Gas-Phase Acid-Induced S_N2' versus S_N2 Mechanism in Allylic Alcohols[**]

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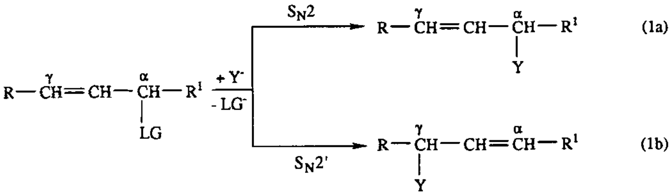
Abstract: A first demonstration of the existence of the concerted S_N2' mechanism in the gas phase was obtained by establishing the regioselectivity of the attack of a neutral nucleophile, such as MeOH, on several allylic oxonium ions. These were generated in the gas phase by the reaction of radiolytically formed GA^+ acids ($GA^+ = C_nH_5^+$ ($n = 1$, 2), $iC_3H_7^+$, and $(CH_3)_2F^+$) with *trans-* (**1**) and *cis*-2-buten-1-ol (**2**) as well as with 1-buten-3-ol (**3**). Firm evidence in favor of the concerted S_N2' pathway accompanying the classical S_N2 one in these systems was obtained after careful evaluation of the extent of conceivable intramolecular isomerization both of the primary oxonium ions from GA^+ attack on **1**–**3** before nucleophilic displacement by MeOH and of their substituted intermediates before neutralization. The intermediacy of free allylic ions in the nucleophilic substitution was ruled out by generating the ions by protonation of 1,3-butadiene and by investigating their behavior in exactly the same media employed in the substitution reactions. The regioselectivity of MeOH with the ionic substrates investigated showed the occurrence of nearly equally extensive S_N2' and S_N2 pathways in the oxonium ions from **1** (S_N2' ($57 \pm 2\%$) and S_N2 ($43 \pm 2\%$)) and **3** (S_N2' ($54 \pm 2\%$) and S_N2 ($46 \pm 2\%$)), whereas, with **2**, the S_N2 ($66 \pm 2\%$) reaction prevailed over the S_N2' one ($34 \pm 2\%$). The role of intrinsic structural factors in determining the S_N2'/S_N2 branching in the selected oxonium ions is discussed.

Keywords
allylic alcohols · gas-phase chemistry · ions · mechanistic studies · nucleophilic substitutions

Introduction

Nucleophilic substitution at saturated carbon proceeds either by a stepwise mechanism involving the intermediacy of ionic species (S_N1) or through a concerted mechanism involving a single transition state between reactants and products (S_N2) wherein the energy released in forming the new bond serves to break the old one. With allylic compounds, the attack of the nucleophile Y can occur at the C_α center (S_N2) [Eq. (1 a)] or at the C_γ one with concerted or stepwise departure of the leaving group LG and migration of the double bond (S_N2') [Eq. (1 b)].[1] Alternatively, rate-determining dissociation of LG may precede attachment of the nucleophile at either the C_α (S_N1) and the C_γ sites (S_N1').



Since the S_N2' mechanism in allylic substitutions was first posited in the late thirties,[2] the search for authentic examples has been intense but lacking in unequivocal success. This failure is mainly a result of the conceivable occurrence in solution of a variety of alternative substitution mechanisms in allylic compounds [Eqs. (2–6)], which makes the unambiguous assignment of the S_N2' one extremely rare.[3] Such mechanistic variety arises from interference of the reaction medium, which may induce a preliminary solvent-, counterion-, or nucleophile-assisted heterolysis of the allylic reactant (and of its substitution products as well) to an intermediate ion pair. Among Equations (2–6), second-order reaction (2) involves rearrangement of the initially formed S_N2 product. In pathways (3–6), formation of an allylic cation–leaving-group pair precedes the substitution process, which leads in reaction (4) to the isomerization of the starting substrate prior to substitution. It follows that observation of the substitution product shown in Equation (1 b) is insufficient per se for assigning the S_N2' label to its formation mechanism. In fact, firm demonstration of a S_N2' mechanism must rely also on the following mechanistic criteria: i) the reaction must follow second-order kinetics; ii) the formation of the substitution product of Equation (1 b) must not proceed through rearrangement of both the starting substrate before substitution and the initially formed S_N2 product; iii) the fast preliminary formation of a free allylic cation must be ruled out.[3a, 4]

