5.85 (2 H, seven line m), 5.9–6.1 (2 H, m), 6.2–6.45 (2 H, m), 6.6–6.8 (2 H, m); UV (MeOH) λ_{\max} 287, 301, 316 nm; GC mass spectrum, m/e (tri-TMS methyl ester derivative) 582 M⁺, 203, 100% peak cleavage of vicinal diol. The same result is obtained for 5(*S*),6(*R*),15(*S*) isomer **1a**.

Acknowledgment. We thank N.S.E.R.C. of Canada for industrial postdoctoral fellowships to Dr. Brian Fitzsimmons and Dr. Jillian Evans.

Supplementary Material Available: Experimental data of **10**, **11**, **15**, **16**, and **18** and ^1H NMR, mass, and RP-HPLC spectra of lipoxins A and B (7 pages). Ordering information given on any current masthead.

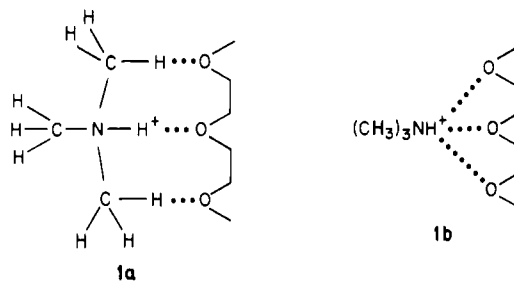
Unconventional Ionic Hydrogen Bonds. 1. CH^{δ+}...X. Complexes of Quaternary Ions with n- and π -Donors

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Contribution from the Chemical Kinetics Division, Center for Chemical Physics, National Bureau of Standards, Washington, DC 20234, and the Department of Chemistry, College of the Holy Cross, Worcester, Massachusetts 01610. Received February 21, 1984

Abstract: CH^{δ+}...X interaction energies are obtained from the clustering of quaternary onium ions with n-donor solvent molecules. The dissociation energies (ΔH°_D) of Me₄N⁺ clustered with the n-donors H₂O, MeOH, MeNH₂, and Me₃N and with the π -donors benzene and toluene range between 8 and 10 kcal mol⁻¹. With the weak, bulky n-donor MeCl the interaction is weaker (6.5 kcal mol⁻¹) while the more polar ligands Me₂CO and MeCONMe₂ attach strongly (14.6 and 18.0 kcal mol⁻¹, respectively) to Me₄N⁺. Strong interactions, 20–23 kcal mol⁻¹, are also observed with polyethers and CH₃CO-gly-OCH₃, indicating polydentate complexing. The attachment energies of ligands to Et₄N⁺ are smaller by 2 kcal mol⁻¹ than those to Me₄N⁺. Ab initio calculations show that in the Me₄N⁺·H₂O, MeOH, MeNH₂, and MeCl complexes the ligands attach electrostatically to a cavity created by protons of three CH₃ groups rather than hydrogen bonding to one proton or to one CH₃ group. Both experiment and theory indicate that a second solvent molecule (H₂O or CH₃OH) attaches preferentially to the first solvent molecule rather than to Me₄N⁺.

Ionic hydrogen bonding between protonated and neutral n-donors has been investigated extensively by mass spectrometric methods.¹ These ionic hydrogen bonds range in strength up to 30 kcal mol⁻¹ in R₂OH⁺...OR₂ and R₂OH⁺...NR₃ and 24 kcal mol⁻¹ in R₃NH⁺...NR₃ type complexes.² In addition to such strong interactions, recent evidence³ suggests that methyl hydrogens of alkylammonium ions may also interact significantly, through more weakly than conventional hydrogen bonds, with n-donors. Thus, the complexes of Me₃NH⁺ with polyethers showed evidence for multiple ion–neutral interactions within the complex,³ even though in Me₃NH⁺ only one NH proton is available for hydrogen bonding. These results indicate that –CH^{δ+}...O– interactions contribute \approx 6 and 4 kcal mol⁻¹ (for the first and the second such interaction) to the stability of **1**.



Other indirect evidence also suggests significant CH^{δ+}...X interactions. For example, Grimsrud and Kebarle⁴ have observed

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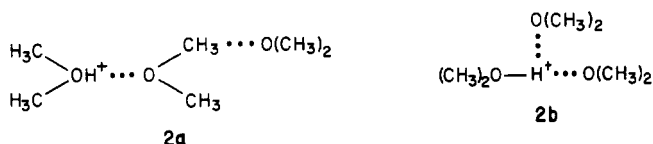
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Table I. Thermochemistry of Dissociation Reactions $A^+ \cdot B \rightarrow A^+ + B$ of Complexes of Quaternary Ammonium Ions A^+ and (for Reference) of Me_3NH^+ , with Ligands B

