Fast Interconversion of $C_4H_7^+$ Cations in the Gas Phase and in a Gaseous Microsolvated Environment

Fulvio Cacace, Barbara Chiavarino, and M. Elisa Crestoni*[a]

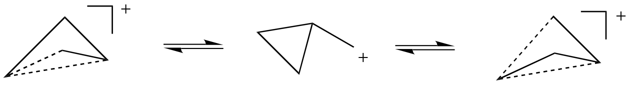
Abstract: The equilibration of cyclobutyl **1** and **1′** and the cyclopropylmethyl cation (**2**) has been studied in the gas phase by utilizing FT-ICR mass spectrometry and high-pressure radiolytic techniques. A suitable gaseous nucleophile, C_6X_6 (X = H,D), was used to sample the equilibration of $C_4H_7^+$ ions, produced from both cyclobutanol and cyclopropylmethanol. These are either dispersed in the bulk gas or confined within a $C_4H_7^+/C_6X_6$ complex that contains a molecule of solvent (H_2O). The analysis of the products shows that, irrespective of their source and of the intermolecular or intracomplex nature of the process, the $C_4H_7^+$ ions undergo equilibration before they are trapped. The equilibrium (**1**+**1′**)/**2** ratio is very close to unity at 300 K, and the results from the intracomplex trapping experiment show that equilibration occurs within a time interval $\leq 10^{-10}$ s.

Keywords: cluster chemistry · gas-phase chemistry · ion-neutral complexes · isomerizations · radiolysis

Introduction

The interest in $C_4H_7^+$ ions, whose study led J. D. Roberts to propose the first nonclassical structure as early as in 1951,[1] is unabated after almost five decades of extensive investigation.[2] Practically all the tools of experimental physical organic chemistry have been utilized, including solvolytic studies, isotope labeling and perturbation techniques, NMR spectroscopy, mass spectrometry, matrix IR spectroscopy, and photoelectron spectroscopy.[3] The experimental studies have been complemented by increasingly sophisticated theoretical investigations by semiempirical and ab initio methods, aimed at the evaluation of the structure, the relative stability, and the barriers for the interconversion of isomeric $C_4H_7^+$ ions, and the methods have also been used to model the results of temperature-dependent NMR spectroscopy.[4]

Based on the evidence from the above theoretical and experimental studies, the current consensus seems to be that the symmetrical bicyclobutonium cations **1** and **1′** (Scheme 1) and the bisected cyclopropylmethyl cation **2** exist as rapidly interconverting species of nearly equal stability that are separated by a very low barrier.[4c, 4d] The barrier probably does not exceed a few tenths of a kcal mol^{-1}.[3g]



1 **2** **1'**

Scheme 1.

Yet, despite such a sustained research effort, certain problems related to the equilibration of $C_4H_7^+$ cations, recently defined as a chemical "chimera" by their first investigator,[5] deserve further investigation. In particular, the equilibrium composition of isomers, deduced from condensed-phase data, may be conceivably affected by environmental factors, for example, differential solvation effects and interactions with the anion in the liquid phase, and lattice effects in the solid state.[6] Although the differential stabilization of the cations by these environmental effects is generally small, it can be significant in this case, because of the nearly identical stability of the isomeric cations. Furthermore, there is no detailed information on the rate of equilibration, except for the inference that it is presumably fast in view of the low barrier suggested by NMR spectroscopy and theoretical results.[3, 4] This state of affairs makes gas-phase studies of the $C_4H_7^+$ system quite appealing. First, the effects of the medium on the equilibrium composition of the isomeric $C_4H_7^+$ ions are greatly reduced, and in principle this makes gas-phase studies a much more reliable means for the investigation of intrinsic properties of the system. Second, only in the gas phase can charged species be thought of as essentially free; this allows a direct comparison with theoret-

