Tetrahedron, Vol. 37, pp 1221 to 1226, 1981
Printed in Great Britain.

0040-4020/81/061221-06$02.00/0
Pergamon Press Ltd.

EFFECTS OF THE REACTION ENVIRONMENT ON GAS-PHASE PROTON-INDUCED NUCLEOPHILIC DISPLACEMENT AT SATURATED CARBON[1]

MARINA ATTINÀ
Istituto di Chimica Farmaceutica, University of Rome, 00100 Rome, Italy

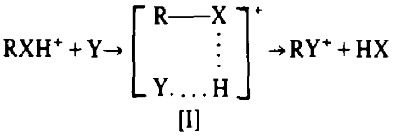
and

GIANCARLO ANGELINI and MAURIZIO SPERANZA*
Istituto di Chimica Nucleare, C.N.R., C.P. 10, 00016 Monterotondo Stazione, Rome, Italy

(*Received in UK* 18 *August* 1980)

Abstract—The H_2O and D_2O chemical ionization (CI) mass spectra of selected methyl halides (CH_3X, X=F, Cl) have been investigated at source temperatures from 330 to 500°K, and at total pressures from 0.1 to 1.1 Torr. Hydronium (H_3O^+) ions, the reactant species formed that predominates in our source under these conditions, were found to promote a gas-phase nucleophilic substitution on the halogenated substrate by H_2O, leading to $CH_3OH_2^+(H_2O)_n$ ($n = 0, 1, 2$) ions. Occurrence of these substitution reactions, which are prevented under ICR conditions, provides direct evidence for contrasting ion reactivities under different experimental conditions, mainly due to the profound influence of the reaction environment on the formation of collision-stabilized intermediate species.

Gas-phase acid-induced nucleophilic displacement reactions are currently observed in mass spectrometry.[2] In an attempt to correlate the available kinetic data concerning substitution at saturated carbon, Beauchamp proposed a reactivity model based upon the hypothesis that occurrence of the exothermic process



$$RXH^+ + Y \rightarrow \left[\begin{array}{c} R\text{—}X \\ \vdots \\ Y\dots H \end{array}\right]^+ \rightarrow RY^+ + HX \qquad (1)$$
$$[I]$$

(1) is allowed only if the proton affinity of the substrate RX exceeds that of the nucleophile Y.[3] Otherwise, the competing proton transfer (2) from the protonated substrate to the nucleophile is expected to prevail over the slower displacement pathway (1).

$$RXH^+ + Y \longrightarrow RX + HY^+ \rightarrow \text{No substitution} \qquad (2)$$

One of the simplest ICR experiments designed to check the validity of this model involves H_2O, as the nucleophile, and CH_3Cl or C_2H_5Cl, as substrates.[3a] On account of their relative proton affinities,[4] only C_2H_5Cl undergoes substitution by H_2O, whereas CH_3Cl follows path (2). However, further careful mass spectrometric investigation on a variety of proton-induced nucleophilic substitutions revealed the only partial applicability of Beauchamp's model, even under ICR conditions. Thus, Caserio *et al.*[5] pointed out that the occurrence and the mechanism of gas-phase nucleophilic substitutions are governed by not only thermodynamic but also structural factors, recalling those recognized in analogous solvolytic systems. In addition, McIver and Fukuda recently reported that nucleophilic substitution mechanism can be drastically affected by clustering the ionic nucleophile with a single solvent molecule.[6] Other facets of the acid-induced nucleophilic displacement problem, which deserve special investigation, concern its dependence on either the energy content of the excited intermediates from the nucleophilic attack (1) and the extent of RXH^+ solvation. A mass spectrometric investigation aimed at focusing both effects is presented in this paper, which reports a chemical ionization (CIMS) mass spectrometric study of process (1), using H_2O (or D_2O) as the reactant gas, and CH_3X (X = F or Cl), as substrate with proton affinity *lower* than that of the nucleophile (H_2O or D_2O).[4]

$$H_3O^+ + CH_3X \longrightarrow CH_3OH_2^+ + HX \qquad (3)$$

Under ICR *conditions*, the nucleophilic displacement (3) does not take place, in agreement with Beauchamp's rules. Here we give direct experimental evidence of sharp reactivity differences under ICR and respectively high-pressure CIMS conditions, which, in view of the limited structural factors involved in the process (3), can be directly linked to the effects of the intermediates excitation level and of the substrate solvation on the substitution mechanism.

