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The Radiolytic Approach to Gas-Phase Ion Chemistry

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An integrated approach to gas-phase ion chemistry based on the coordinated application of mass spectrometric and radiolytic techniques has successfully been applied to problems related to the existence, the structure, and the stability of gaseous cations and has provided new mechanistic insight into many classes of organic reactions, e.g., aromatic alkylation, nitration and silylation, acid-induced nucleophilic displacement, formation of tetrahedral intermediates, pinacol rearrangement, etc.^{1,2} The kinetic, structural, and stereochemical information from the integrated approach is fully comparable with that from solution-chemistry studies, thus allowing meaningful correlation between gas-phase and condensed-phase ion chemistry. The radiolytic technique involves γ irradiation of the substrate of interest, S, highly diluted in a bulk gas, M, whose ionization produces well-defined cations, R⁺, that undergo many thermalizing collisions before reacting with S, much in the same way as in chemical ionization mass spectrometry (CIMS). In the unreactive bulk gas the cations R⁺ are sufficiently long-lived to interact with as little as 10⁻⁵-10⁻⁴ mol % of a reactive substrate prior to neutralization.³ The charged intermediates formed are rapidly (10⁻⁸-10⁻⁶ s) trapped by suitable nucleophiles and converted into neutral end products, amenable to analysis by GC and GC/MS. The most valuable features of the radiolytic approach, i.e., the wide pressure range (from a few Torr to several atmospheres), the meaningful definition and extended range of the temperature, and the structural and stereochemical characterization of the products, pertain exactly to those areas where mass spectrometry suffers from recognized limitations, which makes the two techniques

highly complementary. Such features allow extension to the gas phase of many classical mechanistic tools, including competition kinetics, pressure- and temperature-dependence studies, isotopic labeling, etc., which, coupled with appropriate mass spectrometric techniques, make the integrated approach particularly powerful. It compares favorably with other approaches based on the isolation of the neutral products from gas-phase ionic reactions, i.e., the electron-bombardment flow (EBFlow) technique, limited, as mass spectrometry, to a restricted pressure range,⁴ and the powerful β -decay technique, which requires multiply tritiated precursors and preliminary study of their decay-induced fragmentation.⁵

An inherent complication of the radiolytic technique arises from the incursion of reactive neutral species, i.e., free radicals, cogenerated with the R⁺ ions, which makes it necessary to ascertain the ionic origin of the products of interest. While the problem requires detailed case-by-case consideration, several criteria have proved generally useful. First, the ionic reaction of interest must be shown by preliminary application of CIMS to occur in the specific system investigated. Second, the yields of neutral products of ionic origin are unaffected by the addition of radical scavengers, e.g., O₂ in gaseous alkanes. Third, formation of neutral products from ionic reactions is depressed by additives capable of intercepting their charged precursors, e.g., gaseous nucleophiles that efficiently trap the R⁺ ions. In many systems, application of the above criteria and of additional, more specific tests has ruled out significant

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Table I
Typical Applications of the Radiolytic Technique

bulk gas (M)	ionic reactant (R ⁺)	substrates (S)
H ₂	H ₃ ⁺	PhX (X = F, Cl, Br), ⁶⁻⁹ c-C ₆ H ₁₂ ¹⁰
CH ₄	C _n H ₅ ⁺ (n = 1, 2)	pinacol, ¹¹ diols, ¹² halohydrins, ^{13,14} arenes, ¹⁵ nitriles ¹⁶
H ₂ /H ₂ C=C=CH ₂ H ₂ /CH ₃ C=CH ₂	CH ₃ C ⁺ =CH ₂	arenes, 1,4-dibromobutane ¹⁷
H ₂ /c-C ₃ H ₆ C ₃ H ₈	c-C ₃ H ₇ ⁺ i-C ₃ H ₇ ⁺	arenes ¹⁸ arenes, ¹⁹⁻²¹ monosubstituted benzenes, ²²⁻²⁶ anilines, ^{24,25} benzyl chloride ²⁶
i-C ₄ H ₁₀ , C(CH ₃) ₄	t-C ₄ H ₉ ⁺	arenes, ^{21,27-29} monosubstituted benzenes, ^{30,31} amines, ³² anilines ^{24,25}
CH ₄ /2-C ₄ H ₈ CH ₃ F	sec-C ₄ H ₉ ⁺ (CH ₃) ₂ F ⁺	arenes ³³ arenes, ³⁴⁻³⁶ biphenyls, ³⁷ heteroaromatics, ³⁸ halohydrins, ^{13,14} anilines ^{24,25}
CH ₃ Cl CH ₃ F/CO CH ₄ /MeNO ₃	(CH ₃) ₂ Cl ⁺ CH ₃ CO ⁺ (CH ₃ NO ₃)H ⁺	arenes, ³⁴ heteroaromatics ³⁸ anilines, ^{24,25} aromatics ^{39,40} monosubstituted benzenes, ⁴¹⁻⁴³ diphenylmethanes ⁴⁴
CH ₄ /Si(CH ₃) ₄	Si(CH ₃) ₃ ⁺	arenes ^{45,46}

radical contributions to the formation of the products of interest, allowing successful application of the radiolytic technique, as illustrated in Table I.