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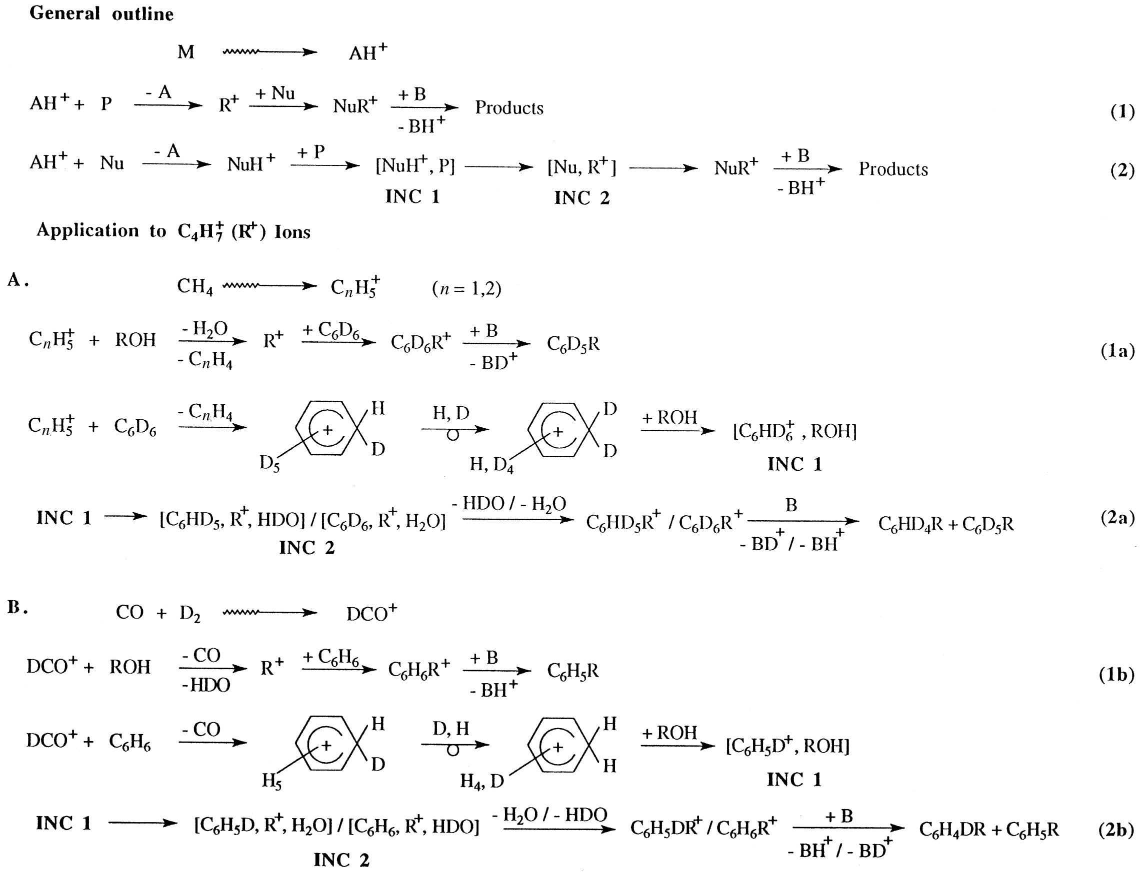
ical results. Furthermore, recent methodological developments allow the same reaction to be studied in the gas phase either in the complete absence of solvent, or in the presence of a controlled, small number of neutral molecules, which provide valuable information on the role of the solvent.[7] Finally, the time resolution of current experimental approaches to the study of fast gas-phase ionic reactions is far superior than that achievable in condensed phases. Whereas the time resolution of structurally diagnostic mass spectrometric techniques is of the order of 10 μs, high-pressure techniques, that is, β-decay and the radiolytic technique,[8, 9] allow ionic reactions to be investigated in the time frame from 10 to 100 ns. Actually, an early β-decay study has provided the first unambiguous evidence for the existence and the interconversion of cyclobutyl and cyclopropylmethyl cations in the gas phase; however, this does not allow the isomerization rate to be evaluated.[10] Recently, with the use of a gaseous ion-neutral complex (INC)[7, 11–17] as a walless reaction "vessel",[18–21] the time resolution of the radiolytic technique has been improved. This method allows the study of reactions in the time frame of approximately 100 ps.[22, 23] Here we report the application of this improved method to the study of the interconversion of $C_4H_7^+$ cations from cyclobutyl and cyclopropylmethyl precursors, both in the free state and in a microsolvated environment that contains the cation, a *single* molecule of the nucleophile, and a *single* molecule of solvent.

Methodology: Our approach to the study of gaseous carbenium ions R^+, which undergo fast isomerization, can be outlined as follows. Ionization of the bulk component of the gaseous system, M, yields a Brønsted acid, AH^+, unreactive towards the parent molecule [see Eqs. (1)–(2b)].

The gas contains low concentrations of a proelectrophile (a species whose protonation gives the R^+ cation), P, and a suitable nucleophile, Nu. Proton transfer to the proelectrophile from AH^+ promotes the reaction sequence (1), namely a conventional electrophilic alkylation.[6, 8] Alternatively, proton transfer to the nucleophile promotes reaction sequence (2), another route to alkylated products.[6, 19] Since both sequences occur concurrently, discrimination of their products is necessary and can be achieved by utilizing isotopically labeled reagents. The R^+ ions from sequence (1) are dispersed in the bulk gas, and their trapping by the nucleophile, present at low concentrations, requires a relatively long time. By contrast, in sequence (2) R^+ is generated together with the nucleophile in the same INC 2, and the high local concentration of both reagents drastically reduces the lifetime and hence the time allowed for isomerization of R^+ before its trapping. Deprotonation of the alkylated cations from both sequences, and hence their conversion into neutral products amenable to separation and characterization by GC-MS, is ensured by a strong gaseous base, for example, triethylamine.[24] The amine is also present at low concentrations in the gas. An example of this application is provided by the isomerization of protonated cyclopropane to the isopropyl cation; the investigation is carried out in the gas phase by utilizing c-C_3H_6 as a proelectrophile and an arene as the nucleophile. The results show that in this system



sequence (1) gives a mixture of *n*-propylated and isopropylated products, which point to extensive isomerization of gaseous $c\text{-}C_3H_7^+$ before its trapping by the nucleophile. In contrast, sequence (2) yields exclusively *n*-propylated products, and this suggests that the extremely short lifetime of the $c\text{-}C_3H_7^+$ ion within INC 2 does not allow its appreciable isomerization.[25]