EXPERIMENTAL

The CIMS experiments were performed on a HP 5980 A quadrupole mass spectrometer, operated in the chemical ionization mode. The materials used were ultra-high pure methyl halides obtained from Matheson, and 99, 95% D_2O from Merck Co. Gaseous mixtures of CH_3X: H_2O (or D_2O) in the ratio 4×10^{-4} to 1, prepared in 1 liter pyrex bulbs, were allowed to bleed into the heated (T = 330–500°K) source of the mass spectrometer through a metering needle valve. The pressures (0.1–1.1 Torr) in both the inlet system and the ion source were measured with a Bourdon-type mechanical gauge. Ionic reactions were initiated by the bombardment of the reaction mixture by 250 V electrons. Each experiment was replicated two to four times. The abundance of the ions identified in all cases accounts for over 99% of the total ion current.

RESULTS

The relative abundances of the ionic products from the experiments carried out at $T = 440°K$ are illustrated in Figs. 1-3, as a function of the total pressure of the system. Similar variations of the intensities $I/\Sigma I$ of the reactant and the product ions with the source pressure were obtained at all source temperatures used ($T = 330$; 380; $500°K$). Unequivocal identification of the *m/e* ratios 33, 51, and 69 was achieved by the use of mixtures containing D_2O, instead of H_2O, as the reactant gas. Despite a certain degree of H/D exchange occurring in the source of the mass spectrometer, these experiments allowed to identify the ionic species of Figs. 1 and 2 as the substituted ions, $CH_3OH_2^+ (H_2O)_n$, with $n = 0, 1, 2$, respectively.

Under our high-pressure chemical ionization conditions, the primary H_2O^+ ions, formed from electron impact on water, react completely with H_2O to yield H_3O^+,[7,8] whose further reactions are only of the clustering type.[9] If compared to related studies on water ion clustering equilibria, the dependence of the relative intensities of $H^+(H_2O)_n$ ($n = 1, 2, 3, \ldots$) observed in the present study as a function of the source pressure and temperature indicates that, even though thermal equilibrium is readily reached in the ionization chamber,[10] we did not attain complete thermodynamic equilibration among the present ionic species. Nevertheless, the same $H^+(H_2O)_n$ distribution observed for both CH_3F and CH_3Cl systems, and for pure water, shows that the presence of traces of methyl halide (molar fraction $= 4 \times 10^{-4}$) in the mixture does not appreciably perturb the ionic processes leading to the major ionic species.

Inspection of the pressure trends of substituted ions intensities reveals that yields of $CH_3OH_2^+ (H_2O)_n$($n = 0, 1$) ions display the same dependence on the pressure at least within the low-pressure range ($P = 0.1$–0.4 Torr), suggesting that the two species can be formed from the same precursors. On the other hand, the pressure dependence of $CH_3OH_2^+ (H_2O)_2$ and, in the CH_3F/H_2O systems that of $CH_3OH_2^+(H_2O)$ in the high-pressure range ($P > 0.4$ Torr), indicates that their formation processes follow a trend similar to that prevailing for the correspondent water-ion clustering reactions.

The effects of varying the source pressure on the relative $CH_3OH_2^+$ ion yields, from both CH_3F and CH_3Cl systems, were investigated at the four selected source temperatures. The trends obtained, shown in Figs. 4 and 5, suggest that the substituted ion intensities increase with the pressure, reaching the maximum value in rather restricted ranges of pressure wherein, at the corresponding source temperature, H_3O^+ is the most abundant reactant species, since its clustering with H_2O molecules is still limited. As water-ion clustering becomes significant, i.e. at high pressures and low temperatures, the $CH_3OH_2^+$ ion yields rapidly fall off. An alternative view of the same effect is given in the Figs. 6 and 7, showing the temperature dependence of the relative yields of the $CH_3OH_2^+$ ion at a fixed pressure. Different temperature effects on the $CH_3OH_2^+$ ion yield are apparent, whose extent is strictly related to either the total pressure of the system and the nature of the halogenated substrate.