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Gas-Phase Models of Ionic Reactions in Solution

In condensed media the intrinsic reactivity of ions is deeply affected by solvation, ion pairing, viscosity, etc., which diversify the mechanistic pattern, preventing the construction of unified reaction models and reducing the impact of theoretical approaches. Indeed, a major incentive to the study of gas-phase ionic reactions is their potential value as extremely simplified and generalized models of the corresponding processes occurring in solution. However, meaningful kinetic and mechanistic correlation with condensed-phase ion chemistry imposes certain constraints on gas-phase studies, requiring, in particular, that thermal kinetics are obeyed and that structural and stereochemical features of mechanistically relevant species are established as accurately as in solution. In both areas, properly designed radiolytic experiments can help overcome the limitations of mass spectrometry, which is restricted to the low-pressure range where collisional thermalization of the reactants is lacking or incomplete and ion-molecule kinetics are dominated by a unique "electrostatic activation" mechanism, which prevents meaningful comparison with thermal solution-chemistry kinetics. In fact, the energy E° released by the electrostatic interaction of the reactants remains stored in the internal degrees of freedom of the ion-molecule complex formed, available to overcome the intrinsic ("chemical") energy barrier E^* to the products. Under this unique set of conditions, ordinary thermal kinetics do not apply, and the reaction rate depends on the $E^{\circ} - E^*$ difference, rather than on E^* . In the frequent case where E° exceeds E^* , the reactions often proceed at the collision rate with *negative* temperature coefficients, becoming chemically featureless.^{47,48} On the other hand, at the higher pressures typical of radiolytic systems, thermalizing collisions remove the excess internal energy E° of the ion-molecule complex prior to reaction, which consequently obeys ordinary thermal kinetics, displaying the normal *positive* dependence on the temperature, which allows meaningful comparison with condensed-phase processes.

Structural characterization of the primary intermediates is also notoriously difficult by mass spectrometry, whose limited structural resolution is compounded by the long delay (10^{-5} s) before structural assay, typical of techniques such as collisionally activated dissociation (CAD) and metastable ion kinetic energy (MIKE) spectrometry. The long lifetime and the inefficient collisional stabilization account for the extensive fragmentation and/or isomerization processes that almost

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Table II
Selectivity of Nitration of Substituted Benzenes by
(MeNO₂)H⁺ in CH₄ at 37 °C and 720 Torr

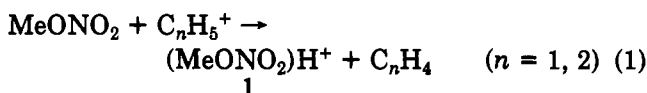
X in PhX	$k_{PhX}:k_{PhH}$	orientation		
		% ortho	% meta	% para
Me	5.1	59	7	34
Et	5.6	47	4	49
<i>n</i> -Pr	7.0	50	4	46
<i>i</i> -Pr	6.0	31	5	64
<i>c</i> -Pr	10.6	72	6	22
<i>t</i> -Bu	8.4	17	8	75
Ph	1.5	40	4	56
OMe	7.6	41		59
F	0.15	14	13	73
Cl	0.19	36	10	54
CF ₃	0.0037		100	
mesitylene	8.1			

invariably affect the results of "structurally diagnostic" mass spectrometric techniques. Pressure-dependence studies of widely different reactions^{10,27} show that the pressures required to ensure that a gas-phase ionic reaction obeys thermal kinetics and to prevent significant changes of its primary products prior to their characterization exceed in general by orders of magnitude the range accessible to mass spectrometry, yet are readily attainable in radiolytic experiments, which is particularly valuable to establish meaningful correlations between gas-phase and condensed-phase ion chemistry, as illustrated by the examples discussed in the next sections.

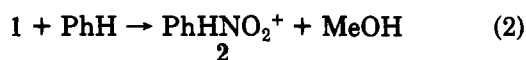
Gas-Phase Aromatic Substitution

Nitration. The central role of nitration in the theory of aromatic reactivity has stimulated many attempts to extend its study to the gas phase. Early ICR approaches met with limited success, since NO₂⁺, the nitrating reagent in solution, undergoes only charge exchange and oxygen-atom transfer to aromatics,⁴⁹⁻⁵¹ while the other cations investigated, CH₂ONO₂⁺ and EtO(NO₂)₂⁺, display a paradoxical selectivity, reacting at higher rate with deactivated substrates.⁵²

Preliminary radiolytic studies, backed by CI, CAD, and ICR spectrometry, have identified protonated methyl nitrate as a suitable reagent, easily obtained, e.g., in CIMS, via the exothermic process



The cation, essentially a nitronium ion "solvated" by methanol with a binding energy of ca. 24 kcal mol⁻¹,^{42,53,54} undergoes nucleophilic displacement by aromatic substrates, e.g.



as shown by CI⁴² and double-resonance ICR⁴⁹ spectrometry. The CAD spectra of 2, recorded ca. 10⁻⁵ s