The bulk gas utilized in most of the present radiolytic experiments is CH_4, whose ionization gives two strong Brønsted acids, CH_5^+ and $C_2H_5^+$, according to well-established processes.[8] Cyclobutanol or cyclopropylmethanol are used as proelectrophiles, based on previous results that show that intracomplex protonation of related alcohols, such as 2-butanol, gives the corresponding carbenium ions as the alkylating agents.[21] Finally, fully deuterated benzene is used as the nucleophile in order to distinguish the products from sequence (1a), namely $C_6D_5-C_4H_7$ isomers, from the products from sequence (2a), namely $C_6HD_4-C_4H_7$ isomers. The two groups of products can be conveniently distinguished by GC-MS methods, and their yields measured.

Confirmatory evidence is provided by mirror experiments, whereby a deuteronating agent, the DCO^+ ion obtained from the ionization of a D_2/CO mixture,[26] is utilized in conjunction with isotopically rarified $^{12}C_6H_6$. In these experiments, sequence (1b) yields $C_6H_5-C_4H_7$ products, whereas sequence (2b) yields $C_6H_4D-C_4H_7$ products.

Finally, FT-ICR mass spectrometry[27] is used to gather relevant thermochemical data, such as the gas-phase basicity (GB) and the proton affinity (PA) of benzylcyclopropane, and low-pressure kinetic data on the reaction of benzenium ions with cyclobutanol and cyclopropylmethanol.

Experimental Section

Materials: The gases used (Ar, O_2, CH_4, D_2, CO) were research grade products from Matheson Gas Products or Aldrich Chemie with a stated purity in excess of 99.95 mol%. The $^{12}C_6H_6$ (99.9 atom% ^{12}C) was purchased from Cambridge Isotope Laboratories, C_6D_6 (99.96 atom% D) and 4-phenyl-1-butene were obtained from Sigma-Aldrich, and benzylcyclopropane (97%) from Lancaster Synthesis. The compound 1-methylindane was prepared from the reaction of CH_3MgI with 1-indanone, and then the alcohol was reduced with H_2, at approximately 2 atm, in the presence of Pd(C) (15%). Other $C_{10}H_{12}$ isomers, namely cyclobutylbenzene, 3-phenyl-1-butene, and 2-methyl-3-phenylpropene, were obtained by treatment of the appropriate Grignard reagents with C_6H_5Br, and their identity was established by GC-MS and NMR spectrometry.

Mass spectrometry: The FT-ICR mass spectra were recorded with an Apex TM 47e Bruker Spectrospin spectrometer, equipped with an external ion source, a computer-controlled pulsed valve, and a XMass data system. $C_6H_7^+$ ions, obtained in the external source by $CI(CH_4)$ of C_6H_6, were driven into the resonance cell at 298 K and thermalized by multiple collisions with Ar admitted through the pulsed valve (up to a peak pressure of approximately 1×10^{-5} Torr). After 1.5 s pumping time, the arenium ions were isolated by a "soft" r.f.-pulse ejection technique and allowed to react with the C_4H_7OH proelectrophile, present at stationary pressures of 10^{-7} to 10^{-8} Torr. The progress of the reaction in the cell was monitored by recording mass spectra at increasing reaction times. A series of thirty time domain signals, each of 32 K data points, was accumulated to improve the S/N ratio. The partial pressures of the individual compounds were read from the Bayard–Alpert ionization gauge, calibrated with the known rate coefficient of the reaction $CH_4^{+\bullet} + CH_4 \rightarrow CH_3^\bullet + CH_5^+$ (equal to 1.1×10^{-9} $cm^3 s^{-1} molecule^{-1}$) and corrected by means of individual response factors based on the polarizability of each gas.[28] The GB and PA of benzylcyclopropane were measured by the equilibrium method at 300 K. In these experiments, the gaseous acid, $C_3H_7^+$, formed by $CI(C_3H_8)$ at approximately 5×10^{-5} Torr in the ion source, was driven into the cell that contained $C_6H_5CH_2-c\text{-}C_3H_5$ and the reference base B ($B = (CH_3)_2O$; $i\text{-}C_3H_7CN$) at a total pressure of approximately 1×10^{-7} Torr. Protonated $C_{10}H_{13}^+$ or BH^+ ions were mass selected, allowed to cool down by a delay time of 2 s, and then allowed to equilibrate. Their constant intensity ratio, together with the measured pressure ratio of the neutrals, was used to calculate the equilibrium constant and hence the ΔG^0_{300} free energy change.