DISCUSSION

(1) *Nature of the displacement process.* The particular purpose of the present investigation requires an analysis

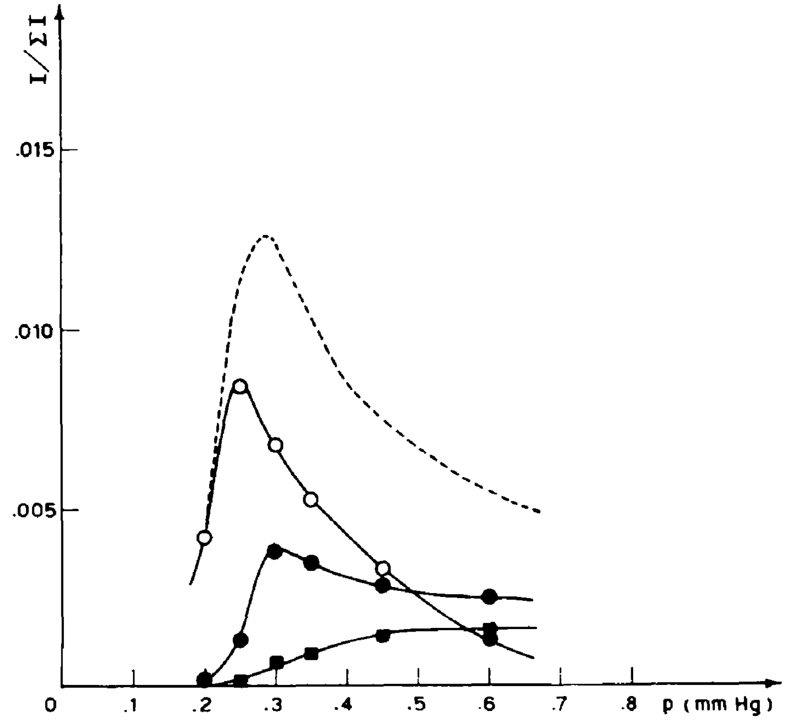


Fig. 1. Pressure dependence of $CH_3OH_2^+(H_2O)_n$ ion abundances from methyl fluoride H_2O–CI spectrum, ⊕, $n = 0$; ●, $n = 1$; ■, $n = 2$. ($T = 440°K$). ----- overall substituted ion intensity ratio.

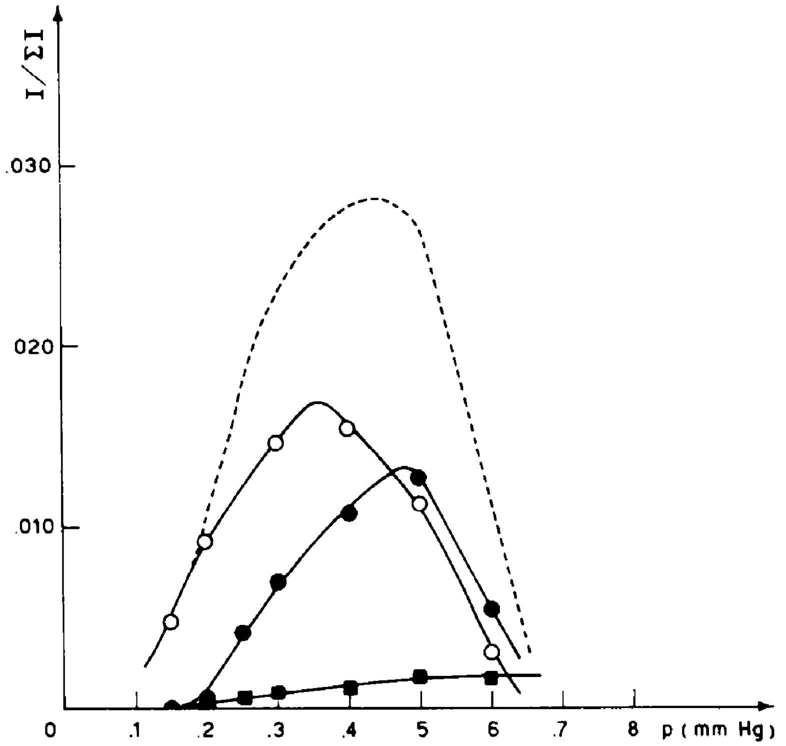


Fig. 2. Pressure dependence of $CH_3OH_2^+(H_2O)_n$ ion abundances from methyl chloride H_2O–CI spectrum. ⊕, n = 0; ●, n = 1; ■, n = 2. (T = 440°K). ----- overall substituted ion intensity ratio.