	B	ΔH°_D ^a	ΔS°_D ^a	ΔG°_D ^a (T, K)	ΔH°_D ^a ((CH ₃) ₃ NH ⁺ ·B)	$\delta^{a,b}$
1. (CH ₃) ₃ NCH ₃ ⁺	H ₂ O	9.0	21.5		15.5 ^c	7
2. (CH ₃) ₃ NCH ₃ ⁺ ·H ₂ O	H ₂ O	9.4 ^d	(22) ^d	3.6 (255)		
3. (CH ₃) ₃ NCH ₃ ⁺	CH ₃ OH	9.8	23.2		18 ^e	8
4. (CH ₃) ₃ NCH ₃ ⁺ ·CH ₃ OH	CH ₃ OH	9.2	24.0			
5. (CH ₃) ₃ NCH ₃ ⁺	(CH ₃) ₂ CO	14.6	24.7		22 ^e	7
6. (CH ₃) ₃ NCH ₃ ⁺ ·(CH ₃) ₂ CO	(CH ₃) ₂ CO	13.0	29.2			
7. (CH ₃) ₃ NCH ₃ ⁺ ·2(CH ₃) ₂ CO	(CH ₃) ₂ CO	11.7 ^d	(25) ^d	4.7 (281)		
8. (CH ₃) ₃ NCH ₃ ⁺	(n-C ₄ H ₉) ₂ O	12.9 ^d	(25) ^d	4.6 (330)	23 ^e	10
9. (CH ₃) ₃ NCH ₃ ⁺	CH ₃ OCH ₂ CH ₂ OCH ₂ CH ₂ OCH ₃	20.6	28.7		32.8 ^f	12
10. (CH ₃) ₃ NCH ₃ ⁺	CH ₃ OCH ₂ CH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ OCH ₃	24.2	33.8		34.6 ^f	12
11. (CH ₃) ₃ NCH ₃ ⁺	CH ₃ CON(CH ₃) ₂	18.0	21.6		27.2 ^e	9
12. (CH ₃) ₃ NCH ₃ ⁺	CH ₃ CONHCH ₂ COOCH ₃ (CH ₃ CO-gly-OCH ₃)	20.1	29.4		29.7 ^e	10
13. (CH ₃) ₃ NCH ₃ ⁺	CH ₃ NH ₂	8.7	17.4		20 ^e	11
14. (CH ₃) ₃ NCH ₃ ⁺	(CH ₃) ₃ N	9.9	20.6		22.6	13
15. (CH ₃) ₃ NCH ₃ ⁺	CH ₃ Cl	6.5	17.9		9 ^g	2
16. (CH ₃) ₃ NCH ₃ ⁺	C ₆ H ₆	9.4 ^d	(20) ^d	3.5 (296)	15.9	7
17. (CH ₃) ₃ NCH ₃ ⁺	C ₆ H ₅ CH ₃	9.5	20.3			
18. (C ₂ H ₅) ₃ NC ₂ H ₅ ⁺	H ₂ O	7.0 ^d	(20) ^d	2.4 (233)		
19. (C ₂ H ₅) ₃ NC ₂ H ₅ ⁺	(CH ₃) ₂ CO	12.4	26.7			
20. (CH ₃) ₂ OCH ₃ ⁺	(CH ₃) ₂ O	13.0	28.4			

^a ΔH° , ΔG° in kcal mol⁻¹, ΔS° in kcal mol⁻¹ K⁻¹, T in K. Based on scatter and reproducibility of van't Hoff plots, error is estimated as ± 1 kcal mol⁻¹ for ΔH° and ± 2 cal mol⁻¹ K⁻¹ for ΔS° . ^b $\delta = \Delta H^\circ_D(CH_3)_3NH^+ \cdot B - \Delta H^\circ_D(CH_3)_3NCH_3^+ \cdot B$. ^c Reference 2. ^d ΔH° obtained from ΔG° at one temperature and ΔS° as estimated from analogous reactions (ref 2). Obtained from correlations of ΔH°_D vs. ΔPA , ref 2. ^e Reference 3. ^f Estimated from ΔH° of $CH_3NH_3^+ \cdot CH_3Cl$.

the (Me₂O)₃H⁺ cluster, and ab initio results suggest a CH^{δ+}...O interaction energy of 8 kcal mol⁻¹ in **2a**, making the structures **2a** and **2b** about equally stable. In addition, -CH^{δ+}...N- in-



teractions of 9 kcal mol⁻¹ involving methyl hydrogens are indicated in the acetonitrile trimer CH₃CN...H⁺...NCCH₃...NCCH₃,^{6,7} and CH^{δ+}...X interactions are indicated in crystals.⁸⁻¹⁰ There exists, however, no direct quantitative data on the strength of CH^{δ+}...X interactions. Moreover, for the above clusters the presence of such interactions is ambiguous since alternative structures **1b** and **2b** may be possible.

To study CH^{δ+}...X interactions unambiguously, we generated quaternary ammonium ions by gas-phase ion-molecule reactions and studied the clustering of those ions with solvent molecules. We have also investigated properties of the clusters via molecular orbital calculations. Interactions of this type are evidently important in the solvation of quaternary onium ions and of the alkyl groups of alkylammonium and carbonium ions. The interaction of acetylcholine ((CH₃)₃N⁺CH₂CH₂OC(O)CH₃) with solvents and neuroreceptors should also involve CH^{δ+}...O interactions.

It should be noted that the term hydrogen bonding is applied to the present complexes only to indicate that the attractive forces result from the interaction of partially charged hydrogen atoms with polar and/or polarizable ligands. Significant n donations into the bonds are not implied.

Experimental and Computational Methods

The measurements were carried out with use of the NBS pulsed high-pressure mass spectrometer.^{2,11} Reactions in the ion source were

initiated by a 1-ms pulse of 500–1000 eV electrons. Ions exiting from the source were observed to reaction times of 2–4 ms.

Typical reaction mixtures for studies on the clustering of Me₄N⁺ contained 60–90% MeCl as carrier gas, ~10% Me₃N, and 1–20% of the ligand. Et₄N⁺ was generated in a mixture of 90% EtI, 1–5% Et₃N, and 1–10% ligand. Me₃O⁺ was generated in 90% MeCl and 10% Me₂O.