According to the sparse unambiguous evidence from solution studies, the efficiency of the concerted S_N2' pathway in allylic compounds appears determined by many factors, including the

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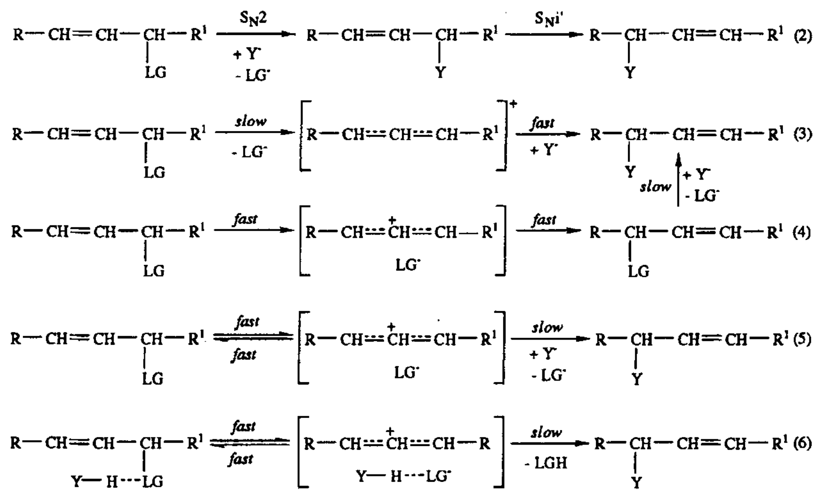
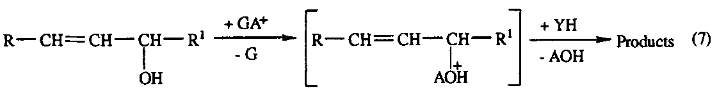
[**] Gas-Phase Acid-Induced Nucleophilic Displacement Reactions, Part 10. Part 9: ref. [1].



nature of the reaction medium as well as the electronic and structural features of the reactants. Indeed, concerted S_N2' reactions (1 b) were found to be best favored in apolar, aprotic media with α-substituted allylic substrates in the presence of neutral nucleophiles.[5] The approach to the electron-rich C=C moiety is indeed easier for neutral than for negatively charged nucleophiles, especially in apolar, aprotic media. Furthermore, when possible, apolar, aprotic solvents favor hydrogen bonding between the nucleophile and the leaving group, which could represent an important driving force for the reaction.

In the search for a genuine S_N2' process, we decided to undertake a comprehensive investigation of acid-catalyzed nucleophilic substitutions on some representative allylic compounds under selected conditions, such as in the gaseous phase and with a neutral nucleophile (MeOH), where the probability that the reaction takes place by the concerted S_N2' pathway is greatest. The kinetic approach adopted, which has recently been reviewed,[6] was based upon the generation of stationary concentrations of gaseous acids ($GA^+ = C_nH_5^+$ (n = 1, 2), $iC_3H_7^+$, and $(CH_3)_2F^+$) obtained in the gas phase by γ-radiolysis (^{60}Co source, $T = 37.5\,°C$) of the corresponding neutral precursor (CH_4, C_3H_8, and CH_3F, respectively) (100–760 Torr), and their attack on the nucleophilic centers of allylic alcohols **1**–**3**, in the presence of an external nucleophile (YH = MeOH). Proton transfer from GA^+ to the oxygen atom of **1**–**3** was expected to generate the corresponding oxonium ions **I**–**III**, wherein the potential leaving group, H_2O (A = H), can be easily displaced by YH = MeOH [Eq. (7)].