Radiolysis: The gaseous samples were prepared in sealed Pyrex vessels (135 mL) according to standard procedures with the aid of a greaseless vacuum line. The irradiations, run to less than 1% of substrate conversion, were performed in a 220 Gammacell (Nuclear Canada) at 25 °C with a total dose of 2.5×10^4 Gy and at a rate of 1×10^4 $Gy h^{-1}$. After the irradiation, the vessels were cooled to 77 K, their contents dissolved in *n*-hexane, and repeated freeze–thaw cycles were performed. The nature of the products, their yields, and the extent of H(D) incorporation were determined by GC/MS with the use of reference standards. The results were corrected for the incomplete deuteration of C_6D_6 (1%), the ^{13}C contribution, and the statistical fraction of product isotopomers from proton transfer in Equation (2a) and deuterium transfer in Equation (2b). The following columns were used: i) a fused silica column (50 m long, 0.20 mm i.d.) coated with a layer of crosslinked methylsilicone phase (0.5 μm, PONA column from Hewlett Packard) operated in the temperature range from 60 to 240 °C, and ii) a fused silica column (30 m long, 0.25 mm i.d.) coated with a layer of poly(alkylene glycol) bonded phase (0.25 μm, PAG column from Supelco) operated in the temperature range from 40 °C to 190 °C. The analyses were performed with a Hewlett Packard 5890 series II gas chromatograph in line with a quadrupole mass spectrometer model 5989B from Hewlett Packard.

Results

Mass spectrometry: The GB of benzylcyclopropane was determined in this study by the evaluation of prototropic equilibria with $(CH_3)_2O$ and $i\text{-}C_3H_7CN$ as the reference bases (B). The results of experiments, in which equilibrium was approached from either side with $C_{10}H_{13}^+$ or BH^+ ion populations, allowed the $GB_{300}(C_6H_5CH_2-c\text{-}C_3H_5)$ to be set at 187.3 ± 2 $kcal mol^{-1}$, which corresponds to a PA of approximately 194 $kcal mol^{-1}$. The formation of small amounts of the dimer $[BH^+B]$, which occurs at a much lower rate than proton transfer, does not appreciably affect the equilibrium constant evaluation.

We exploited the unique ability of FT-ICR mass spectrometry to establish parent–daughter relationships in consecutive ion–molecule reactions. This was done to study the relative efficiency of the competing processes that follow the formation of (arene R^+) (ICN) adducts produced in sequence (2). Benzenium ions, obtained in the external source of the ICR mass spectrometer by $CI(CH_4)$ of benzene, were isolated and allowed to react with a stationary concentration of the proelectrophile, ROH ($R = c\text{-}C_4H_7$ or $c\text{-}C_3H_5\text{-}CH_2$), in the cell. Among the conceivable processes, the predominant ones are proton transfer (3) to ROH that yields ROH_2^+ as well as the protonation-induced dissociation (4) to give free R^+. The barely detectable formation (5) of the $C_{10}H_{13}^+$ alkylated

$$C_6H_7^+ + ROH \longrightarrow C_6H_6 + ROH_2^+ \qquad (3)$$

$$C_6H_7^+ + ROH \longrightarrow C_6H_6 + R^+ + H_2O \qquad (4)$$

$$C_6H_7^+ + ROH \longrightarrow C_6H_6R^+ + H_2O \qquad (5)$$

adduct, that has an efficiency as low as 2% at the low pressure (2×10^{-8} Torr) of the resonance cell, increased significantly at higher pressures of the proelectrophile, that is, when ROH was introduced by the pulsed valve to a peak pressure of approximately 10^{-5} Torr. This favors collisional stabilization of the adduct. In any case, occurrence of the alkylation reaction was positively established by accurate mass analysis of the $C_{10}H_{13}^+$ product.

Radiolysis: Table 1 reports the composition of the irradiated systems as well as the identity, the yields, and the isotopic composition of the products of interest, namely those formed by alkylation of benzene by the $C_4H_7^+$ cations.

Table 1. Gas-phase reaction of $C_4H_7^+$ ions with C_6D_6.