The theoretical calculations were carried out ab initio at the 3-21G basis set level with use of the GAUSSIAN 80 series of programs.¹² All computations were done on a VAX 11/780 computer. The 3-21G basis was utilized in lieu of the larger 4-31G basis, since the complexes studied are so big. The former basis set yields results comparable to the latter, but considerably less CPU time is expended.¹³ Relative solvation enthalpies along a series of related molecules are reproduced well at the 4-31G level for many ionic complexes,^{5,7,14,15} and this is expected to be true at the 3-21G level as well.

Five systems were investigated, Me₄N⁺·H₂O, Me₄N⁺·(H₂O)₂, Me₄N⁺·CH₃OH, Me₄N⁺·CH₃NH₂, and Me₄N⁺·CH₃Cl. The geometries of the solvent molecules were the completely optimized ones.¹⁶ The N–C bond lengths and N–C–H bond angles were optimized for Me₄N⁺; the C–H bond length was assumed to be 1.08 Å. These optimized structures were retained in the complexes, and only selected bond distances and angles between Me₄N⁺ and the solvent molecules were varied. This approach of partially optimizing the structures of complexes has been used by many other research groups.^{7,17,18}

Geometry optimizations were done by the force relaxation method.¹⁹ Reported bond lengths represent convergence to 0.001 Å and bond angles to 0.1°.

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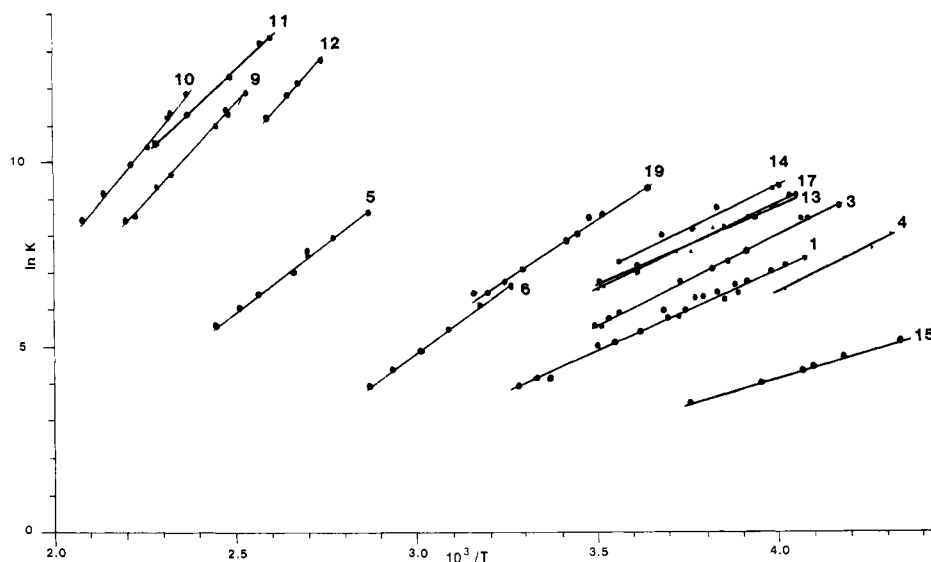


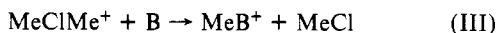
Figure 1. van't Hoff plots for clustering reactions of quaternary ions. Numbers refer to Table I.

Results

Ion-molecule reactions in MeCl generate the alkylating agent MeClMe⁺ which methylates Me₃N (reaction I). The product Me₄N⁺ clusters with added bases B. Other reactions in the



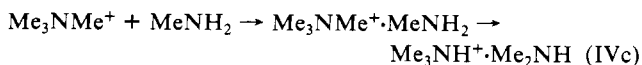
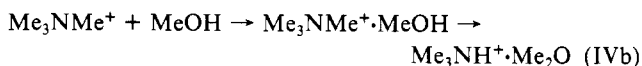
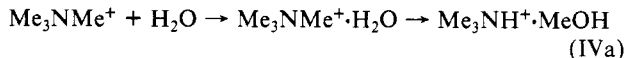
mixture produce Me₃NCH₂Cl⁺, Me₃NH⁺, (Me₃N)₂H⁺, and Me₃NH⁺·B. These are in general the major ionic species; however, their presence does not affect equilibrium II. With most bases B in Table I, reaction III also occurs. However, all of the MeB⁺



product ions, except where B is an ether, protonate Me₃N to yield Me₃NH⁺ and are thus eliminated from the reaction system. This is important since MeB⁺·Me₃N and Me₄N⁺·B cannot be distinguished by mass spectrometry. To check equilibrium II when B is an ether (reactions 8–10, Table I), we determined whether K_{II} is independent of the concentration of B, i.e., whether $(\text{Me}_4\text{N}^+\cdot\text{B})/(\text{Me}_4\text{N}^+) \propto (\text{B})$, where the concentrations of the ethers varied from 0.3 to 12% of the reaction mixture. Similar checks on the independence of K_{II} on (B) and total source pressure (between 0.3 and 0.8 torr) were performed on other equilibria as well.

Reactions analogous to reaction I can be applied to generate other ions such as Et₄N⁺ in a mixture of Et₃N in EtI (for reactions 17 and 18, Table I) and Me₃O⁺ in a mixture of Me₂O in CH₃Cl (for reaction 19, Table I).