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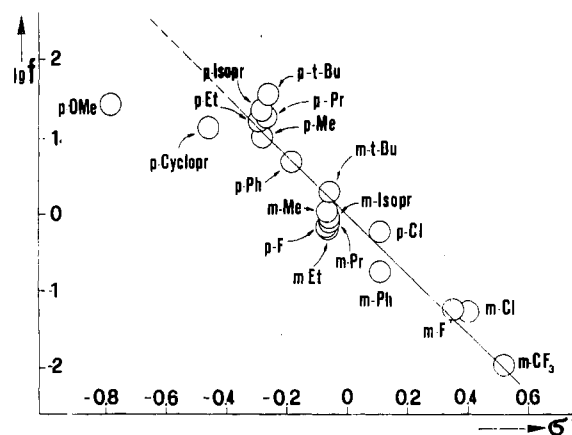
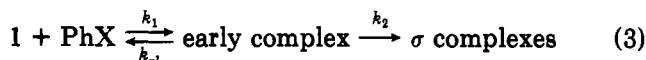


Figure 1. Logarithmic plot of the partial rate factor vs the substituent constant in the nitration of PhX substrates by (MeNO₂)H⁺ in CH₄ at 37 °C and 720 Torr.

after its formation, are identical with those of a model ion from the selective O-protonation of PhNO₂,⁴² suggesting actual formation of a C-N covalent bond from (2). Ab initio calculations of the proton affinity (PA) of the "ipso" position of PhNO₂ show that formation of a σ complex from (2) is energetically allowed.⁴²

Radiolysis of systems containing CH₄, MeNO₃, and PhX in the typical molar ratios 10³:20:1 gives high yields of the corresponding nitrated aromatics of assuredly ionic origin, according to sequence (1-2), followed by deprotonation of intermediates 2.⁴² The selectivity of the reaction, illustrated in Table II, conforms to solution-chemistry trends, characterizing 1 as the first well-behaved gaseous nitrating cation. The partial rate factors fit a Hammett type plot (Figure 1) whose ρ value, -3.87, is appreciably less negative than those of conventional nitrations, e.g., $\rho = -6.53$ in Ac₂O or MeNO₂ and -9.7 in H₂SO₄,⁵⁵ as expected for a free gaseous cation. Another intriguing analogy with solution is the limiting nitration rate reached by highly activated substrates, as apparent in Figure 1 in the case of anisole and cyclopropylbenzene, and confirmed by later studies of other substrates.⁴⁴ Crucial evidence on this point has been obtained from the nitration of benzylmesitylene, containing two rings whose activation corresponds roughly to that of toluene (T) and respectively of isodurene (I). While the k_I/k_T ratio is as low as 1.5, the activated ring of benzylmesitylene reacts at least 20 times faster than the other one, despite the unfavorable (2/5) statistical ratio. This suggests formation of an "early" electrostatic complex, followed by a product-determining step



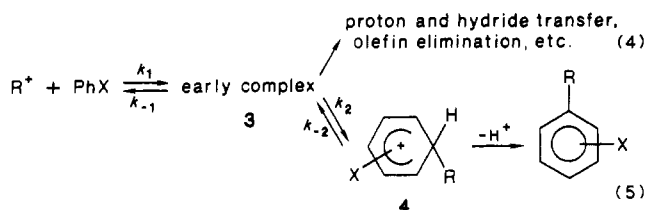
Whenever activation of PhX is sufficient to make $k_2 > k_{-1}$, the first step is rate determining, and the reaction proceeds at the limiting (collision) rate, losing substrate, but not positional selectivity. This is the gas-phase counterpart of the "encounter-controlled" nitration observed in solution, whose rate depends as well, according to the original suggestion by Olah,⁵⁶ on the formation of an "early complex", kinetically distinct

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from the product-controlling formation of the σ complexes. While the factors that stabilize in solution the early adduct, perceived as a π complex⁶⁶ or an "encounter pair" confined in a solvent cage by a viscosity barrier,⁵⁵ can be physically different from the electrostatic interactions that stabilize ion-molecule complexes in the gas phase, their kinetic role is the same. The temperature dependence of the substrate selectivity in the competitive nitration of benzene (B) and toluene (T) has been measured in CH_4 at a sufficiently high pressure (720 Torr) to ensure that the reaction obeys thermal kinetics and that its primary products undergo no significant isomerization, as shown by pressure-dependence studies. From the slope of the Arrhenius plot an empirical $E_B^* - E_T^*$ difference of $4.2 \pm 0.3 \text{ kcal mol}^{-1}$ has been estimated.⁴³ The influence of the leaving group on the reactivity of different $(\text{RNO}_3)\text{H}^+$ cations is consistent with the mechanism suggested, since inductively stabilizing groups depress the nitrating ability; e.g., the ion is unreactive when $\text{R} = i\text{-C}_6\text{H}_{11}$, and alkylation, rather than nitration, occurs when $\text{R} = i\text{-C}_3\text{H}_7$. On the other hand, electron-withdrawing groups make the reagent more energetic and indiscriminate; e.g., both substrate and positional selectivity decrease in passing from $\text{R} = \text{CH}_3$ to $\text{R} = \text{CF}_3\text{CH}_2$ and to $\text{R} = (\text{CF}_3)_2\text{CH}$.⁴³