We hoped thus to determine the regiochemistry of the gas-phase nucleophilic displacement on **I**–**III** by MeOH as a function of the structural features of the oxonium intermediates, under conditions ensuring their efficient thermalization as well as neutralization of their substituted derivatives **IV**–**VI**, whose isomeric distribution could therefore be determined from the relative concentration of the corresponding deprotonated derivatives. The study was of special interest because it would allow identification of a genuine S_N2' reaction and its dependence upon intrinsic structural factors under conditions excluding the complicating interference of the solvent and counterion effects.



	R, R^1
1	*trans*-Me, H
2	*cis*-Me, H
3	H, Me

I (A = H) ; **IV** (A = Me)
II (A = H) ; **V** (A = Me)
III (A = H) ; **VI** (A = Me)

Experimental Section

Materials: Methane, propane, methyl fluoride, oxygen and trimethylamine were supplied as high purity gases by Matheson and used without further purification. *trans*-2-Buten-1-ol (**1**), *cis*-2-buten-1-ol (**2**), 1-buten-3-ol (**3**), and 1,3-butadiene (**7**) were research-grade chemicals from Aldrich. *trans*-1-Methoxy-2-butene (**4**), *cis*-1-methoxy-2-butene (**5**), and 2-methoxy-3-butene (**6**) were synthesized by the sodium hydride/dimethyl sulfate method [7]. The alcohols **1**–**3** were purified by preparative GLC on a 5 m long, 4 mm i.d. stainless steel column packed with 5% FFAP on Chromosorb G-AW-DMCS at 110 °C. Their final purity exceeded 99.95%. The identity of the alcohols **1**–**3** and of ethers **4**–**6** was verified by NMR spectroscopy and their purity assayed by GLC and GLC-MS on the same columns employed for the analysis of the irradiated mixtures.

Procedure: The gaseous mixtures were prepared by conventional techniques; a greaseless vacuum line was used. The reagents and the additives were introduced into carefully outgassed 250-mL Pyrex bulbs, each equipped with a break-seal tip. The bulbs were filled with the required mixture of gases, cooled to liquid-nitrogen temperature, and sealed off. The irradiation was carried out at 37.5 °C in a 220 Gammacell from Nuclear Canada to a dose of 2×10^4 Gy at a rate of 10^4 Gy h^{-1}, as determined by a neopentane dosimeter. Control experiments, carried out at doses ranging from 1×10^4 to 1×10^5 Gy, showed that the relative yields of products are largely independent of the dose. The radiolytic products were analyzed by GLC by means of either a Hewlett–Packard 5890 series II or a HP 5730 A gas chromatograph equipped with a flame ionization detector. The following columns were employed: i) a 30 m long, 0.32 mm i.d. Supelcowax 10 fused silica capillary column operated at temperatures ranging from 25 to 180 °C, 5 °C min^{-1}; ii) a 3 m long, 2 mm i.d. glass column, packed with 0.1% SP 1000 on 80–100 Carbopack C, operated at temperatures ranging from 50 to 150 °C, 4 °C min^{-1}. The products were identified by comparison of their retention volumes with those of authentic standard compounds and their identity confirmed by GLC-MS with a Hewlett–Packard HP 5971 A mass spectrometer. Their yields were determined from the areas of the corresponding eluted peaks by means of individual calibration curves.