Another possible complication could occur via a CH₃ shift in the complex, as illustrated in reactions IVa–c. These reactions could be facilitated by the formation of strong hydrogen bonds in the products. These rearrangements are, however, contradicted



by thermochemistry and/or deuterium labeling experiments, as follows. For reaction IVa, the overall ΔH° , including rearrangement, is calculated^{20–22} to be –3 kcal mol^{–1}, which is in-

consistent with the experimental value of –9 kcal mol^{–1}. For reaction IVb, when (CH₃)₃NCH₃⁺ and CD₃OH are used, the rearrangement would produce (CH₃)₃NH⁺·CD₃OCH₃; under the observed equilibrium conditions, reverse rearrangement and dissociation would produce about 50% (CH₃)₃NCD₃⁺, and further cycles would produce further enrichment in CD₃ up to (CD₃)₃NCD₃⁺. Analogous reactions would also occur in (CH₃)₃NCH₃⁺·CD₃NH₂. However, these sequences are not seen, even though in IVc the rearrangement should be exothermic by 6 kcal mol^{–1}. Apparently, the activation requirement of N–C bond dissociation renders the rearrangement unavailable.

The van't Hoff plots for equilibria II are shown in Figure 1. The results are summarized in Table I. Table II tabulates the optimized parameters, total energies, and solvation energies of the clusters. Figure 2 presents the atomic charges.

Discussion

Complexes of Me₄N⁺ with Oxygen and Nitrogen Ligands: Geometries, Stabilities, and Charge Distributions. The interaction energies of Me₄N⁺ with most neutral molecules are 8–10 kcal mol^{–1}, as was expected from the indirect data mentioned in the introduction. These –CH^{δ+}...X-interactions are substantially weaker than conventional ionic hydrogen bonds, as can be observed by comparing the Me₄N⁺...X and Me₃NH⁺...X complexes (Table I). Indeed, the differences are fairly constant, 7–10 kcal mol^{–1} for monofunctional oxygen ligands and 11–13 kcal mol^{–1} for nitrogen ligands (Table I, last column). We note the strong bonding of Me₄N⁺ to Me₂CO and MeCONMe₂, whose dipole moments are 2.9 and 3.8 D, respectively. These interactions are significantly stronger than those of the other ligands whose dipole moments are 1.2–1.8 D. Strong bonding to the polar ligands suggests that the interactions are predominantly electrostatic.

The predominantly electrostatic nature of the interactions is also confirmed by the ab initio results. In the calculations on Me₄N⁺·H₂O two types of conformations were considered, which will be termed linear and cavity types. For the linear conformation, H₂O is the electron donor and it attaches to a hydrogen of a methyl group of Me₄N⁺, which is the proton donor. Two types of cavity conformations were considered. In the first, the 3-Me-cavity conformation, the H₂O attaches to a cavity created by three hydrogens, each from a *different* methyl group. In the second, the 1-Me-cavity conformation, the H₂O attaches to a cavity created by three hydrogens, each on the *same* methyl group. The

(20) For these estimates, $\Delta H^\circ_f(\text{Me}_4\text{N}^+)$ is extrapolated from the corresponding values of MeNH₃⁺, Me₂NH⁺, and Me₃NH⁺; the other values are obtained from proton affinity data and from clustering data (ref 2).

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Table II. Structures, Total Energies (E_T), and Solvation Energies (ΔE_D) of the Me_4N^+ Complexes

complex	R_{NX}^a	$R_{\text{XH}_1}^a$	R_{XH}^a	E_T^b	ΔE_D^c
$\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}$ (3-Me)	3.488	2.612	2.266	-287.14146	17.90
$\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}$ (1-Me)	4.241	2.588	2.588	-287.13191	11.91
$\text{Me}_4\text{N}^+\cdot 2\text{H}_2\text{O}$ (water-water)	3.488 ^d	2.612	2.266	-362.75455	17.02
$\text{Me}_4\text{N}^+\cdot 2\text{H}_2\text{O}$ (two-cavity)	3.488	2.612	2.266	-362.75255	15.77
$\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{OH}$ (3-Me)	3.506	2.699	2.254	-325.95284	17.47
$\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{OH}$ (1-Me)	4.241	2.589	2.589	-325.94333	11.50
$\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{NH}_2$ (3-Me)	3.803	2.671	2.612	-306.23058	13.77
$\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{NH}_2$ (1-Me)	4.484	2.813	2.813	-306.22433	9.85
$\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{Cl}$ (3-Me)	4.029	2.824	2.825	-708.23073	8.95
$\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{Cl}$ (1-Me)	4.843	3.151	3.151	-708.22647	6.28

^a Bond lengths in Å. X = N, O, Cl. ^b Energies in atomic units. ^c Energies in kcal. ^d R_{00} was assumed to be 2.85 Å.

calculations showed that even when starting with the linear conformation, optimization caused the H_2O group to move down into the 3-Me cavity. Consequently, only the cavity conformations were considered for CH_3OH , CH_3NH_2 , and CH_3Cl . The total energies (Table II) show that the 3-Me-cavity conformation of all of these complexes is more stable than the corresponding 1-Me-cavity conformation. Therefore, the 3-Me complexes will be discussed first.

Only one orientation of the solvent molecule was examined for each singly solvated 3-Me complex. In each case, X = O, N, Cl was placed in the N-C-H₁ plane (see drawing below for the case X = O; note the N-C-H₁-X plane defines the identity of the hydrogen labeled H₁) as was either each atom bonded to X (H_2O , CH_3OH , CH_3Cl) or one atom bonded to it (the carbon in CH_3NH_2). The N of Me_4N^+ and the H or CH_3 groups bonded to X are on opposite sides of X. The methyl group of CH_3OH points toward H₁; the methyl group of CH_3NH_2 points away from H₁. Given this positioning, the N-X and X-H₁ distances and the orientation of the lone pairs on X were then optimized. The X-H' distances are fixed by this optimization.