Alkylation. Gas-phase radiolytic alkylation by carbenium ions and dialkylhalonium ions conforms in general to the scheme



easily adaptable to R_2X^+ ions as well. At low pressures, e.g., in CIMS experiments, the "blind" channel (4) often predominates,⁵⁷ while ions 4, formed in the kinetically controlled step, rearrange into more stable isomers, which occurs as well in low-pressure radiolytic studies.^{19,58} The individual steps of the above scheme will be illustrated by referring to pertinent examples. Formation of early complex 3 has characteristic effects on the substrate selectivity and orientation. Whenever k_2 exceeds k_{-1} , as in the alkylation of PhH and of PhMe by primary and secondary carbenium ions and by Me_2F^+ , formation of 3 is rate determining, and the alkylation proceeds essentially at collision frequency, characterized by k_T/k_B ratios even lower than unity, e.g., 0.8 in ethylation and 0.6–0.9 in isopropylation, owing to the higher efficiency of processes 4 in the case of PhMe , well documented by CIMS.⁵⁷ In contrast with the loss of substrate selectivity, measurable positional discrimination is retained, reflected by para:1/2 meta ratios higher than unity, e.g., 1.3 in ethylation and 1.6 in isopropylation. This state of affairs is analogous to the "encounter rate" nitration discussed earlier, although the much higher reactivity of C_2H_5^+ and $i\text{-C}_3\text{H}_7^+$ than of 1 causes the limiting rate to be attained by less activated substrates in alkylation than in nitration. On

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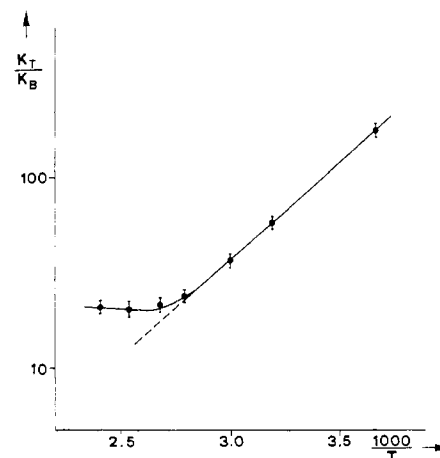
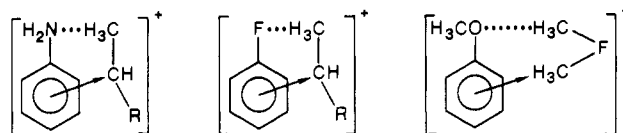


Figure 2. Temperature dependence of the relative *tert*-butylation rate of benzene and toluene in isobutane at 720 Torr.

the other hand, whenever k_{-1} exceeds k_2 , as in the case of $t\text{-C}_4\text{H}_9^+$, Me_2Cl^+ , and Me_2Br^+ ions, formation of 3 is not rate determining, and the alkylation displays a remarkable substrate and positional selectivity; e.g., $k_T/k_B = 55$, para:1/2 meta = 35 in *tert*-butylation.²⁷

Even if not rate determining, and therefore not affecting substrate selectivity, intervention of 3 can nevertheless be inferred from the high extent (up to 90%) of ortho orientation in the alkylation of substrates containing n-type nucleophilic substituents, e.g., F, Cl, Br, OH, OMe, and NH_2 groups, by $i\text{-C}_3\text{H}_7^+$ and $t\text{-C}_4\text{H}_9^+$. This has been traced²² to the preliminary formation of oriented electrostatic complexes, where the charge is effectively delocalized by interaction of the cation with both the π system of the substrate and the lone pair of the substituent, forming a sort of "chelate", e.g.



Recently, such a model has been extended to systems containing two π centers, e.g., biphenyl, whose alkylation by Me_2F^+ is characterized by predominant (75%) ortho orientation. Significantly, when coordination of the electrophile with both rings is prevented by their increased dihedral angle, due to the presence of ortho substituents, the extent of ortho orientation decreases, e.g., to only 38% in 2-methylbiphenyl.³⁷

Passing to the second step of sequence 5, there is no evidence that alkylation by R_2X^+ or by most carbenium ions is reversible. An interesting exception is represented by $t\text{-Bu}^+$, whose substrate and positional selectivity have been measured as a function of the temperature, using benzene and toluene as the competing aromatics.²⁹ The Arrhenius plot (Figure 2) is linear over the 0–100 °C range, the reactivity of PhH relative to PhMe increasing regularly with the temperature. Above 100 °C, however, an inflection is apparent, traced to the fact that the equilibrium constant of the addition of $t\text{-C}_4\text{H}_9^+$ to PhH decreases markedly with the temperature, as documented by CIMS measurements.⁵⁹ This accounts for the curvature of the plot, since the analogous dissociation of the *tert*-butylated adducts from

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toluene becomes significant only at higher temperatures.