Results

Table 1 lists the absolute and relative yields of the products formed from allylic alcohols **1**–**3** and 1,3-butadiene (**7**) undergoing gas-phase attack from the radiolytically generated GA^+ acids in the presence of H_2O or MeOH as nucleophiles, and NMe_3 as a base when required. The table gives $G_{(M)}$ values, expressed as the number of molecules of the product M formed per 100 eV of energy absorbed by the gaseous mixture at the total dose of 2×10^4 Gy (dose rate: 1×10^4 Gy h^{-1}). The reported figures represent the mean $G_{(M)}$ values obtained from several separate irradiations carried out under the same experimental conditions, whose reproducibility is expressed by the uncertainty level quoted. The table also summarizes the total absolute yields of products, expressed as a percentage ratio of their combined $G_{(M)}$ values to the $G_{(GA^+)}$ of their gaseous acid precursor available from the literature.[8]

The ionic character of these reactions was demonstrated by the sharp decrease of the overall product yields (over 60%) caused by the addition to the gaseous mixture of 0.4 mol% of NMe_3, an efficient positive-ion interceptor.

The experiments reported in Table 1 can be grouped in four categories: i) those to evaluate the extent of rearrangement in oxonium intermediates **I**–**III** from GA^+ attack on **1**–**3** (entries 1–6); ii) those to estimate the extent of rearrangement in their substituted intermediates, namely, the O-protonated *trans*-1-methoxy-2-butene (**IV**), *cis*-1-methoxy-2-butene (**V**), and 2-methoxy-3-butene (**VI**) prior to neutralization to the corresponding ethers **4**–**6** (entries 7–21); iii) those to investigate the behavior of free 1-methylallyl cation (**VII**) towards selected gaseous nucleophiles (entries 22–27); iv) those concerning the attack of MeOH on **I**–**III** (entries 28–36).

The results of the first group of experiments indicated that protonation of allylic alcohol **1** in the presence of approximately

Table 1. Product yields from the gas-phase attack of GA^+ acids on allylic compounds.