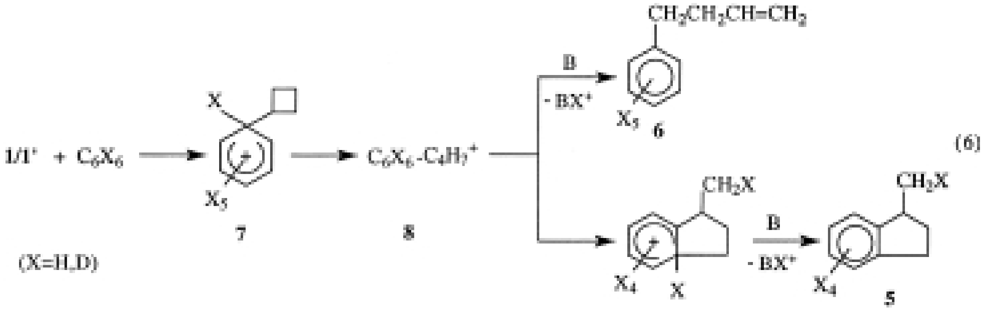
System Composition [Torr][a]				Products: C_4H_7-substituted benzenes[b, c] Isomeric composition [%]			
Substrate	Additive(s)	Bulk gas		3	4	5	6
C_6D_6 (4.0)	cyclobutanol (4.9)	CH_4 (650)	F.C.	26.4	51.1	15.4	7.0
			C.F.	33.6	50.5	9.0	6.9
$^{12}C_6H_6$ (4.0)	cyclobutanol (5.5)	D_2 (650)	F.C.	25.2	46.4	20.4	7.9
	CO (20)		C.F.	28.9	44.4	23.3	3.4
C_6D_6 (3.0)	cyclobutanol (6.5)	CH_4 (620)	F.C.	29.2	48.7	12.9	9.3
	NEt_3 (1.2)		C.F.	36.3	46.8	12.3	4.3
C_6D_6 (3.8)	cyclopropylmethanol (5.2)	CH_4 (660)	F.C.	25.0	50.6	15.8	8.6
			C.F.	29.7	47.8	12.0	10.5
C_6D_6 (3.5)	cyclopropylmethanol (5.8)	CH_4 (630)	F.C.	23.8	51.5	16.6	8.1
	NEt_3 (1.1)		C.F.	30.4	49.3	10.7	9.6
C_6D_6 (2.9)[d]	cyclobutanol (6.4)	CH_4 (610)	F.C.	25.0	37.9	20.9	16.2
			C.F.	31.6	28.5	27.7	12.2

[a] All reactions carried out at 25°C in the presence of O_2 (10 Torr). [b] Standard deviation of ±10%. [c] Isotopic composition of the products: FC = $C_6D_5-C_4H_7$; CF = $C_6HD_4-C_4H_7$. [d] Reaction carried out at 160°C.

The table does not include other products, for example, ethylbenzene formed by direct alkylation of benzene by $C_2H_5^+$, a major ion from the ionization of methane.[8] Table 1 reports the relative yields of the relevant products, namely cyclobutylbenzene **3**, benzylcyclopropane **4**, 1-methylindane **5**, and homoallylbenzene **6**. Their absolute yields are expressed by the $G_{(+M)}$ value (molecules formed per 100 eV); in the absence of deliberately added bases, the cumulative yield of products **3** to **6** amounts to approximately 1×10^{-2}. The ionic origin of the products is demonstrated by control experiments, which are performed in systems that contain CH_4 as the bulk gas. These experiments show declining, and eventually vanishing yields upon addition of increasing amounts of strong bases such as NEt_3, which efficiently intercept the charged intermediates.[29, 30] Remarkably, no radiation-induced isomerization of ROH proelectrophiles occur, that is, no detectable amounts of cyclopropylmethanol (cyclobutanol) are formed upon irradiation of systems that contain cyclobutanol (cyclopropylmethanol) as the proelectrophile. This is not the case for cyclobutyl bromide, which undergoes appreciable radiation-induced isomerization into cyclopropylmethyl bromide (up to 20% at the end of the irradiation), and this, of course, prevents its use as the proelectrophile in experiments to evaluate the extent of the interconversion of c-$C_4H_7^+$ ions.

Direct versus intracomplex alkylation: The isotopic composition of the products (Table 1) demonstrates the simultaneous operation of two pathways: sequence (1) whose products, denoted as FC, correspond to $C_6D_5-C_4H_7$ isomers formed by a conventional (Friedel–Crafts) alkylation, and sequence (2) whose isomeric $C_6HD_4-C_4H_7$ products are denoted as CF (Crafts–Friedel) to stress the inversion of the conventional roles of the electrophilic and the nucleophilic agents. Direct information on the extent of H incorporation on the aromatic ring has been provided by the integration of the GC-MS profiles of both the molecular ions and diagnostic fragments of the alkylated products. The fraction of the CF pathway has been found to correspond to approximately 30% of the total amount of the alkylation process.

Isomeric composition of the products: The paramount feature is that sequences (1) and (2) give products of nearly the same isomeric composition, almost unaffected by the nature of the ROH proelectrophile (cyclobutanol or cyclopropylmethanol) and by the presence of NEt_3. Even more remarkably, a closely similar product pattern is obtained from the mirror experiments, except for an appreciable increase of the relative yield of 1-methylindane **5**. This noticeable consistency of the results from both sets of experiments is mechanistically significant, if one considers their difference in two important parameters: i) the nature of the bulk gas, a CO/D_2 mixture instead of CH_4,



Scheme 2.

and ii) the different isotopic composition of the reagents, and hence the conceivably different kinetic isotope effects (KIE) in the two sets of experiments.