Analysis of the linear portion of the Arrhenius plot leads to a difference in the empirical activation energies $E_B^* - E_T^* = 3.6 \pm 0.4$ kcal mol⁻¹. The orientation changes as well at higher temperature in favor of *m*-*tert*-butyltoluene. Assuming that the isomeric composition of the products measured at 720 Torr reflects indeed that of the intermediates 4, one obtains $E_{\text{meta}}^* - E_{\text{para}}^* \approx 3$ kcal mol⁻¹, not inconsistent with the $E_B^* - E_T^*$ difference.²⁹

Besides depressing the rate of alkylation of hindered positions, the bulk of the cation can affect as well the deprotonation step, making intermediates 4 long-lived and consequently prone to reversible dealkylation and/or to isomerization. Thus, the yield of 1,3-dimethyl-4-*tert*-butylbenzene, the "kinetic" product from the *tert*-butylation of *m*-xylene, decreases from 65% at 725 Torr to 8% at 20 Torr, in favor of the more stable 1,3-dimethyl-5-*tert*-butylbenzene, unless the bulk gas (neopentane) contains strong bases.²¹

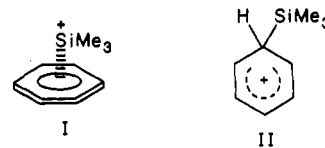
Evidence for steric hindrance to deprotonation has been found in a study of the *tert*-butylation of crowded polymethylbenzenes primarily aimed at evaluating the intrinsic steric requirements of free *t*-C₄H₉⁺, whose salient features can be summarized as follows: (i) Activation of a ring position by *one* ortho Me group is insufficient to balance steric hindrance: e.g., no ortho substitution occurs in toluene, while *p*-xylene is unreactive. (ii) The activation by *two* Me groups, ortho and para to a ring position, overcomes steric hindrance by the ortho substituent, making the position nearly as reactive as position 4 of toluene. (iii) No *tert*-butylation occurs *ortho* to *two* Me groups; e.g., mesitylene is unreactive.

Steric hindrance to deprotonation is suggested by the influence of NH₃ on the reactivity and orientation of *m*-xylene and of trimethylbenzenes. In the absence of bases, the relative reactivity of hemimellitene (5) and of pseudocumene (6) is measured by a k_5/k_6 ratio of 10, far in excess of the 2:1 ratio expected from the number of comparably activated and sterically accessible ring positions. The leveling effect of small, strong bases (NH₃) reduces the k_5/k_6 ratio nearly to the expected value, providing strong evidence for the rate-determining role of the deprotonation step.²⁷ It should be noted that *t*-C₄H₉⁺ has considerably smaller steric requirements in the gas phase than in solution, where, *inter alia*, pseudocumene is unreactive.⁶⁰

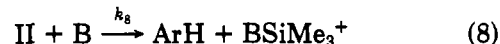
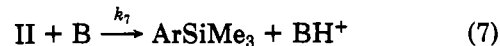
Silylation. Electrophilic aromatic silylation is a unique example of a reaction first demonstrated by radiolytic techniques, being unprecedented in solution, nor detected by mass spectrometry. In fact, the results of a mass spectrometric study of the reaction



had been interpreted by excluding substitution, i.e., formation of a localized C-Si bond, characterizing 7 as a mere π complex I, rather than a σ complex II, based on its inability to undergo deprotonation by gaseous bases.⁶¹ The radiolytic study was based on the hy-



pothesis that adduct II had actually formed, but its deprotonation was prevented by faster, competitive desilylation by the bases used in the mass spectrometric work, i.e., $k_8 > k_7$.



Preliminary ICR experiments showed in fact that oxygenated bases react exclusively as desilylating agents, while certain amines appeared more promising as Brønsted bases.^{45,46} Radiolytic silylation involved irradiation of CH₄/SiMe₄/arene mixtures, yielding the electrophile according to the process



well characterized by CIMS.⁶² No silylation occurs unless the system contains NEt₃, which incidentally alleviates the usual need of demonstrating the ionic origin of the radiolytic aromatic products. Introducing NEt₃ into the system promotes aromatic silylation, whose yield in the case of toluene increases up to ca. 20% at a NEt₃ pressure of 1.2 Torr. Further increasing [NEt₃] causes the decline, and eventually the suppression, of the ArSiMe₃ yields. The actual isolation of its products demonstrates the occurrence of electrophilic aromatic silylation, providing compelling evidence for the formation of II from reaction 6. The dependence of the yields on [NEt₃] verifies the hypothesis based on the competition of processes 7 and 8. In fact, in the absence of NEt₃, the oxygenated nucleophiles invariably present as impurities (H₂O) or formed from the radiolysis (H₂O, CH₃OH, CH₂O, etc.) desilylate II, preventing formation of silylated aromatics. Added NEt₃, which promotes deprotonation 7, tends to increase the ArSiMe₃ yields by competing with purely desilylating nucleophiles. However, NEt₃ effectively intercepts C_nH₅⁺ and SiMe₃⁺ ions, which tends to depress the ArSiMe₃ yields. Combination of such opposite effects neatly accounts for the otherwise peculiar dependence of the yields on [NEt₃]. The validity of the model and the purely kinetic nature of the bias in favor of desilylation by oxygenated bases have been confirmed by using bidentate nucleophiles, e.g., Me₂NCH₂CH₂OH, that promote desilylation, despite their high PA.⁴⁵

Electrophilic aromatic silylation being unprecedented in the liquid as in the gas phase, its selectivity, orientation, and steric requirements, summarized in Table III, are of special interest. They characterize SiMe₃⁺ as a typical, if moderately selective, electrophile, whose reactivity is dominated by steric factors that prevent substitution ortho to *two* methyl groups. Substitution ortho to *one* methyl group occurs only at highly activated positions, or in the lack of alternative sites. There exists a close analogy with *t*-Bu⁺, although SiMe₃⁺ appears *less* selective and characterized by *lower* steric

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(61) Wojtyniak, A. C. M.; Stone, J. A. *Int. J. Mass Spectrom. Ion Processes* 1986, 74, 59.

