Bull Soc Chim Fr (1996) 133, 59-64

Thermoneutral nucleophilic substitution of β-distonic ions $^{\bullet}CH_2CH_2XH^+$ in the gas phase (X = OH, OCH_3, OC_2H_5, NH_2)

Henri-Edouard Audier* , Jacques Fossey, Danielle Leblanc, Philippe Mourgues

Laboratoire des mécanismes réactionnels, URA CNRS 1307, École polytechnique, 91128 Palaiseau, France

(Received 3 October 1995; accepted 16 November 1995)

Summary – The gas-phase bimolecular reactivity of the β-distonic ions $^{\bullet}CH_2CH_2XH^+$ **1–4** (X = OH, OCH_3, OC_2H_5, NH_2) has been studied by FT-ion cyclotron resonance mass spectrometry. Substitution of the XH group by a neutral species is generally considered to be the most characteristic reaction of such ions. It is shown in this work that the degree of substitution strongly depends on the nature of the β-distonic ion. Thermoneutral substitution of the XH group by a labeled neutral molecule $^*XH$ is rapid for ion **1** and not observed for ion **4**. The behavior of ions **2** and **3** is intermediate. Ab initio calculations at the MP2(FU)/6-31G* level of theory provide a rationale for these observations: the transition structure for substitution lies below the reactants in energy for X = OH (ion **1**) but it becomes higher in energy than the reactants when X = NH_2 (ion **4**).

gas-phase ion – molecule reactions / mass spectrometry FT-ion cyclotron resonance / nucleophilic substitution / distonic ions

Résumé – Substitution nucléophile thermoneutre d'ions β-distoniques $^{\bullet}CH_2CH_2XH^+$ en phase gazeuse (X = OH, OCH_3, OC_2H_5, NH_2). *La réactivité bimoléculaire en phase gazeuse des ions β-distoniques $^{\bullet}CH_2CH_2XH^+$* **1–4** *(X = OH, OCH_3, OC_2H_5, NH_2) a été étudiée en spectrométrie de masse par résonance cyclotronique ionique et transformé de Fourier. La substitution du groupe XH par un neutre est généralement considérée comme étant la réaction la plus caractéristique de ces ions. Ce travail montre que la substitution dépend fortement de la nature de l'ion β-distonique. En particulier, la substitution thermoneutre du groupe XH par le neutre marqué $^*XH$ est rapide pour l'ion $^{\bullet}CH_2CH_2OH_2^+$ (**1**) mais n'est pas observée pour l'ion $^{\bullet}CH_2CH_2NH_3^+$ (**4**). Le comportement des ions $^{\bullet}CH_2CH_2OH^+CH_3$ (**2**) et $^{\bullet}CH_2CH_2OH^+C_2H_5$ (**3**) est intermédiaire. Les calculs ab initio au niveau MP2(FU)/6-31G* permettent de rationaliser ces observations: la structure de l'état de transition pour la substitution possède une énergie inférieure à celle des réactifs pour X = OH (ion **1**), mais supérieure à celle des réactifs pour X = NH_2 (ion **4**).*

réaction ion – molécule en phase gazeuse / spectrométrie de masse TF-résonance cyclotronique ionique / substitution nucléophile / ion distonique

Introduction

Gas-phase ion chemistry allows the precise study of unimolecular or bimolecular reactions of organic ions in the absence of solvent or by modeling its role. Good methods now exist for the determination of the structure of the products, and for the measurement of transition or final states energies. However, it often remains difficult to obtain evidence for the stable intermediates which intervene in the reaction.

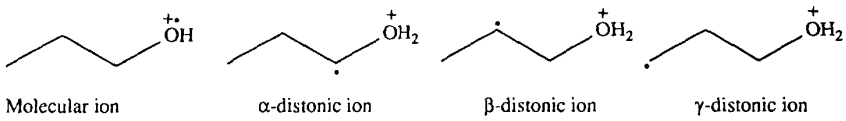
Distonic ions are the most frequently invoked intermediates [1]. Distonic ions are radical cations which can formally be generated by ionization of a zwitterion or a diradical [1, 2]. As a consequence, in a conventional valence bond description such ions have the charge and the radical localized on separate atoms (scheme 1).