The optimized N-X, X-H₁, and X-H' bond lengths of the 3-Me complexes studied are tabulated in Table II. The optimized N-C bond length and N-C-H bond angle of Me_4N^+ are 1.517 Å and 108.7°, respectively. The geometries utilized for the solvent molecules are from ref 16. For each 3-Me dimer, the solvent molecule lies below and to the right of H₁ and the two H' atoms, rather than in between H₁ and the two H's. The lone pairs on X tilt upward toward the three hydrogens.

Although the 3-Me conformations of $\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}$, $\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{OH}$, $\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{NH}_2$, and $\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{Cl}$ all involve an electrostatic interaction between the solvent molecule and H₁ and the two H's, the detailed structures of $\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}$ and $\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{OH}$ are very similar to one another but differ from the structures of $\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{Cl}$ and $\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{NH}_2$. The X's (X = N, Cl) of the latter two complexes are essentially equidistant from H₁ and the two H' atoms, while the X's of the former two complexes are further from H₁ than from the H's. Since the nitrogen atom of NH_2CH_3 has only one lone pair and the chlorine atom of CH_3Cl has three lone pairs, the most effective disposition of these atoms is to have them interact equally with all three of the hydrogens that form the 3-Me-electrostatic cavity. In contrast, attachment of H_2O or CH_3OH to Me_4N^+ produces a more stable complex when the two lone pairs on the oxygens are directed toward one hydrogen apiece rather than in between all three hydrogens.

The differences between the oxygen, nitrogen, and chlorine ligand geometries are also evident from the Mulliken overlap populations²³ of X-H' vs. X-H₁, which for $\text{H}_2\text{O}(\text{CH}_3\text{OH})$ are 0.0640 (0.0678) vs. 0.0175 (0.0118). In contrast, in the latter

complexes the Mulliken overlap populations are 0.0372 (X-H') and 0.0326 (X-H₁) for X = N and 0.00808 (X-H' and X-H₁) for X = Cl.

Table II also lists the total energies, E_T , and the solvation energies, ΔE_D , of the 3-Me complexes. The calculated total energy of Me_4N^+ is -211.52698 au. The optimized energies of the solvent molecules were obtained from ref 16. They are -75.58596 au (H_2O), -114.39802 au (CH_3OH), -94.68166 au (CH_3NH_2), and -496.68948 au (CH_3Cl). All of the ΔE_D 's are too large compared to the corresponding ΔH_D 's (see Table I). This was not unexpected since dipole moments are overestimated at the 3-21G basis set level¹³ and the ΔE_D 's have not been corrected for zero-point energies, correlation energies, or basis set superposition error.

The theoretically determined ΔE_D 's of the 3-Me complexes fall in the order $\text{H}_2\text{O} \approx \text{CH}_3\text{OH} > \text{CH}_3\text{NH}_2 > \text{CH}_3\text{Cl}$, whereas the experimentally determined ΔH_D 's fall in the order $\text{CH}_3\text{OH} \approx \text{H}_2\text{O} \approx \text{CH}_3\text{NH}_2 > \text{CH}_3\text{Cl}$. As expected, the calculated relative solvation energies can be correlated with both the N-X and X-H' distance. For H_2O , CH_3OH , and CH_3NH_2 , as the number and bulk of the substituents bonded to X increase, the magnitudes of the N-X and X-H' distances increase and ΔE_D decreases. For CH_3Cl , the chlorine itself is so large that its equilibrium position is substantially further from the Me_4N^+ nitrogen and the three hydrogens than the other X's. Consequently, one rationalization for the incorrect relative ΔE_D of H_2O is the following. In their calculations on the interaction energy of F^- with H_2O , Kistenmacher et al.¹⁷ found that when the geometry of the H_2O molecule in the complex is allowed to vary from its monomer geometry the main change is a relatively large decrease in the magnitude of the H-O-H angle, i.e., from 105° in the monomer to 95° in the complex. This change in geometry corresponded to approximately a 1 kcal increase in ΔE_D . Since CH_3OH and CH_3NH_2 are considerably bulkier than H_2O , steric interactions will be larger in the complexes of these molecules and the constraint of rigid solvent geometry should have a more significant effect on their solvation energies. This suggests that the relative positions of the computed ΔE_D 's of H_2O and CH_3OH will change and the difference between ΔE_D of H_2O and of CH_3NH_2 will decrease if the geometry of the solvent molecule is allowed to vary.

Atomic charges from Mulliken population analysis²³ are given in Figure 2 for the monomers and dimers. The total positive charge on Me_4N^+ in the 3-Me dimers $\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}$, $\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{OH}$, $\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{NH}_2$, and $\text{Me}_4\text{N}^+\cdot\text{CH}_3\text{Cl}$ is 0.927, 0.926, 0.946, and 0.989, respectively. Thus, there is very little charge transfer from the n-donor molecules to Me_4N^+ . However, a comparison of the charge distributions of unsolvated and solvated Me_4N^+ shows that complex formation produces a considerable rearrangement of electron density within Me_4N^+ . With the exception of H_2O , the rearrangement is significant for the n-donors as well.

The results of the Mulliken population analysis suggest that the stabilization of the 3-Me dimers arises primarily from electrostatic and polarization effects. However, although the charge distributions in Figure 2 indicate that there is little charge transfer from the n-donor molecule to Me_4N^+ , the amount of charge transferred does increase in the order of increasing ΔE_D . Hirao et al.⁷ obtained similar results from their calculations on $\text{Li}^+(\text{CH}_3\text{CN})_n$ and $\text{Na}^+(\text{CH}_3\text{CN})_n$ clusters.