(62) Klevan, L.; Munson, B. *Int. J. Mass Spectrom. Ion Phys.* 1974, 13, 261.

Table III
Reactivity of Methylbenzenes Relative to Toluene and Orientation in Gas-Phase Silylation

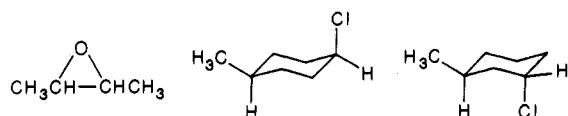
	substrate				
	toluene	<i>o</i> -xylene	<i>m</i> -xylene	<i>p</i> -xylene	mesitylene
app k_S/k_T	1.0 (1.0) ^a	3.3 (2.0)	1.5 (1.6)	0.6 (<0.05)	<0.05 (<0.05)
orientation, ^b %	ortho: 0 (0) meta: 14 (6) para: 86 (94)	1,2,3: 0 (0) 1,2,4: 100 (100)	1,2,3: 0 (0) 1,3,4: 70 (87) 1,3,5: 30 (13)	1,2,4: 100 (100)	

^a Values in parentheses refer to gas-phase *tert*-butylation. ^b Position of the SiMe₃ group italicized.

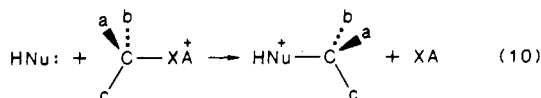
requirements, consistent with the longer C–Si bond, 1.88 vs 1.54 Å of the C–C bond, which appreciably reduces its effective bulk.

Stereochemical Course of Gas-Phase Ionic Reactions

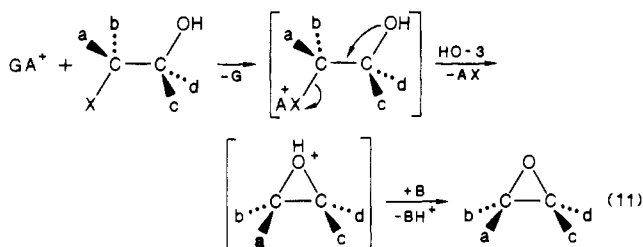
In a study of acid-induced nucleophilic displacement at saturated carbon, onium ions RXA⁺ from the reactions of radiolytic GA⁺ acids, e.g., CH₅⁺, C₂H₅⁺, and Me₂F⁺, with monofunctional RX substrates, e.g.



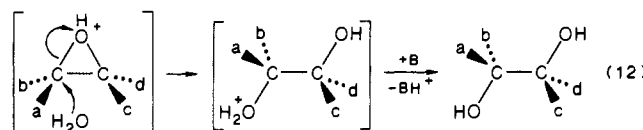
were allowed to react with nucleophiles, HNu:, e.g., H₂O.^{12,13} Analysis of the neutral end products demonstrates occurrence of *backside* attack, leading to predominant (64–98%) inversion



Attack of GA⁺ acids on bifunctional substrates, e.g., halohydrins, followed by the reaction of the RXA⁺ ions with H₂O, yields mostly *inverted* (80–93%) epoxybutanes and smaller amounts of predominantly (73–98%) *retained* 2,3-butanediols. The reaction involves fast intramolecular HO-to-XA displacement, a HO-3 process, that eventually yields *inverted* epoxybutanes.



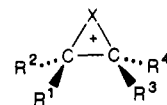
Formation of the *retained* glycols is traced instead to two consecutive displacements, the second one promoted by intermolecular attack of water



The above results resolve earlier discrepancies between low-pressure ICR results and well-established solution-chemistry reactivity patterns.

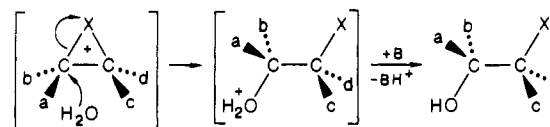
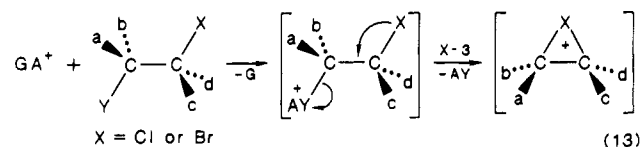
The study of gas-phase acid-induced nucleophilic displacement on RXA⁺ ions from 2,3-dihalobutanes has provided convincing stereochemical evidence on the

occurrence of cyclic chloronium and bromonium, but not fluoronium, ions^{13,14}

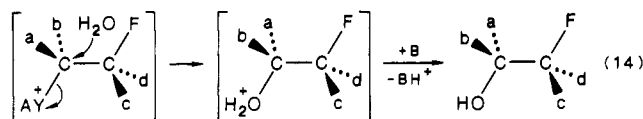


X = halogen
R¹–R⁴ = alkyl groups or H

Reaction with H₂O of the RXA⁺ ions from the protonation (C_nH₅⁺) or methylation (Me₂F⁺) of the chlorinated and brominated substrates yields predominantly *retained* chloro- and bromohydrins, whereas predomi-



nantly *inverted* fluorohydrins are obtained from fluorinated substrates. The results suggest intermediacy of cyclic chloronium and bromonium ions formed by participation of vicinal substituent groups. The predominant formation of *inverted* fluorohydrins, which excludes participation of the vicinal F atom in the displacement reaction, is traced instead to the sequence