Distonic ions can be prepared selectively and characterized in both the gas phase and the condensed phase [1]. They are considered to be key intermediates in some reactions in solution, eg, the Hofmann–Löffler reaction [3].

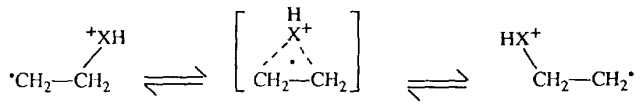
The most characteristic unimolecular reaction of β-distonic ions of the type $^{\bullet}CH_2CH_2XH^+$ in the gas phase is their isomerization by a 1,2-XH shift [2, 4] (scheme 2). Calculations indicate that β-distonic ions generally correspond to minima on the potential energy surface and that the 1,2-XH shift only requires 3 kcal/mol when XH = OH_2 but considerably higher energy when XH = NH_3 [5, 6]. Bimolecular reactions of β-distonic ions have been reported in several studies [7–10] and the transfer of the $CH_2CH_2^{\bullet+}$ moiety to a neutral is considered to be a characteristic reaction of these ions.

This transfer can also be considered as a substitution of the XH group by the neutral molecule M (reaction **a**, scheme 3). The thermoneutral substitution with labeled neutrals (reaction **b**) is reported in this work. It will be

* Correspondence and reprints

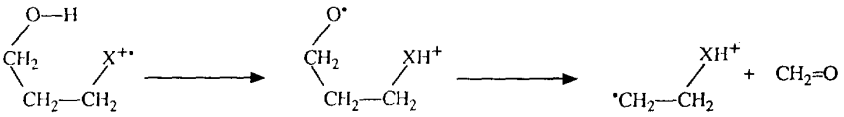


Scheme 1



Scheme 2

Scheme 3



Scheme 4

shown that the rate of substitution strongly depends on the nature of the β-distonic ion.

Experimental section

The bimolecular reactions were studied with a Bruker (Bremen, Germany) CMS-47X FT-ICR spectrometer equipped with an external ion source. The neutral reactants were introduced into the cell through a leak valve (Balzers, Liechtenstein) at a pressure of 2×10^{-8} to 5×10^{-8} mbar depending on the experiment, and then diluted with argon, to give a total pressure of $2\text{–}3 \times 10^{-7}$ mbar.

The $^{\bullet}CH_2CH_2XH^+$ reactant ions were formed in the external ion source by fragmentation of $HOCH_2CH_2CH_2X^{\bullet+}$ [2] (scheme 4) and isolated after transfer to the ICR cell by RF ejection of all the other ions. After a 1 s delay, which was found to be enough to bring the ions near to thermal energies by successive collisions with argon, the isolation procedure was repeated by the use of low-voltage single RF pulses (soft shots) at the resonance frequencies of all undesired ions.

The exact composition of all ions produced in the reactions was checked by systematic high resolution mass measurements, reducing the argon pressure to 4×10^{-8} mbar, and increasing the relaxation time to 2 s.

For kinetic measurements, the exact pressure of the neutral species was determined after correction for the sensitivity of the ionization gauge towards it. Calibration of the ionization gauge was performed with reactions of known first-order rate constant, such as protonation of methane by $CH_4^{\bullet+}$ ($k = 1.17 \times 10^{-9}$ cm^3 molecule^{-1} s^{-1}).

Standard ab initio molecular orbital calculations [11] were carried out using the GAUSSIAN 92 [12] and GAUSSIAN 94 [13] program packages. Calculations were performed at the MP2(FU) [14] levels of theory using the split-valence shell 6-31G* basis set [15] which has polarization basis functions (*d*-type on nonhydrogen atoms). The spin-unrestricted method was used for open shell systems.

A diagonalization of the analytically calculated Hessian matrix at the MP2(FU)/6-31G* level was used to calculate harmonic vibrational frequencies, from which critical points of the potential energy surface (PES) were characterized as minima or first-order saddle points. Zero-point energy (ZPE) and thermodynamic quantities (E_{298}, S_{298}) were also determined (cf table I).