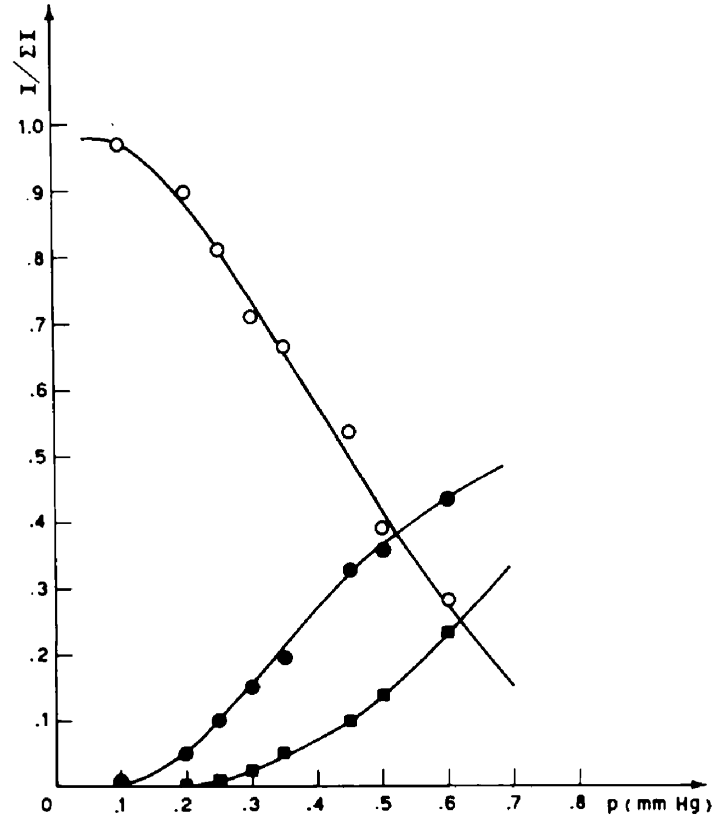


Fig. 3. Pressure dependence of $H_3O^+(H_2O)_n$ ion abundances from both methyl fluoride and methyl chloride H_2O–CI spectra. ⊕, n = 0; ●, n = 1; ■, n = 2 (T = 440°K)

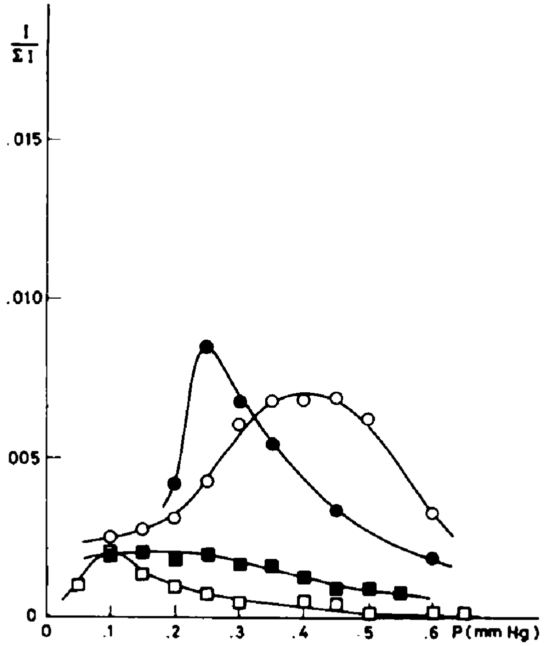


Fig. 4. Pressure dependence of $CH_3OH_2^+$ ion abundances from methyl fluoride H_2O–CI spectra at: □, T = 330°K; ■, T = 380°K; ●, T = 440°K; ⊕, T = 500°K.