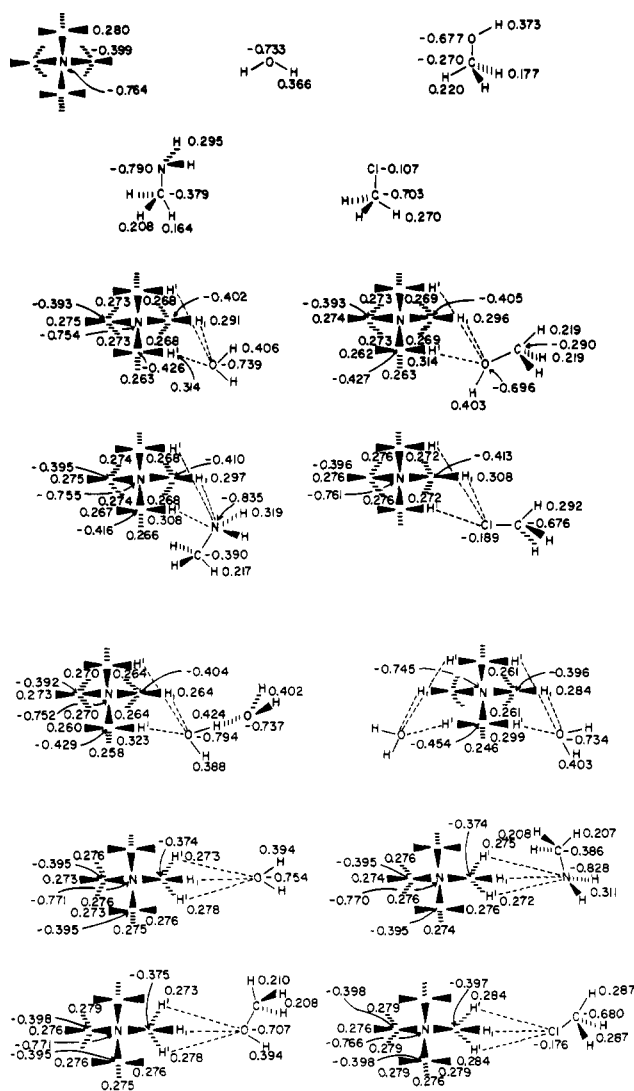
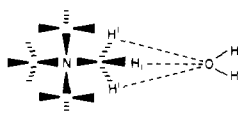


Figure 2. Atomic charges from population analysis for monomers, dimers, and trimers of the Me_4N^+ complexes.

In the 1-Me-cavity complexes (see drawing below for the case where H_2O is the solvent), only one orientation of the atoms bonded to X ($\text{X} = \text{N}, \text{O}, \text{Cl}$) with respect to the methyl hydrogens, H_1 and H' , was considered for each complex, since the overlap populations show that the nonbonded interactions between these atoms are negligible. The $\text{N}-\text{C}-\text{X}$ bond was assumed to be linear, and the $\text{C}-\text{X}$ bond distance and orientation of the lone pairs on X were optimized. For comparison with the 3-Me-cavity complexes, the $\text{N}-\text{X}$ ($\text{C}-\text{X} = 1.517 \text{ \AA}$), $\text{X}-\text{H}_1$, and $\text{X}-\text{H}'$ bond lengths, total energies, and solvation energies of the 1-Me-cavity complexes are reported in Table II.



The lone pair on the nitrogen of methylamine in $\text{Me}_4\text{N}^+\cdot\text{MeNH}_2$ points towards one of the hydrogens (H_1) rather than the carbon of the methyl group to which the NH_2CH_3 complexes. Consequently, the methylamine nitrogen interacts more effectively with H_1 than with the H' 's. The $\text{N}-\text{H}_1$ overlap population is 0.00636; the $\text{N}-\text{H}'$ overlap populations are 0.00502. One of the lone pairs on the oxygen in $\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}$ and in $\text{Me}_4\text{N}^+\cdot\text{MeOH}$ points toward H_1 . The other lone pair is directed in between the two H' 's. Again there is a stronger interaction between X and H_1 than between X and the H' 's. The $\text{O}-\text{H}_1$ overlap population for $\text{H}_2\text{O}(\text{MeOH})$ is 0.00782 (0.00754); the $\text{O}-\text{H}'$ overlap populations are 0.00548 (0.00558) and 0.00320. Each lone pair on

the chlorine in $\text{Me}_4\text{N}^+\cdot\text{MeCl}$ is directed toward a methyl hydrogen, and the chlorine interacts weakly but equally with all of them. The $\text{Cl}-\text{H}$ overlap populations are 0.00129.

The stabilization of the 1-Me-cavity complexes also arises primarily from electrostatic and polarization effects (see Figure 2). Again there is very little charge transferred from the n-donor to Me_4N^+ in these complexes (0.034, 0.032, 0.031, and 0.005 e for H_2O , MeOH , MeNH_2 , and MeCl , respectively). The 1-Me conformation of each complex is less stable than the 3-Me conformation, since for the 1-Me dimers there is/are (1) less polarization of the Me_4N^+ group; (2) less charge transferred to Me_4N^+ ; (3) a tenfold weaker $\text{X}-\text{H}_1$ and $\text{X}-\text{H}'$ overlap; and (4) considerably longer $\text{N}-\text{X}$, $\text{X}-\text{H}_1$, and $\text{X}-\text{H}'$ distances.