The interaction energy ΔE_{MP2} (table II) was calculated as the difference between the energy of the neutral-distonic supersystem, $E_{MP2}(ND)$ and the sum of energies of neutral $E_{MP2}(N)$ and distonic $E_{MP2}(D)$:

$$\Delta E_{MP2} = E_{MP2}(ND) - (E_{MP2}(N) + E_{MP2}(D))$$

The counterpoise method for correcting for the basis set superposition error (BSSE) is not entirely satisfatory and it is often better to use a larger basis set. Nevertheless, because the finite basis set was used, it was necessary to eliminate BSSE. Estimates of the BSSE were calculated (table II) using the full counterpoise method of Boys and Bernardi [16]:

$$\text{BSSE} = E_{MP2}(N_{def})_{ND} - E_{MP2}(N_{def})_N + E_{MP2}(D_{def})_{ND} - E_{MP2}(D_{def})_D$$

where $E_{MP2}(N_{def})_{ND}$ and $E_{MP2}(N_{def})_N$ correspond to the energy of the neutral calculated using its geometry within the dimer (N_{def}) and the basic function of N plus D and N alone respectively.

ΔH_{298}, the enthalpy of the reaction between the distonic ion and the neutral towards the critical points of the neutral-distonic supersystem, was calculated as:

$$\Delta H_{298} = \Delta U_{298} - RT = \Delta E_{MP2} + \text{BSSE} + \Delta E_{298} - RT$$

Results and discussion

It appears that the occurrence of the substitution reaction (scheme 3) depends strongly on the nature of the β-distonic ion $^{\bullet}CH_2CH_2XH^+$. This is often observed with $^{\bullet}CH_2CH_2OH_2^+$ **1** [10a] but only rarely with $^{\bullet}CH_2CH_2NH_3^+$ **4** [9a, 17]. Ions **3** and **4** (X = OCH_3, OC_2H_5) represent intermediate cases [9, 10].

Arguments based on thermochemistry provide a preliminary explanation of these differences. For instance,

(c) $^{\bullet}CH_2CH_2^{+}OH_2 + CH_2O \longrightarrow {}^{\bullet}CH_2CH_2^{+}OCH_2 + H_2O \quad \Delta H_f = -6$ kcal/mol

(d) $^{\bullet}CH_2CH_2^{+}NH_3 + CH_2O \longrightarrow {}^{\bullet}CH_2CH_2^{+}OCH_2 + NH_3 \quad \Delta H_f = 32$ kcal/mol

Scheme 5

on the basis of the enthalpies of formation published so far [5, 18, 19], reaction (c) of ion **1** with CH_2O (scheme 5) is exothermic and observed [10a], while the corresponding reaction (d) with ion **4** is endothermic and not observed [9a, 17].

However, the thermochemistry alone does not explain the differences observed in reactivity. The thermoneutral $C_2H_4^{+\bullet}$ transfer (ie, the substitution of XH by labeled *XH; reaction b, scheme 3) appears to differ for the various ions, as shown by kinetic measurements. The experimental rate constants k_{exp} for these thermoneutral reactions have been determined and compared with the calculated capture collision rate constant k_{coll} [20]. The results show that:

- the substitution of H_2O by $H_2{}^{18}O$ (fig 1) is rapid for the $^{\bullet}CH_2CH_2OH_2^{+}$ ion **1** ($k_{coll} = 2.4 \times 10^{-9}$ cm^3 molecule^{-1} s^{-1}, $k_{exp}/k_{coll} = 0.3$);
- the substitution of CH_3OH by CD_3OD in $^{\bullet}CH_2CH_2OHCH_3^{+}$ **2** is slow ($k_{exp}/k_{coll} = 0.05$, $k_{coll} = 2.0 \times 10^{-9}$ cm^3 molecule^{-1} s^{-1}) while that of C_2H_5OH by C_2D_5OD in $^{\bullet}CH_2CH_2OH^{+}C_2H_5$ **3** is very slow; and
- the substitution of NH_3 by $^{15}NH_3$ in $^{\bullet}CH_2CH_2NH_3^{+}$ **4** is not observed at all [21].