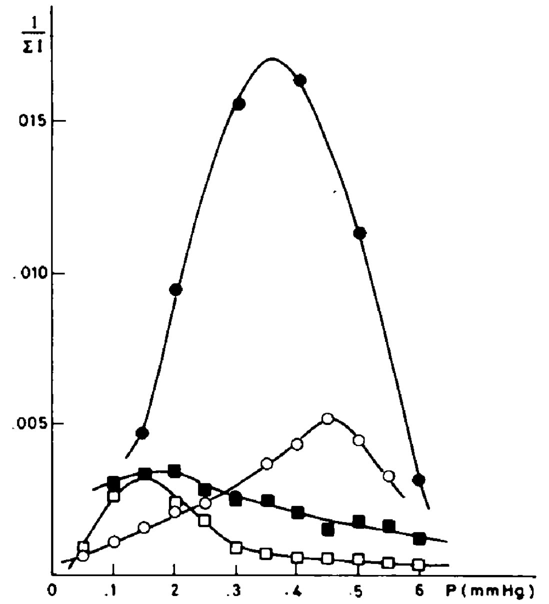


Fig. 5. Pressure dependence of $CH_3OH_2^+$ ion abundances from methyl chloride H_2O–CI spectra at: □, T = 330°K; ■, T = 380°K; ●, T = 440°K; ⊕, T = 500°K.

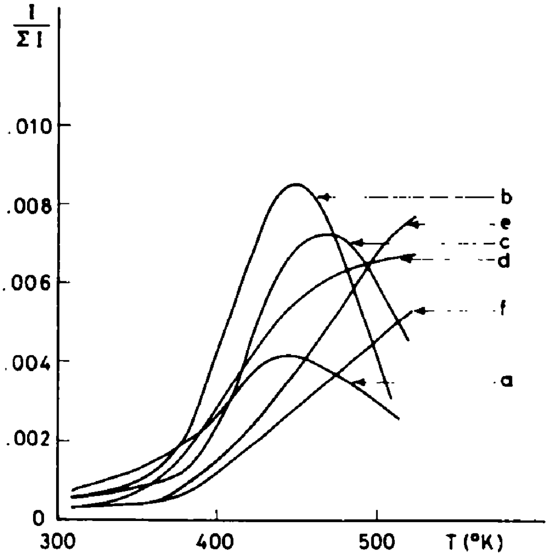


Fig. 6. Temperature dependence of $CH_3OH_2^+$ ion abundances from methyl fluoride H_2O–CI spectra at different source pressures: (a) 0.20; (b) 0.25; (c) 0.30; (d) 0.35; (e) 0.45; (f) 0.55 Torr†.

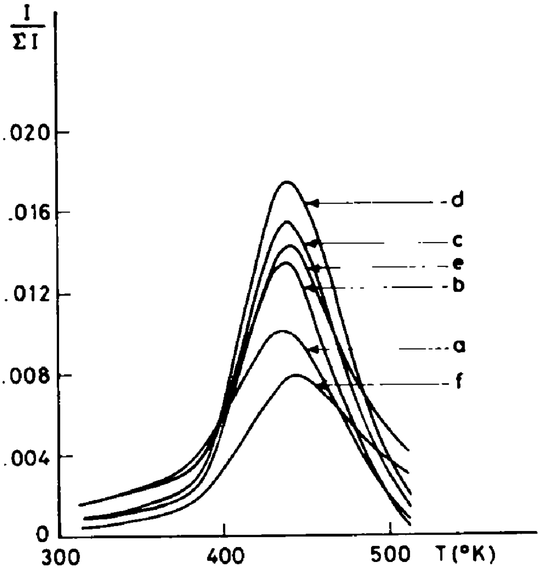


Fig. 7. Temperature dependence of $CH_3OH_2^+$ ion abundance from methyl chloride H_2O–CI spectra at different source pressures: (a) 0.20; (b) 0.25; (c) 0.30; (d) 0.35; (e) 0.45; (f) 0.55 Torr†.

of the nature of the ionic processes occurring in our system. The extremely large excess of H_2O in the mixture prevents direct electron impact ionization of CH_3X, as demonstrated by the complete absence in the recorded spectra of typical reaction pattern of CH_3X ions (CH_3X^+, CH_2X^+, CH_3^+, X^+, CX_3XH^+, $CH_3XCH_3^+$, etc.). Thus, any conceivable exothermic process involving these ionic species, including the following processes:

$$\left.\begin{matrix} CH_3^+ \\ CH_3XH^+ \\ CH_3XCH_3^+ \end{matrix}\right\} + H_2O \rightarrow CH_3OH_2^+ + \left\{\begin{matrix} HX \\ CH_3X \end{matrix}\right. \qquad (4)$$

can be safely ruled out as significant routes to the formation of the $CH_3OH_2^+$ $(H_2O)_n$ ions. In addition, the large third-body (H_2O) densities (1.2×10^{15}–$2.6 \times 10^{16}\,cm^{-3}$) typical of the present experiments, and the relatively high efficiency of reactive collisions between H_2O and the ionic species formed,[7,8] exclude *excited* water molecules, radicals, or ions as precursors of the observed ionic products. Thus, formation of $CH_3OH_2^+$ $(H_2O)_n$ ions must be ascribed to the attack of thermal H_3O^+ ions on CH_3X. According to Beauchamp's model,