Multiple Solvation of Me_4N^+ . The multiple solvation of Me_4N^+ by two H_2O or MeOH molecules (reactions 2 and 4, Table I) is unusual in that the attachment energy of the second ligand molecule is comparable in both cases to the energy of the first step. This is in contrast to the large majority of hydrogen-bonded clusters where the second step is usually weaker than the first step by 25–30%. Indeed, the $\text{Me}_4\text{N}^+\cdot n\text{Me}_2\text{CO}$ clusters behave in the usual way (Table I). The unusual behavior of $\text{Me}_4\text{N}^+\cdot 2\text{H}_2\text{O}$ (or 2 MeOH) can be explained by the attachment of the second H_2O molecule to the first H_2O molecule to form a strong hydrogen bond rather than to Me_4N^+ to form a second weak one, as will be seen from the ab initio results.

For the ab initio calculations, two sites were examined for the second H_2O in $\text{Me}_4\text{N}^+\cdot 2\text{H}_2\text{O}$. In one calculation the two H_2O molecules are located in two 3-Me cavities on opposite sides of Me_4N^+ , and both H_2O molecules assume the optimized geometry found for one H_2O molecule (no reoptimization was performed). In the other calculation, the second H_2O molecule is hydrogen bonded to the first one. For this complex, the first water was put at its optimum position in the 3-Me dimer and the second H_2O was placed 2.85 Å from it, in accordance with the 4-31G result for the $\text{O}\cdots\text{O}$ bond length in $(\text{H}_2\text{O})_2$.¹⁸ The hydrogen bond was assumed to be linear, and the plane of the second water molecule was assumed to be perpendicular to the plane of the first one. Again no geometry optimization was carried out.

The results (Table II) show that the second, i.e., $\text{Me}_4\text{N}^+\cdot \text{H}_2\text{O}\cdots\text{H}_2\text{O}$, complex is the more stable one. The larger drop calculated for the second solvation step of the two-cavity complex is believed to be real, since the magnitudes of the forces on the atoms in the unoptimized two-cavity complex indicate that the system is close to its equilibrium structure.

Mulliken population analysis²³ was performed on the two types of $\text{Me}_4\text{N}^+\cdot 2\text{H}_2\text{O}$ complexes (see Figure 2). In the $\text{Me}_4\text{N}^+\cdot \text{H}_2\text{O}\cdots\text{H}_2\text{O}$ complex the waters donate much less electron density (0.0850 e) than twice that observed for $\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}$ (0.146 e) to Me_4N^+ . However, the addition of the second water molecule does produce further charge redistributions in Me_4N^+ . Most of the electron density transferred to Me_4N^+ now comes from the second H_2O . The oxygen of the first H_2O has gained negative charge, which is characteristic of proton donors in hydrogen-bonded complexes.¹⁸ In comparison, the two-cavity complex exhibits a total charge transfer from the n-donor to Me_4N^+ (0.142 e) only slightly less than twice that observed for $\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}$ (0.146 e).

In the latter complex, the smaller positive charges on the hydrogens that participate in the attachments and the slightly smaller negative charge on the oxygens of $\text{Me}_4\text{N}^+\cdot(\text{H}_2\text{O})_2$ compared to $\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}$ lead to weaker electrostatic and polarization interactions in the second than in the first step. In comparison, the calculated second attachment energy in $\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}\cdots\text{H}_2\text{O}$ is close to the energy of the first solvation step, in agreement with the experimental results. The energies would become still closer if R_{NX} , $R_{\text{XH}'}$, R_{XH_1} , and the hydrogen-bonded distances were optimized for the trimer. The additional stabilization energy gained by attaching the second water molecule in $\text{Me}_4\text{N}^+\cdot\text{H}_2\text{O}\cdots\text{H}_2\text{O}$ originates from the following: (1) the formation of the hydrogen bond; (2) the polarization and electrostatic effects brought about by the additional charge redistributions induced in Me_4N^+ by the $(\text{H}_2\text{O})_2$ group and the larger negative charge on the oxygen of

the first water molecule; (3) the somewhat larger charge transfer to Me_4N^+ .

One consequence of the above results is that any solvent that cannot participate in a solvent-to-solvent hydrogen bond, i.e., Me_2CO and MeCl , would be expected to have a lower ΔE_D for the second attachment than for the first. This is in complete agreement with the experimental results for Me_2CO .

Interaction of Me_4N^+ with Polyfunctional Ligands. The interaction energies of Me_4N^+ with ethers are shown in reactions 8-10, Table I. The interaction with the large, polarizable $n\text{-Bu}_2\text{O}$ is somewhat stronger than that with H_2O and MeOH . While the triether in reaction 9 has a polarizability comparable to that of $n\text{-Bu}_2\text{O}$, the polydentate ligands give considerably more stable complexes than any of the other ligands. The strong interaction energies here clearly indicate multiple interactions of the ion with the multiple ether functions. A comparison of the $n\text{-Bu}_2\text{O}$ and diglyme complexes indicates 8 kcal mol⁻¹ for the second plus third $\text{CH}^{\delta+}\cdots\text{O}$ interactions in the latter. Interestingly, this is similar to the 10 kcal mol⁻¹ interactions assigned for two $\text{CH}^{\delta+}\cdots\text{O}$ interactions in the analogous complex $\text{Me}_3\text{NH}^+\cdots\text{diglyme}$.³ Apparently the exchange of a strong vs. weak bond in the first interaction does not significantly affect the additional $\text{CH}^{\delta+}\cdots\text{O}$ interactions.