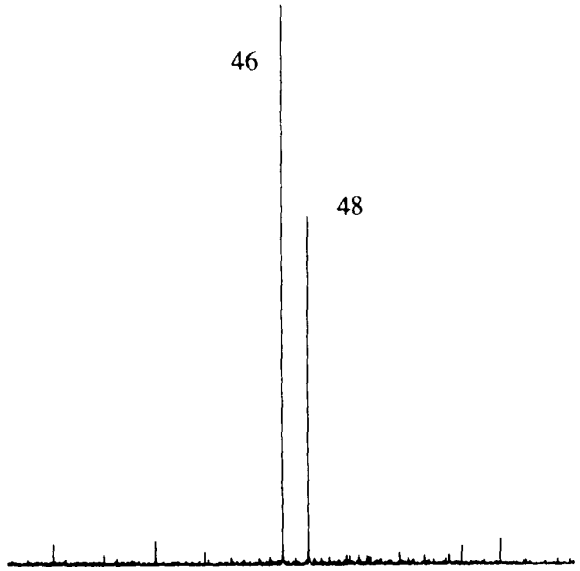


Fig 1. Reaction of $^{\bullet}CH_2CH_2OH_2^{+}$ ($m/z = 46$) with $H_2{}^{18}O$ giving $^{\bullet}CH_2CH_2{}^{18}OH_2$ ($m/z = 48$) (pressure 3×10^{-8} mbar) in the cell of an instrument FT-ICR (reaction time 750 ms).

A qualitative explanation of these observations is based on the following. Early calculations [5] indicate that in ion **1** the C–O bond is long ($d = 1.65$ Å), and the 1,2 shift is very easy. Since the ionization energy (IE) of ethylene (10.5 eV) is lower than that of water (11.35 eV) [19], $^{\bullet}CH_2CH_2OH_2^{+}$ can be considered as a structure in which the C–O bond is stretched and in which a significant positive charge resides on the carbon atoms. Such a structure may be prone to a nucleophilic attack of $H_2{}^{18}O$ on the carbon.

In the ion $^{\bullet}CH_2CH_2NH_3^{+}$ **4**, the C–N bond appears to have a normal length, while the 1,2-NH_3 shift requires a significant energy barrier to be overcome. Since the IE of ethylene (10.5 eV) is higher than that of ammonia (10.15 eV), the positive charge is dominantly located at the NH_3 group. Therefore a nucleophilic attack on a carbon atom should not be favored.

Ab initio calculations allow a quantitative approach. Various computations were performed for the ions **1** and **4**, and the systems $^{\bullet}CH_2CH_2OH_2/H_2O$ and $^{\bullet}CH_2CH_2NH_3^{+}/NH_3$, which represent the extreme cases in the behavior of this kind of ions. The results are reported in tables I and II.

Table I. EUMP2/6-31G*//6-31G* in hartrees. ZPE in kcal/mol. E_{298} (thermal energy in kcal/mol) and S_{298} (entropy in cal/mol·K) at 298 K under 1 atm.

	EUMP2	*ZPE*	E_{298}	S_{298}
$^{\bullet}CH_2CH_2OH_2^{+}$	−154.176733	49.9	52.9	68.0
$^{\bullet}CH_2CH_2OH_2 + H_2O$	−230.375977	63.4	68.2	113.1
INC1	−230.395491	64.6	70.1	89.9
TS1	−230.389699	63.0	68.6	89.6
HBC1	−230.422203	65.3	70.0	84.1
$^{\bullet}CH_2CH_2NH_3^{+}$	−154.392353	59.8	62.8	66.6
$^{\bullet}CH_2CH_2NH_3^{+} + NH_3$	−190.749731	82.0	86.7	112.6
INC4	−190.776783	83.0	88.1	89.8
TS4	−190.737825	82.1	87.0	82.2
HBC4	−190.792450	83.7	88.7	88.2

Table II. Critical points of the potential energy surface (PES). Energies in kcal/mol at 298 K under 1 atm. $\Delta H_{298} = \Delta U_{298} - RT = \Delta E_{MP2} + \text{BSSE} + \Delta E_{298} - RT$ with $RT = 0.6$ kcal/mol.