---

†For the sake of clarity, only the interpolated trends are reported without showing the obtained experimental values.

this interaction should lead to no observable ionic product, as shown under ICR conditions. As a consequence, detection of $CH_3OH_2^+(H_2O)_n$ ions in the CIMS experiments suggests occurrence of an alternative substitution mechanism, which is prevented under ICR conditions by the absence of those specific environmental effects on ion-molecule reactions typical of high-pressure CIMS.

(2) *Mechanism of the proton-induced nucleophilic displacement.* On account of the large excess of H_2O, and of the observed effects of water ion clustering on the substituted ion yields, the plots of Figs. 1-7 can be interpreted as arising from a substitution mechanism involving the preliminary attack of H_3O^+ ions on the n-center of the substrate giving the proton-bound intermediate $[II]^{**}$ whose occurrence is confirmed by the actual observation of a minute peak at the corresponding *m/e* value. Formation

$$H_3O^+ + CH_3X \underset{K_-}{\overset{K_+(M)}{\rightleftharpoons}} [CH_3X\text{---}H\text{---}OH_2]^+_{exc} \tag{5}$$

$$[II]^{**}$$

of the intermediates $[II]^{**}$, excited by the exothermicity of the electrostatic interaction (5),[11] is allowed by effective third-body ($M = H_2O$) stabilization,[9] which substantially reduces back dissociation. Alternative dissociation pathways of $[II]^{**}$, such as reactions (6) and (7), are thermodynamically unfavored.[12]

$$[II]^{**} \not\longrightarrow H_2O + CH_3XH^+ \tag{6}$$

$$[II]^{**} \not\longrightarrow [I] \longrightarrow CH_3OH_2^+ + HX \tag{7}$$

Further collisions of $[II]^{**}$ with H_2O molecules lead either to less excited proton-bound intermediates $[II]^*$ or directly to the substituted $CH_3OH_2^+\ (H_2O)_n$ ($n = 0, 1$) ions, as shown in Scheme 1.

As collisional quenching of $[II]^{**}$ goes along path (b), formation of naked $CH_3OH_2^+$ becomes less and less significant, since the substitution path (a) is endothermic for proton-bound intermediates with insufficient energy content (for instance $[II]^\circ$ in the Scheme). In this case, the only possible substitution process is the H_2O-for-HX displacement with the direct formation of $CH_3OH_2^+\ (H_2O)$ (path (c)). The occurrence of the suggested reaction network and the identification of path (c) as an additional source of $CH_3OH_2^+\ (H_2O)$ ions, apart from the common clustering pattern (paths (d) and (e)), are consistent with the observed trend of $CH_3OH_2^+\ (H_2O)_n$ ion intensities as a function of the source pressure and temperature.

When successive clustering of the substituted ionic products is limited, and the substitution paths (a) and (c) are still exothermic, namely at sufficiently low pressures, an estimate of the order of magnitude of the corresponding rate constants is possible. Thus, at 440°K and at a third-body density of $7 \times 10^{15}\ \mathrm{cm^{-3}}$, direct comparison of the substituted ion yields with the corresponding $H^+(H_2O)_2$ ion abundance from the competitive water-ion clustering process,[9d] leads to k_a and k_c values ranging between 10^{-9} and $10^{-10}\ \mathrm{cm^3\ molecule^{-1}\ sec^{-1}}$, showing that only a few unreactive collisions between $[II]^{**}$ and H_2O occur before the substitution event.