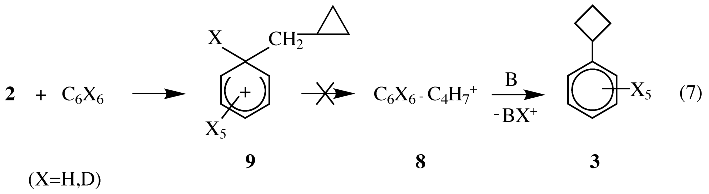
An appreciable modification of the product pattern is observed when the reaction temperature is increased from 25 to 160 °C, and this causes an increase in the yields of **5** and **6** at the expense of benzylcyclopropane **4**.

Control experiments on the deuterium distribution: Several tests were performed in order to verify the assignment of the products to sequence (1) or (2) and to assess the role of conceivable secondary reactions. In the first place, the position of the H(D) isotopic label in the molecules of the products, particularly with regard to the discrimination between the aromatic ring and the side chain (deduced from the EI fragmentation patterns in the GC-MS analyses), was checked by comparison with the spectra of authentic, specifically labeled samples. In the case of 1-methylindane **5** from the alkylation of C_6D_6, a mixture of $C_6D_4-C_4H_6D$ and $C_6HD_3-C_4H_6D$ from sequences (1) and (2), respectively, was collected. The high (80 %) D incorporation found in the methyl group of **5**, indicative of a significant D transfer from the phenyl ring to the methyl group, is a mechanistically informative feature. Such a label migration into the side chain was not observed to any detectable extent in the case of cyclobutylbenzene **3**, benzylcyclopropane **4**, and homoallylbenzene **6**.

Assignment of the ionic precursors of the products: We address first the origin of 1-methylindane **5** and homoallylbenzene **6**. With regard to the latter, it is most unlikely that it could derive from the reaction of a homoallyl cation, a species too unstable to be present to any significant concentration in the $C_4H_7^+$ mixture.[4] A more reasonable route to **6** is a process in which an *ipso* arenium ion **7**, the not particularly stable, primary intermediate from the attack of **1** and **1′** on the benzene,[31] evolves into an intermediate **8** by means of the opening of the cyclobutyl moiety, as shown in Equation (6) (Scheme 2). Subsequently, formation of **5** and **6** can occur by cyclization followed at this point by deprotonation and by direct deprotonation of **8**, respectively. In order to verify such a hypothesis, we performed control experiments whereby the *ipso*-protonated arenium ion is produced by an independent route, namely the protonation of cyclobutylbenzene by a gaseous acid. Of course, ring protonation is not expected to be selective, and the ipso position is certainly not favored over other positions. However, once the "*ipso*" protonated arenium ion is formed, it can irreversibly evolve into the $C_6H_5-C_4H_7X^+$ isomer. Thus, the problem is reduced to produce an appreciable amount of the *ipso* ion **7**, and the sizeable barriers to 1,2-H(D) shifts in arenium ions[32] are overcome as well as the energy barrier associated with the presumably lower PA of the *ipso* position compared with those of the *ortho*, *meta*, and *para* positions.[15, 31] We utilized the highly exothermic protonation of cyclobutylbenzene ($C_6D_5-C_4H_7$) by D_3^+ ions upon irradiation of a **3**/D_2 mixture (Table 1). The results show that indeed both 1-methylindane ($C_6D_4-C_4H_6D$) and homoallylbenzene ($C_6D_5-C_4H_7$) are formed with a radiochemical yield ($G_{(+M)} = 0.24$ and 0.25, respectively) that accounts for the isomeric composition reported in Table 1. This allows one to trace the formation of **5** and **6** to the trapping of the bicyclobutonium ions **1** and **1′**. Furthermore, the hypothesis based on the cyclization of the intermediate **8** was verified by the exothermic protonation of 4-phenyl-1-butene by $C_nH_5^+$ ($n = 1,2$) that gave 1-methylindane **5** with $G_{(+M)} = 0.2$. Finally, control experiments performed by the protonation of benzylcyclopropane by $C_nH_5^+$ showed no appreciable isomerization, for example, no detectable amounts of other $C_6H_5-C_4H_7$ isomers were formed upon irradiation of **4** diluted in CH_4 as the bulk gas. In conclusion, the above results allow one to assign products **3**, **5**, and **6** to the reaction promoted by the bicyclobutonium ion **1** and **1′**, whereas **4** derives from the cyclopropylmethyl cation **2**. This is an important result in that it allows one to estimate the equilibrium composition of the $C_4H_7^+$ mixture in a gaseous environment at atmospheric pressure and room temperature. From the above considerations, the ratio of the sum of the yields of the alkylated products **3**, **5**, and **6** from the reaction of ion **1** and **1′**, and the yield of the product **4** from the attack of ion **2** is close to unity. Most remarkably, the same ratio characterizes both sequences (1) and (2).