	ΔE_{MP2}	*BSSE*	ΔE_{298}	ΔH_{298}
$^{\bullet}CH_2CH_2OH_2^{+} + H_2O$	0	0	0	0
INC1	−12.2	2.0	1.9	−8.9
TS1	−8.6	3.1	0.4	−5.7
HBC1	−29.0	2.7	1.8	−25.1
$^{\bullet}CH_2CH_2NH_3^{+} + NH_3$	0	0	0	0
INC4	−17.0	1.9	1.4	−14.3
TS4	7.5	5.2	0.3	12.4
HBC4	−26.8	2.6	1.0	−23.8

The structures of ions **1** and **4** are represented in figure 2. Compared to protonated ethanol (1.547 Å), the C–O bond in ion **1** is longer (1.604 Å), albeit somewhat less than that previously calculated at a lower level of theory [5]. For ion **4** the length of the C–N bond is only slightly larger than in protonated ethylamine (1.538 Å versus 1.519 Å).

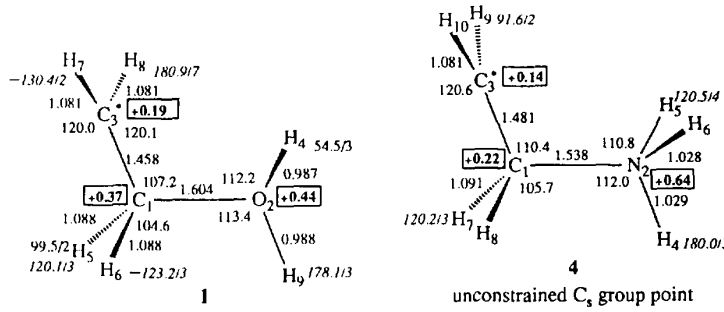


Fig 2. EUMP2/6-31G*//6-31G* optimized geometries for the β-distonic ions. Bond lengths are given in Å, angles ($X_1X_2X_3$) and dihedral angles ($X_1X_2X_3X_4$) in degrees (value of X_3 or X_4 may be specified after a slash). Dihedral angles in italics. Net charges (framed numbers) were obtained through natural population analysis of the MP2 density matrix.

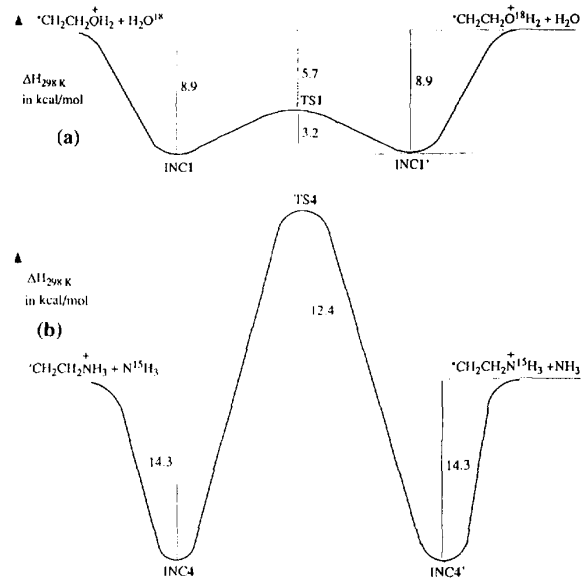


Fig 3. Energy diagrams for reactions between ion $^{\bullet}CH_2CH_2OH_2^+$ and H_2O (a) and $^{\bullet}CH_2CH_2NH_3^+$ and NH_3.

The distribution of the positive charge is more significant. Some 56% of the charge is carried by the CH_2CH_2 moiety in ion **1**, but only 36% in ion **4**.

Finally, the α-CH_2 group bears some of the positive charge in ion **1** (37%), a value which is significantly less for ion **4** (22%) This confirms the qualitative explanation outlined above.