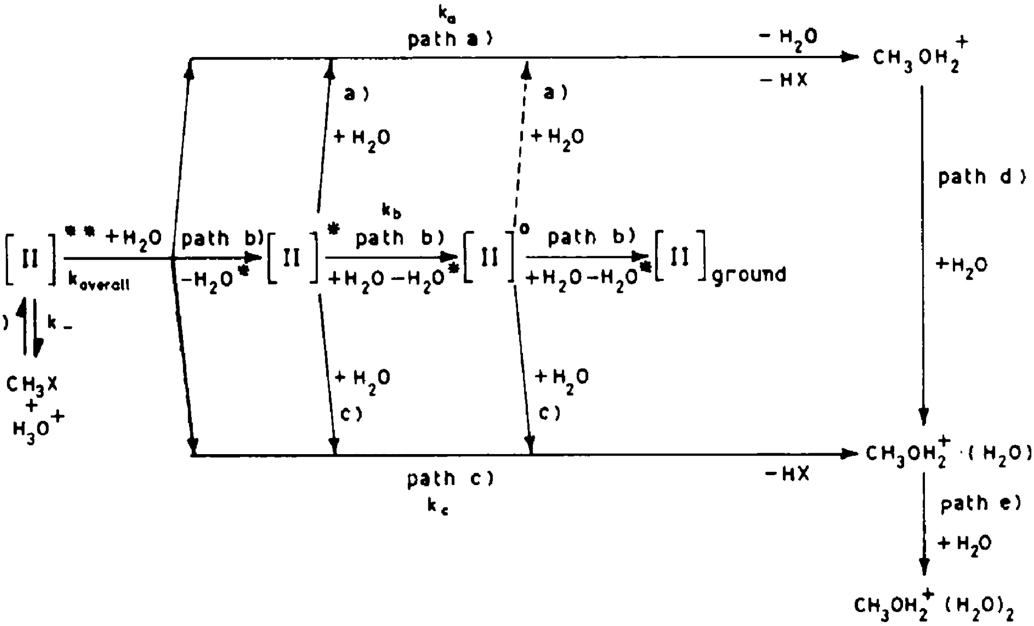
According to the suggested reaction Scheme, the rate of formation of $CH_3OH_2^+$ is given by:

$$\frac{d[CH_3OH_2^+]}{dt} = \frac{k_a k_+ [CH_3X][H_2O]}{k_- + k_{over}[H_2O]}[H_3O^+] \tag{8}$$

which semplifies at low pressures to:

$$\frac{d[CH_3OH_2^+]}{dt} = k_a K_{eq}[CH_3X][H_2O][H_3O^+] \text{ with } K_{eq} = k_+/k_-. \tag{9}$$

Both the steady-state $[H_3O^+]$ concentration and the $k_a K_{eq}$ quantity are temperature-dependent. In particular,



Scheme 1.

at a given total pressure, the relative abundance of the free (unclustered) H_3O^+ ions decreases at lower temperatures.[9a] On the other hand, the T-dependence of the k_aK_{eq} product cannot be defined *a priori* since the rate constant k_a of the bimolecular nucleophilic displacement increases with the temperature, while the equilibrium constant K_{eq} of the exothermic clustering process between H_3O^+ and CH_3X to form the adduct [II]** is expected to decrease.[9d] Under conditions where formation of $[CH_3OH_2^+]$ follow third-order kinetics (eqn 9) namely in the low-pressure region of the present experiments, the relative intensity of $CH_3OH_2^+$ ion vs T is described by the bell-shaped curves *a*, *b* and *c*, of Figs. 6 and 7. This indicates that, within the high-temperature range ($T > 450°K$, right part of the curves), namely in a region where the H_3O^+ concentration is virtually T-independent,[13] the observed negative temperature dependence of $[CH_3OH_2^+]$ must arise from a greater temperature effect on K_{eq} than on k_a. In this view, the overall positive T-dependence of $[CH_3OH_2^+]$, observed in the low-temperature range ($T < 450°K$, left part of the curves) suggests that the positive T-effect on $[H_3O^+]$ overcomes the overall negative one on the k_aK_{eq} product.

The different shape of curves *d*, *e* and *f* (Figs. 6 and 7) pertaining CH_3F and CH_3Cl systems at higher pressures ($P > 0.30$ Torr) can be traced to several factors, including a different stability of the corresponding proton-bound intermediate [II]** which, therefore, can modify the range of applicability of the semplified third-order eqn (9).