Detection and Characterization of Transient Intermediates

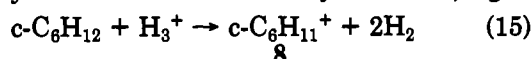
Efficient collisional stabilization and fast trapping, combined with the positive structural assignment allowed by the actual isolation of neutral products, make the radiolytic approach particularly useful for the study of transient ionic species that defy detection by mass spectrometry. Thus, the cyclohexyl cation (8), long recognized as an intermediate in solution, could never be detected by CAD and MIKE spectrometry⁶⁴ nor by the EBFLOW technique,⁶⁵ which had led to the conclusion that it does not exist in the gas phase, rearranging immediately into the more stable 1-methylcyclopentyl isomer (9). Successful demonstration of gaseous 8 was first achieved in radiolytic experiments, involving exo-

(63) (a) Holz, D.; Beauchamp, J. L.; Woodgate, S. D. *J. Am. Chem. Soc.* 1970, 92, 7484. (b) Staley, R. H.; Cordeman, R. R.; Foster, M. S.; Beauchamp, J. L. *J. Am. Chem. Soc.* 1974, 96, 1260.

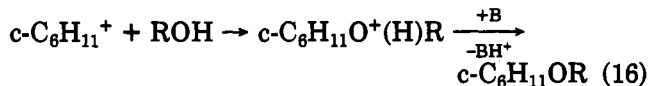
(64) Wesdemiotis, C.; Wolfshütz, R.; Schwartz, H. *Tetrahedron* 1979, 36, 275.

(65) Marinelli, W. J.; Morton, T. H. *J. Am. Chem. Soc.* 1978, 100, 3536; 1979, 101, 1908.

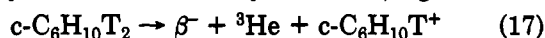
thermic hydride abstraction from cyclohexane, e.g.



and subsequent trapping by gaseous nucleophiles, e.g.

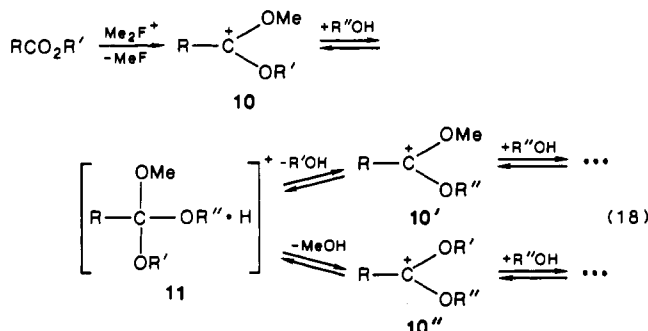


Both cyclohexyl and 1-methylcyclopentyl derivatives were isolated, whose proportions displayed the expected dependence on the exothermicity of (15), on the pressure of the bath gas, and on [ROH]. The results provide direct evidence for the existence of gaseous **8** with a lifetime of $\sim 10^{-7}$ s, while confirming its facile isomerization into **9**.¹⁰ Such conclusions are supported by a β -decay study, where the labeled daughter ions from the decay of multitritiated cyclohexane, e.g.



were trapped with different nucleophiles both in solution and in gases at various pressures.⁶⁶ The radiolytic and β -decay studies conclusively demonstrate that gaseous **8** corresponds to a local minimum on the $\text{C}_6\text{H}_{11}^+$ energy surface, whose depth has been estimated around 10 kcal mol⁻¹.⁶⁶

Intervention of tetrahedral cationic intermediates in the gas-phase alcoholysis of esters has recently been demonstrated by the integrated approach.⁶⁷ Tetrahedral intermediates are well established in solution,⁶⁸ while gas-phase reactions at the carbonyl group, e.g., cation-induced esterification, have been assigned a different mechanism, involving concerted transfer of the acyl group, on the grounds of ICR evidence.⁶⁹⁻⁷¹ Radiolytic alcoholysis of esters, $\text{RCO}_2\text{R}'$, has been accomplished by methylation with Me_2F^+ ions, followed by reaction with a $\text{R}''\text{OH}$ alcohol, occasionally in the presence of gaseous bases. The results, in particular the isolation of ortho esters accomplished in favorable cases, suggest the addition-elimination sequence promoted by predominant methylation at carbonyl oxygen



Eventually, **10**–**10''** evolve into neutral esters by releasing an alkyl cation to a suitable nucleophile. The sequence (18) has independently been demonstrated by isobutane-CIMS, allowing the $\text{MeC}(\text{OMe})_2^+$ ions from the protonation of $\text{MeC}(\text{OMe})_3$ to react with suitably labeled alcohols, e.g., CD_3OD and $\text{CH}_3^{18}\text{OH}$. More direct evidence is provided by the formation of ortho

(66) Attinà, M.; Cacace, F.; Cipollini, R.; Speranza, M. *J. Am. Chem. Soc.* **1985**, *107*, 4824.

(67) Fornarini, S. *J. Am. Chem. Soc.* **1988**, *110*, 963.

(68) March, J. *Advanced Organic Chemistry*; Wiley: New York, 1985; p 334.