The results of computations for the systems $^{\bullet}CH_2CH_2OH_2/H_2O$ and $^{\bullet}CH_2CH_2NH_3^+/NH_3$ are summarized in the energy profiles depicted in figure 3, and provide an even clearer interpretation of the experimental results.

Figure 3a shows the energy diagram for the reaction between the ion $^{\bullet}CH_2CH_2OH_2^+$ **1** and H_2O. When a molecule of water approaches the oxygen side of the distonic ion **1**, the H-bonded complex HBC1 is formed (see fig 4 for the geometry). This complex is characterized by the presence of a H-bond between the hydroxylic hydrogen of the ion and the oxygen of the water molecule and it is highly stabilized ($\approx$ 25.1 kcal/mol). Nevertheless this complex is a dead end in the reaction pathway [22].

The attack of water on the radical carbon in the β-position gives a repulsive three-electron bond and no critical point (minimum or transition structure) is found in this region.

However, when the water molecule approaches the α-carbon, the energy of the system decreases until the ion-neutral complex INC1 (fig 4). In this complex electrostatic interactions exist between the charge carried by the α-carbon and the water molecule. The interaction energy is 8.9 kcal/mol.

A nucleophilic substitution can take place within this INC1 complex via a symmetric transition structure TS1 (fig 4). This transition structure lies 5.6 kcal/mol in energy below the reactants. Therefore in ion **1** the thermoneutral nucleophilic substitution is facile.

The energy diagram for the reaction of the $^{\bullet}CH_2CH_2NH_3^+$ ion **4** and NH_3 is reported in figure 3b. When a molecule of NH_3 approaches ion **4**, the H-bonded complex HBC4 or the ion-neutral complex INC4 is formed (fig 5). Their interaction energies are 23.8 and 14.3 kcal/mol, respectively. However, the transition structure for substitution TS4 (fig 5) now lies

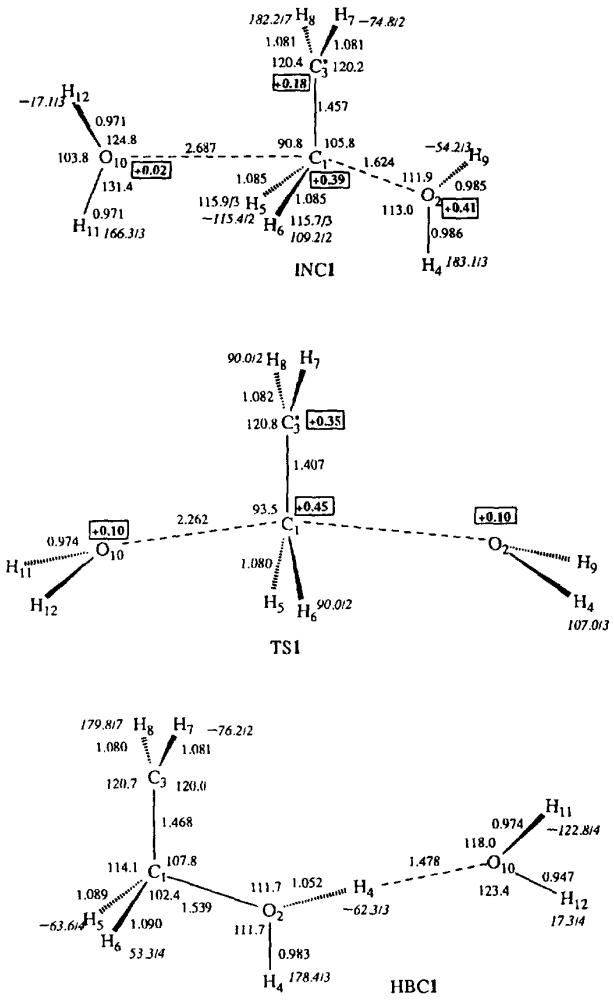


Fig 4. EUMP2/6-31G*//6-31G* optimized geometries for INC1 (minima), TS1 (transition structure, unconstrained C_{2v} point group) and HBC1 (minima). See comments for figure 2.