Discussion

The salient feature of the experimental picture is that nearly the same isomeric composition of the products is obtained with cyclobutanol or cyclopropylmethanol as the proelectrophile, and from both alkylation sequences (1) and (2). This evidently requires that the C_4H_7 group undergoes isomerization at some stage of the alkylation sequence. To simplify matters, it is appropriate to consider first the possibility of the isomerization of the C_4H_7 group within the arenium ion *following* the primary alkylation step, for example, in process (7) (Scheme 3). This process is ruled out by the results of control experiments that reveal no protonation-induced isomerization of benzylcyclopropane to cyclobutylbenzene and vice versa, as shown in the summary list of Table 2. This leaves only ROH_2^+ and R^+ as the species whose isomerization can lead to a common product pattern that contains both cyclobutyl and cyclopropylmethyl derivatives. At this point, assessment of the roles of ROH_2^+ and R^+ ions, in particular with regard to intracomplex alkyation (2), is in order.



Scheme 3.

The nature of the electrophile: The alkylation step can be envisaged to occur according to Equation (8).

Table 2. Control experiments on skeletal isomerization of C_4H_7-substituted benzenes.

System composition [Torr][a]		Products: C_4H_7-substituted benzenes			
Substrate	Bulk gas	**3**	**4**	**5**	**6**
cyclobutylbenzene (1,5)	CH_4 (640)	–	[b]	[b]	[b]
cyclobutylbenzene (1,8)	D_2 (620)	–	[b]	yes	yes
benzylcyclopropane (2,2)	CH_4 (650)	[b]	–	[b]	[b]
benzylcyclopropane (1,6)	D_2 (600)	[b]	–	[b]	[b]
homoallylbenzene (1,5)	CH_4 (650)	[b]	[b]	yes	–

[a] See Table 1. [b] Below detection limit.

$$ROH_2^+ + C_6H_6 \rightarrow C_6H_6R^+ + H_2O \quad (8)$$

This reaction occurs by means of the nucleophilic displacement of water by benzene in the protonated alcohol, or by the electrophilic addition below [Eq. (9)].

$$R^+ + C_6H_6 \rightarrow C_6H_6R^+ \quad (9)$$

The addition is promoted by the $C_4H_7^+$ ions. Accordingly, the complex formed in alkylation can be envisaged as a binary cluster, INC 2a [C_6H_6, ROH_2^+], or a ternary cluster, INC 2b [C_6H_6, R^+, H_2O].

The role of R^+ is strongly supported by the following considerations.

1) The analogy with a strictly related reaction: the intracomplex aromatic alkylation, in which (*R*)(−)-*sec*-butyl chloride was used as the proelectrophile, is promoted by the *s*-$C_4H_9^+$ cation, as shown by compelling stereochemical evidence.[21]
2) Comparison with the conventional alkylation sequence (1): since both sequence (1) and (2) give a mixture of isomeric products of nearly the same composition, it appears extremely unlikely that they are promoted by different electrophiles. ROH_2^+ ions can be ruled out as the electrophiles involved in sequence (1), since it was found that ROH proelectrophiles undergo no appreciable protonation-induced isomerization, in contrast with the extensive isomerization of the C_4H_7 group in the alkylated products. Since both sequences (1) and (2) are most likely to be promoted by the same electrophile, the role of ROH_2^+ can be excluded in the intracomplex alkylation as well.
3) The low-pressure FT-ICR experiments reported in a previous section showed that dissociative proton transfer (4) is the predominant reaction channel of the thermalized benzenium ion towards ROH proelectrophiles. In the case of the cyclobutyl structure for the $C_4H_7^+$ ion, the most recent thermochemical data allow a ΔH^0_{300} change of 0.7 ± 2 kcal mol^{-1} to be computed for process (4).[24]

Such a small endothermicity and the favorable ΔS° change account for the occurrence of dissociative proton transfer (4) under the low-pressure conditions typical of FT-ICR experiments. In the case of atmospheric-pressure experiments when the INC is collisionally stabilized, the energetics of the process, a key step of sequence (2), are probably more favorable. This is a result of the differential solvation effects that stabilize INC2b with respect to INC1 [Eq. (10)].

$$[C_6H_7^+, c\text{-}C_4H_7OH]\ (\text{INC1}) \rightarrow [C_6H_6, c\text{-}C_4H_7^+, H_2O]\ (\text{INC2b}) \quad (10)$$

In any case, even the small endothermicity of process (10) calculated for isolated species would not represent a significant thermochemical barrier for INC1 → INC2b conversion, which accounts for the occurrence of sequence (2) when ROH proelectrophiles are utilized. It should be noted, in this connection, that the subsequent steps of sequence (2) are energetically downhill, as in the reaction in Equation (11).

$$C_6H_7^+ + c\text{-}C_3H_5CH_2OH \rightarrow [C_6H_6\text{-}CH_2-c\text{-}C_3H_5]^+ + H_2O \quad (11)$$

The overall reaction is estimated to be exothermic by approximately 35 kcal mol^{-1}, based on the PA of benzylcyclopropane from FT-ICR measurements reported in a previous section.