The question of multiple interactions is also of interest in the complex of Me_4N^+ with the amino acid derivative $\text{CH}_3\text{CONH}\cdot\text{CH}_2\text{COOCH}_3$, i.e., $\text{CH}_3\text{CO}\cdot\text{gly}\cdot\text{OCH}_3$ (reaction 11, Table I). The geometries of the two carbonyl functions in $\text{CH}_3\text{CO}\cdot\text{gly}\cdot\text{OCH}_3$ are similar to those in two adjacent amide oxygens in a peptide. Therefore, the complex simulates the interactions of the charged group in acetylcholine with two adjacent amide links in an unionized peptide. The experimental results show that the interaction, 20 kcal mol⁻¹, is substantial. However, a comparable interaction energy is observed with a single amide group, i.e., dimethylacetamide (reaction 12, Table I). Molecular models

demonstrate that, with the oxygen of one amide group of $\text{CH}_3\text{CO}\cdot\text{gly}\cdot\text{OCH}_3$ in a three-proton cavity of Me_4N^+ , the other carbonyl oxygen could interact only with the same protons, whose charge is already delocalized in the first interaction. This may explain the small effects of multiple interaction for this group as opposed to the polyether complexes, for which the oxygen can interact with different groups of methyl protons. Of course, with larger peptides, non-neighboring amide groups could bind the ion in a more efficient polydentate conformation.

Complexes of Other Quaternary Ions. Complexes of Quaternary Ions with π -Donors. With increased size of the quaternary ion, i.e., in Et_4N^+ , the charge on each proton should be decreased and, consequently, the interaction energy with solvents should decrease. Indeed, the interaction energies with H_2O and Me_2CO are decreased by 2 kcal mol⁻¹ (reactions 18 and 19, Table I) compared to the analogous complexes of Me_4N^+ .

Finally, the complex $\text{Me}_3\text{O}^+\cdots\text{Me}_2\text{O}$ is comparable in stability to the complexes of Me_4N^+ with oxygen ligands. This suggests that there are similar charge distributions in the quaternary ammonium and tertiary oxonium ions. Reactions 16 and 17 show that the interaction of Me_4N^+ with the π -donor ligands benzene and toluene is similar to that with the oxygen and nitrogen ligands. Interestingly, benzene also shows an interaction energy with Me_3NH^+ comparable to regular n -donor ionic hydrogen bonds as will be seen in the following article in this issue. The complexes of Me_4N^+ with benzene and toluene represent a special type, $\text{CH}^{\delta+}\cdots\pi$, where no n -donors are involved on either side.

Registry No. $(\text{CH}_3)_3\text{NCH}_3^+$, 51-92-3; $(\text{C}_2\text{H}_5)_3\text{NC}_2\text{H}_5^+$, 66-40-0; $(\text{CH}_3)_2\text{OCH}_3^+$, 43625-65-6; H_2O , 7732-18-5; CH_3OH , 67-56-1; $(\text{C}_2\text{H}_5)_2\text{CO}$, 67-64-1; $(n\text{-C}_4\text{H}_9)_2\text{O}$, 142-96-1; $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OC}\cdot\text{H}_3$, 111-96-6; $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_3$, 112-49-2; $\text{CH}_3\text{CON}(\text{CH}_3)_2$, 127-19-5; $\text{CH}_3\text{CONHCH}_2\text{COOCH}_3$, 1117-77-7; CH_3NH_2 , 74-89-5; $(\text{CH}_3)_3\text{N}$, 75-50-3; CH_3Cl , 74-87-3; C_6H_6 , 71-43-2; $\text{C}_6\text{H}_5\text{CH}_3$, 108-88-3; $(\text{CH}_3)_2\text{O}$, 115-10-6.

Unconventional Ionic Hydrogen Bonds. 2. $\text{NH}^+\cdots\pi$. Complexes of Onium Ions with Olefins and Benzene Derivatives

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Abstract: Unconventional strong ionic hydrogen bonds of the $\text{-XH}^+\cdots\pi$ type, where the electron donor is a π -bond or an aromatic π -system, are formed in the clustering reactions of NH_4^+ and MeNH_3^+ with C_2H_4 and benzene derivatives. The interaction energies range from 10 to 22 kcal mol⁻¹. The experimental results and ab initio calculations on $\text{C}_2\text{H}_4\cdots\text{NH}_4^+$, $\text{C}_6\text{H}_6\cdots\text{NH}_4^+$, and $\text{C}_6\text{H}_5\text{F}\cdots\text{NH}_4^+$ indicate that the interaction is primarily electrostatic in nature with little π -donation into the bond. The most stable structure of $\text{C}_2\text{H}_4\cdots\text{NH}_4^+$ is the conformer where one N-H^+ bond points at the center of the double bond. For $\text{C}_6\text{H}_6\cdots\text{NH}_4^+$ and $\text{C}_6\text{H}_5\text{F}\cdots\text{NH}_4^+$, the lowest energy π -dimers have two NH_4^+ hydrogens directed toward the ring. The $\text{F}\cdots\text{H-NH}_3^+$ σ -complex was studied also for $\text{C}_6\text{H}_5\text{F}\cdots\text{NH}_4^+$. The latter complex is the more stable of the two at this level of calculation.

Conventional ionic hydrogen bonds between protonated and neutral n -donors $\text{-XH}^+\cdots\text{X-}$, ranging in strength up to 30 kcal mol⁻¹, have been investigated extensively.^{1,2} Fewer studies have been done on unconventional ionic bonds, i.e., those where the atom on either side of the bonding, partially charged hydrogen is not an n -donor. In the preceding paper³ we observed unconventional bonds of the $\text{CH}^{\delta+}\cdots\text{X}$ type ranging in strength from

6 to 18 kcal mol⁻¹. In the present paper we examine strong ionic hydrogen bonds where the proton is attached to an n -donor, but the electron donor is a π -bond or an aromatic π -system.

While the thermochemistry of $\text{XH}^+\cdots\pi$ interactions has not been investigated previously, Sunner and co-workers⁴ have studied a

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