12.4 kcal/mol above the reactant's energy and this effectively prevents the substitution reaction.

Conclusions

In this work it has been shown that $^{\bullet}CH_2CH_2OH_2^+$ easily undergoes a thermoneutral nucleophilic substitution of water while $^{\bullet}CH_2CH_2NH_3^+$ does not react with ammonia. This has been explained by a difference in the structure of these ions, and supported by calculations on the ion-neutral reacting systems.

Interaction between β-distonic ions $^{\bullet}CH_2CH_2XH^+$ and a neutral species leads to two kinds of intermediates: i) an ion-neutral complex in which the interaction between the neutral species and the α-carbon is mainly electrostatic; and ii) a more stable H-bond complex, in which the neutral is H-bonded to the XH group of the ion. When the proton affinity of the neutral is low this structure is a dead end on the reaction pathway. We will report in a subsequent paper [17] that when the proton

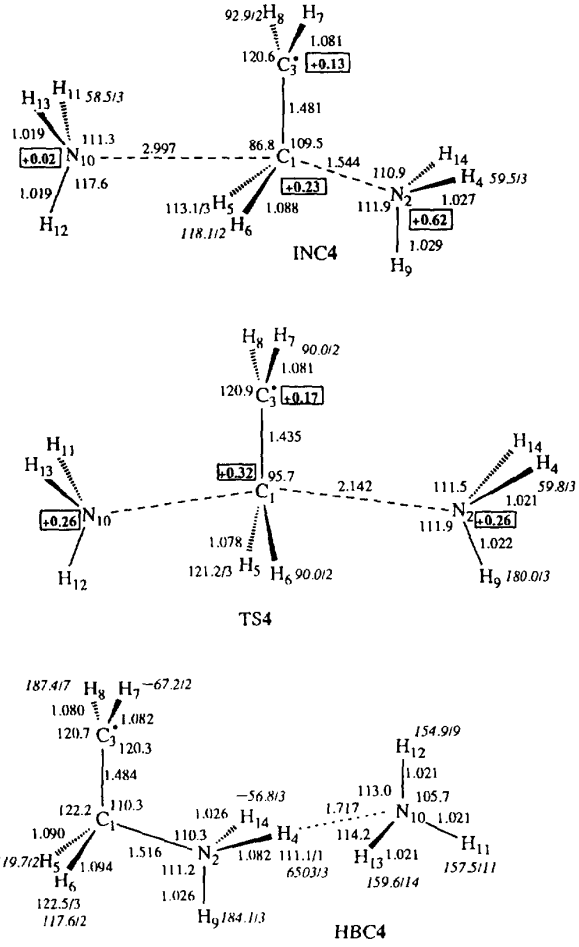


Fig 5. EUMP2/6-31G*//6-31G* optimized geometries for INC4 (unconstrained C_s point group), TS4 (transition structure, unconstrained C_{2v} point group) and HBC4 (minima). See comments for figure 2.

affinity of the neutral is high enough, this complex is the reactive intermediate for the protonation of the neutral species.

References

1 Hammerum S, *Mass Spectrom Rev* (1988) 7, 123.

2 Radom L, Bouma WJ, Nobes RH, Yates BF, *Pure Appl Chem* (1984) 56, 1,1831.

3 For instance, the Hofmann-Löffler-Freytag reaction, see:
a) Wawzonek S, Thelen PJ, *J Am Chem Soc* (1950) 72, 2118
b) Corey EJ, Hertler WR, *J Am Chem Soc* (1960) 82, 1657
c) Wawzonek S, Culbertson TP, *J Am Chem Soc* (1960) 82, 441
d) Wolff ME, *Chem Rev* (1963) 63, 55
e) Stella L, *Angew Chem Int Ed Engl* (1983) 22, 337

4 Bjornholm T, Hammerum S, Kuck D, *J Am Chem Soc* (1988) 110, 3862.

5 a) Bouma W, Nobes R, Radom L, *J Am Chem Soc* (1983) 105, 1743
b) Yates B, Radom L, *J Am Chem Soc* (1987) 109, 2910

c) Yates B, Radom L, *Org Mass Spectrom* (1987) 22, 430.