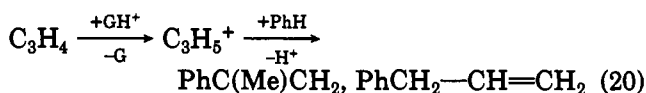
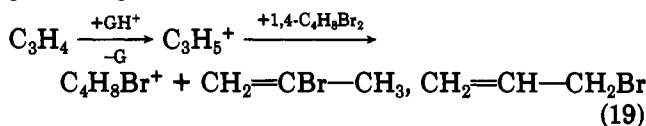
(69) Riveros, J. M.; Jose, S. M.; Takashima, K. *Adv. Phys. Org. Chem.* **1985**, *21*, 197.

(70) Kim, J. K.; Caserio, M. C. *J. Am. Chem. Soc.* **1981**, *103*, 2124.

(71) Caserio, M. C.; Kim, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6896.

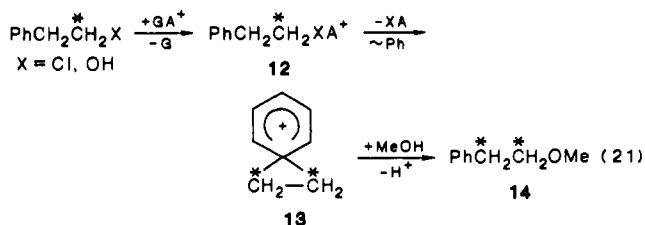
esters from the deprotonation of **11** with strong bases of low nucleophilicity, e.g., NEt_3 , especially successful when the substrate contains electron-withdrawing groups (Ph, F, etc.) that destabilize ions **10** with respect to **11**. The combination of CIMS and radiolytic techniques provides compelling evidence for the addition-elimination mechanism (18) and for the intervention in the gas-phase acid-induced alcoholysis of esters of tetrahedral intermediates, undetectable under ICR conditions.

The protonation of propyne and allene by H_3^+ and C_7H_5^+ ions has been investigated in the range 150–760 Torr,¹⁷ trapping the C_3H_5^+ ions with different nucleophiles, e.g.



Dibromobutane has proved particularly useful, since the isomeric composition of $\text{C}_3\text{H}_5\text{Br}$ neutral products has showed that *2-propenyl ions are formed almost exclusively from both propyne and allene in the kinetically significant step of the protonation*. Such remarkable selectivity must arise from purely kinetic factors, since 2-propenyl cation is known to be considerably *less stable* than the allyl cation.⁷² This is confirmed by the increase of the relative yield of the allyl bromide as the pressure of the radiolytic system is decreased.¹⁷ Benzene, on the other hand, has proved less satisfactory, giving allylbenzene and α -methylstyrene in different ratios, depending on the presence of gaseous bases (NMe_3 , pyridine). This suggests that isomerization occurs within the ion-molecule adducts formed by C_3H_5^+ with benzene, even in high-pressure radiolytic systems, and provides a caveat against the use of benzene as a derivatizing reactant in CAD studies.⁷³

An elegant radiolytic experiment has recently demonstrated the intermediacy of gaseous ethylenebenzenium ion **13** (phenonium ion).⁷⁴ Selectively ¹³C-labeled β -phenylethyl derivatives have been protonated with radiolytically formed acids, such as H_3^+ or C_7H_5^+ , trapping the ions formed with suitable nucleophiles, e.g.



The isolation of **14** by preparative GC and its analysis by MS, as well as by ¹H and ¹³C NMR, accomplished despite the minute amount (~ 0.2 mg) of the radiolytic product, demonstrate complete ¹³C randomization between the methylene groups, ruling out intermediacy of $\text{PhCH}_2\text{CH}_2^+$ ions or direct nucleophilic displacement of AX by MeOH in ion **12** and providing strong evi-

(72) Schwartz, H. In *The Chemistry of Functional Groups: The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: Chichester, 1987.

(73) Lay, J. O.; Gross, M. L. *J. Am. Chem. Soc.* **1983**, *105*, 3445.

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dence for the occurrence of **13** in the gas phase. This conclusion is supported by the stereochemical evidence for the formation of gaseous *substituted* phenonium ions from radiolytic experiments involving the protonation of 2-Ph-1-X-propane, 2-Ph-2-X-propane, and 2-Ph-3-X-butane (X = Cl, OH) by gaseous Brønsted acids.^{75,76}

Concluding Remarks

The integrated approach based on the coordinated application of mass spectrometric and radiolytic tech-

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(76) Fornarini, S.; Sparapani, C.; Speranza, M. *J. Am. Chem. Soc.* **1988**, *110*, 42.

niques is a powerful and versatile tool for the study of gas-phase ion chemistry. The unique features of the radiolytic experiments, i.e., the extended pressure range and the high structural resolution, are particularly useful in two important areas, namely, the study of gas-phase ionic reactions under conditions that allow meaningful *kinetic* comparison with the corresponding processes in solution, and the detection and the structural characterization of otherwise elusive transient ions.

I acknowledge with gratitude the contributions of my colleagues and co-workers whose names appear in the references and M. L. Fabrizi for preparation of the manuscript. The work described here has been supported by the Italian National Research Council (CNR) and the Ministero della Pubblica Istruzione.