In conclusion, the present results give direct evidence for contrasting ion reactivities under different experimental conditions, mainly due to the strong influence of the reaction environment on the formation of collision-stabilized ionic species, which becomes decisive in highly polar gaseous media. Such discrepancies confirm the view that gas-phase proton-induced nucleophilic displacement at saturated carbon is governed by factors much more complex than the simple relative proton affinities of the encounter pairs and the overall exothermicity of the process. Apart from the marked structural effects on substitutions involving relatively complex molecules, both clustering of the ionic species and collisional deactivation of the excited reaction complex are found to play a decisive role in determining the mechanism of such reactions, even though occurring between very simple species. As a consequence, any simple reactivity model for gas-phase ionic displacements based on correlations of kinetic data obtained under particular conditions, namely in the rather restricted range of low pressures typical of ICR techniques, is bound to fail, if extended to gaseous processes occurring under different experimental conditions, and, therefore, any further generalizations stemming from it are unwarrented.

Acknowledgements—The authors are indebted to Prof. F. Cacace for his active interest in their work, and to Mrs. C. Sparapani for her skilled technical assistance.

REFERENCES

[1] Part 1: G. Angelini and M. Speranza, *J. Chem. Soc. Chem. Commum.* 213 (1978); Part 2: M. Speranza and G. Angelini, *J. Am. Chem. Soc.* **102**, 3115 (1980).

[2] W. J. Richter and H. Schwarz, *Angew. Chem. Int. Ed. Engl.* **17**, 424 (1972).

[3a] D. Holtz, J. L. Beauchamp and S. D. Woodgate, *J. Am. Chem. Soc.* **92**, 7484 (1970); [b]D. Holtz and J. L. Beauchamp, *Nature*, **231**, 204 (1971); [c]J. L. Beauchamp, D. Holtz, S. D. Woodgate and S. L. Patt, *J. Am. Chem. Soc.* **94**, 2798 (1972); [d]R. H. Staley, R. R. Cordeman, M. S. Foster and J. L. Beauchamp, *Ibid.* **96**, 1260 (1974).

[4] Proton affinities (kcal mol^{-1}): $CH_3Cl = 165$; $H_2O = 170$; $C_2H_5Cl = 172$; $CH_3F = 156$; J. F. Wolf, R. H. Staley, I. Koppel, M. Taagepera, R. T. Mc Iver, Jr., J. L. Beauchamp and R. W. Taft, *J. Am. Chem. Soc.* **99**, 5417 (1977).

[5a] J. K. Kim, M. C. Findley, W. G. Henderson and M. C. Caserio, *Ibid.* **95**, 2184 (1973); [b]J. K. Pau, J. K. Kim and M. C. Caserio, *Ibid.* **100**, 3831 (1978); [c]*Ibid.* 3838; [d]J. K. Pau, M. B. Ruggera, J. K. Kim and M. C. Caserio, *Ibid.* 4242.

[6] E. K. Fukuda and R. T. Mc Iver, Jr., *Ibid.* **101**, 2498 (1979).

[7] M. M. Mann, A. Hustralid and J. T. Tate, *Phys. Rev.* **58**, 340 (1940).

[8] F. W. Lampe, F. H. Field and J. L. Franklin, *J. Am. Chem. Soc.* **79**, 6132 (1957).

[9a] P. Kebarle, S. K. Searles, A. Zolla, J. Scarborough and M. Arshadi, *Ibid.* **89**, 6393 (1967); [b]E. P. Grimsrud and P. Kebarle, *Ibid.* **95**, 7939 (1973); [c]K. Hiraoka, E. P. Grimsrud and P. Kebarle, *Ibid.* **96**, 3359 (1974); [d]M. Maot-Ner and F. H. Field, *Ibid.* **99**, 998 (1977).

[10] F. H. Field, *Ion Molecule Reactions* (Edited by J. L. Franklin), Vol. 1, p. 261. Plenum Press, New York (1972).

[11] The enthalpy change for the formation of proton-bound complexes, similar to [II]**, is estimated to range around 30 kcal mol^{-1} (ref. 3–8, R. L. Woodin, D. S. Bomse and J. L. Beauchamp, *J. Am. Chem. Soc.* **100**, 3248 (1978).

[12] Path 6 is endothermic. According to Ref. 3, the exothermic path 7 as well as the following direct one-step substitution:

$$H_3O^+ + CH_3X \longrightarrow CH_3OH_2^+ + HX$$

is forbidden on account of its unfavoured free energy requirements.

[13] At low pressures ($P < 0.3$ Torr) and high temperatures ($T > 450°K$) naked H_3O^+ is the only water ion observed in our source.