6 Postma R, Ruttink P, van Baar B, Terlouw JK, Holmes JL, Burgers PC, *Chem Phys Lett* (1986) 123, 409.

7 Morton TH, Beauchamp JL, *J Am Chem Soc* (1975) 97, 2355

8 Busch KL, Nixon WB, Bursey MM, *J Am Chem Soc* (1978) 100, 1621.

9 a) Leblanc D, Thèse, Université Paris XI (1990)
b) Audier HE, Mourgues P, Leblanc D, Hammerum S, *C R Acad Sci Paris* (1993) 317, Série II, 27.

10 a) Mourgues P, Audier HE, Hammerum S, *Rapid Comm Mass Spectrom* (1994) 8, 53
b) Brenner V, Milliet A, Mourgues P, Ohanessian G, Audier HE, *J Phys Chem* (1995) 99, 10837
c) Troude V, Leblanc D, Mourgues P, Audier HE, *J Mass Spectrom*, in press.

11 Hehre WJ, Radom L, Schleyer PvR, Pople JA, Ab-initio *Molecular Orbital Theory*, Wiley, New York, 1986.

12 *Gaussian 92*, Revision B, Frisch MJ, Trucks GW, Head-Gordon M, Gill PNW, Wong MW, Foresman JB, Johnson BG, Schlegel HB, Robb MA, Replogle ES, Gomperts R, Andres JL, Raghavachari K, Binkley JS, Gonzalez C, Martin RL, Fox DJ, Defrees DJ, Baker J, Stewart JP, Pople JA, Gaussian, Inc, Pittsburgh, PA 1992.

13 *Gaussian 94*, Revision B2, Frisch MJ, Trucks GW, Schelgel HB, Gill PNW, Johnson BG, Robb MA, Cheeseman JR, Keith TA, Petersson GA, Montgomery JA, Raghavachari K, Al-Lahman MA, Zakrzewski VG, Ortiz JV, Foresman JB, Cioslowski J, Stefanov BB, Nanayakkara A, Challacombe M, Peng CY, Ayala PY, Chen W, Wong MW, Andres JL, Replogle ES, Gomperts R, Martin RL, Fox DJ, Binkley JS, Defrees DJ, Baker J, Stewart JP, Head-Gordon M, Gonzalez C, Pople JA, Gaussian, Inc, Pittsburgh, PA 1995.

14 Moller C, Plesset MS, *Phys Rev* (1934) 46, 618. Krishnan R, Pople JA, *Int J Quantum Chem Symp* (1980) 14, 91.

15 Hariharan PC, Pople JA, *Chem Phys Lett* (1972) 66, 217.

16 Boys SF, Bernardi F, *Mol Phys* (1970) 19, 553.

17 A detailed study of the different bimolecular reactions of these four β-distonic ions will be published elsewhere.

18 Wittneben D, Grützmacher HF, *Int J Mass Spectrom Ion Proc* (1990) 100, 545.

19 Lias SG, Bartmess JE, Holmes JL, Levin RD, Mallard WG, *J Chem Phys, Ref data* (1988) 17, suppl N°1.

20 The decay of the reacting ions follows a first-order kinetic law, and k_{exp}/k_{coll} is defined as the efficiency of the reaction. However, in this case, the transition state is symmetric and so maximum efficiency is reached when $k_{exp}/k_{coll} = 0.5$. The theoretical capture rate constant is derived from the average dipole orientation (ADO) theory, and was determined according to Su T and Chesnavitch WJ, *J Chem Phys* (1982) 76, 5183.

21 Nevertheless, the reaction of ND_3 with $^{\bullet}CH_2CH_2NH_3^+$ **4** shows that hydrogen exchange occurs one by one between ammonia and the NH_3 group of the distonic ion. No other reaction is observed [17].

22 Hammerum S, Vulpius T, Audier HE, *Org Mass Spectrom* (1992) 27, 369.