The reaction is represented as follows [Eq. (12)].

$$C_6H_7^+ + c\text{-}C_4H_7Br \rightarrow C_6H_6 + c\text{-}C_4H_7^+ + HBr \quad (12)$$

Significantly, the overall reaction is endothermic by 8.5 ± 4 kcal mol^{-1}, based on available thermochemical data. Such a sizeable endothermicity is likely to represent a significant thermochemical barrier to the following conversion [Eq. (13)].

$$[C_6H_7^+, RBr] \rightarrow [C_6H_6, R^+, HBr] \quad (13)$$

This conversion accounts for the inefficiency of sequence (2) when cyclobutyl bromide is used as the proelectrophile. In the conventional alkylation (1), the electrophile is generated by protonation of the proelectrophile by a strong Brønsted acid, for example, $C_nH_5^+$. This process is highly exothermic in the case of cyclobutyl bromide and accounts for the efficiency of the alkylation channel (1).

In summary, the occurrence of intracomplex alkylation depends on whether formation of the R^+ cation is energetically allowed or only slightly endothermic, according to a trend established for other "Crafts–Friedel" reactions.[19] Based on the previous considerations, the R^+ ions, $C_4H_7^+$, can be identified as the electrophilic agents in both sequences (1) and (2).

The equilibrium composition of $C_4H_7^+$ isomers: The previously reported assignment of the ionic precursors allows one to evaluate an equilibrium composition, deduced from the ratio $([\mathbf{3}]+[\mathbf{5}]+[\mathbf{6}])/\mathbf{4} \cong 1$. This result is of interest, because it refers to ions that equilibrate in gaseous systems at room temperature, and under these conditions, the frequent collisions with the bulk gas molecules allow complete thermalization of the interconverting species. In both alkylation sequences (1) and (2), the same equilibrium mixture is observed, and the mixture points to the negligible role played, in this case, by the single solvent molecule present in the INC (CF reaction) with respect to the unsolvated reactants pair (FC reaction).

The remarkably good agreement with the solvolytic results and also with the 1:1 ratio of the bicyclobutonium and the bisected cyclopropylmethyl cations deduced from the recently reported matrix-infrared spectrum[31] confirms the comparable stability of the $C_4H_7^+$ ion. This rules out significant differential solvation effects and is consistent with the theoretical results.

The equilibration rate of $C_4H_7^+$ ions: After the identification of the R^+ ions, namely **1**, **1'**, and **2**, as the species whose interconversion yields the observed mixture of isomeric derivatives **3** to **6**, the estimation of their interconversion rate is of interest. From the kinetic standpoint, the present gas-phase results have significantly reduced the upper limit of the time required for **1/1'** $\rightleftharpoons$ **2** equilibration, as apparent from the following considerations. The limit set by condensed-phase approaches based on NMR spectrometry was $\leq 10^{-5}$ s, which corresponds to the temporal resolution of the technique utilized. This limit is pushed down to approximately 10^{-8} s by the results of radiolytic experiments on conventional alkylation (1) studied in dense gases (720 Torr) in the presence of known amounts of additives, such as strong bases, that are known to quench the reaction. The limit is further reduced to $\leq 10^{-10}$ s by the results of the experiments on intracomplex alkylation (2), based on the lifetime of closely similar arene/electrophile complexes, which were recently evaluated by two independent kinetic approaches.[22, 23] Such a fast equilibration is consistent with the results of previous theoretical studies, that characterize the relevant portion of the $C_4H_7^+$ potential energy surface as very flat and hence devoid of appreciable barriers to interconversion.[4]

Conclusion

The joint application of FT-ICR mass spectrometry and of atmospheric-pressure radiolytic techniques with suitably labeled reagents has proved particularly useful in the case of interest. Whereas FT-ICR has allowed detection of the charged intermediates, the rapid sampling and the positive identification of the products typical of the radiolytic approach have allowed the equilibrium composition of the cyclopropylmethyl/bicyclobutonium system to be evaluated in the gas phase. Consistent with condensed-phase results and theoretical estimates, the present study points to the remarkably close stability of gaseous ions **1/1'** and **2** and to their very fast ($\leq 10^{-10}$ s) equilibration time, which suggests a very low barrier to isomerization.

As a final remark, we note that this study provides the first experimental results on the interconversion of gaseous $C_4H_7^+$ ions under conditions that allow meaningful comparison with the theoretical predictions. Indeed, metastable ion (MI) mass spectrometric evidence showed that in the time window typical of this technique (approximately 1 μs) $C_4H_7^+$ ions from different sources reach a common structure, or mixture of structures.[33] However, these observations concern $C_4H_7^+$ cations sufficiently excited to undergo highly endothermic unimolecular fragmentation processes. Clearly, the large excess of internal energy of the decomposing species prevents generalization of MI spectrometric results, and this does not allow the derivation of kinetic and equilibrium parameters of thermal isomerization processes characterized by low barriers, which are typical of the system of interest.

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