		System composition [a]				Product yields, $G_{(M)}$ (%) [b]			Total
Group No.	Entry No.	Substrate (Torr)	Bulk gas (Torr)	YH (Torr)	GA^+	**4** or **1**	**5** or **2**	**6** or **3**	Absolute yield (%) [c]
i	1	**1** (0.5)	CH_4 (760)	H_2O (1.9) [d]	$C_nH_5^+$		–	*0.09 (100)*	3
	2	**2** (0.5)	CH_4 (760)	H_2O (2.0) [d]	$C_nH_5^+$	*0.23 (69)*		*0.10 (31)*	12
	3	**3** (0.5)	CH_4 (760)	H_2O (1.9) [d]	$C_nH_5^+$	*0.13 (100)*	–		5
	4	**1** (0.5)	C_3H_8 (760)	H_2O (2.0)	$iC_3H_7^+$			*0.02 (100)*	1
	5	**2** (0.5)	C_3H_8 (760)	H_2O (2.1)	$iC_3H_7^+$	*0.10 (76)*		*0.03 (24)*	4
	6	**3** (0.5)	C_3H_8 (760)	H_2O (2.1)	$iC_3H_7^+$	*0.05 (100)*			2
ii	7	**4** (0.5)	CH_4 (760)	[e]	$C_nH_5^+$			0.06 (100)	2
	8	**4** (0.6)	CH_4 (760)		$C_nH_5^+$			0.20 (100)	7
	9	**4** (0.6)	CH_4 (100)		$C_nH_5^+$			0.32 (100)	11
	10	**5** (0.6)	CH_4 (760)	[e]	$C_nH_5^+$	0.02 (100)		–	1
	11	**5** (0.6)	CH_4 (760)		$C_nH_5^+$	0.06 (67)		0.03 (33)	3
	12	**5** (0.6)	CH_4 (100)		$C_nH_5^+$	0.12 (63)		0.07 (37)	7
	13	**6** (0.5)	CH_4 (760) [e]		$C_nH_5^+$	–			<0.2
	14	**6** (0.5)	CH_4 (760)		$C_nH_5^+$	0.14 (100)			5
	15	**6** (0.6)	CH_4 (100)		$C_nH_5^+$	0.24 (100)			9
	16	**1** (0.4)	CH_3F (760)		Me_2F^+	0.71 (72)	0.02 (2)	0.25 (26)	29
	17	**2** (0.6)	CH_3F (760)		Me_2F^+	0.08 (9)	0.74 (85)	0.05 (6)	26
	18	**3** (0.5)	CH_3F (760)		Me_2F^+	0.07 (6)	–	1.05 (94)	33
	19	**1** (0.4)	CH_3F (100)		Me_2F^+	1.18 (68)	0.07 (4)	0.49 (28)	51
	20	**2** (0.6)	CH_3F (100)		Me_2F^+	0.15 (15)	0.73 (74)	0.11 (11)	29
	21	**3** (0.6)	CH_3F (100)		Me_2F^+	0.26 (18)	–	1.17 (82)	42
iii	22	**7** (1.5)	CH_4 (760)	H_2O (2.0) [e,f]	$C_nH_5^+$			*0.92 (100)*	33
	23	**7** (1.5)	CH_4 (760)	H_2O (2.0) [f]	$C_nH_5^+$			*2.32 (100)*	83
	24	**7** (1.6)	CH_4 (100)	H_2O (2.1) [f]	$C_nH_5^+$			*2.52 (100)*	90
	25	**7** (1.3)	CH_4 (760)	MeOH (1.1) [e]	$C_nH_5^+$			–	<0.2
	26	**7** (1.2)	CH_4 (760)	MeOH (1.0)	$C_nH_5^+$	0.14 (38)	0.04 (10)	0.20 (52)	13
	27	**7** (1.2)	CH_4 (100)	MeOH (1.2)	$C_nH_5^+$	0.18 (32)	0.08 (15)	0.29 (53)	20
iv	28	**1** (0.5)	CH_4 (760)	MeOH (0.6) [e]	$C_nH_5^+$	0.08 (40)	–	0.12 (60)	7
	29	**2** (0.5)	CH_4 (760)	MeOH (0.6) [e]	$C_nH_5^+$	0.01 (6)	0.10 (59)	0.06 (35)	6
	30	**3** (0.5)	CH_4 (760)	MeOH (0.5) [e]	$C_nH_5^+$	0.09 (37)	–	0.16 (63)	9
	31	**1** (0.4)	CH_4 (760)	MeOH (0.5)	$C_nH_5^+$	0.30 (35)	0.007(1)	0.55 (64)	31
	32	**2** (0.4)	CH_4 (760)	MeOH (0.5)	$C_nH_5^+$	0.09 (9)	0.48 (51)	0.38 (40)	34
	33	**3** (0.5)	CH_4 (760)	MeOH (0.6)	$C_nH_5^+$	0.42 (42)	–	0.58 (58)	36
	34	**1** (0.6)	CH_4 (100)	MeOH (0.7)	$C_nH_5^+$	0.64 (35)	0.02 (1)	1.19 (64)	66
	35	**2** (0.6)	CH_4 (100)	MeOH (0.6)	$C_nH_5^+$	0.39 (22)	0.57 (32)	0.82 (46)	64
	36	**3** (0.5)	CH_4 (100)	MeOH (0.5)	$C_nH_5^+$	0.75 (40)	–	1.12 (60)	67

[a] A racemic mixture of **3** and **6** was used. O_2: 4 Torr. Radiation dose 2×10^4 Gy (dose rate: 1×10^4 Gyh^{-1}). [b] All figures in italics refer to alcohols **1**–**3** as the products; the other figures refer to ethers **4**–**6** as the products. For the sake of clarity, the yields of the elimination product 1,3-butadiene (up to 19% relative to those of substitution products) are omitted. $G_{(M)}$ as the number of molecules M produced per 100 eV of absorbed energy. Percentages as the ratios between the $G_{(M)}$ of each product and the combined $G_{(M)}$ values of all products identified. The dash (–) denotes that the absolute yield of the corresponding products is below the detection limit of approximately 0.2%. Each value is the average of several determinations, with an uncertainty level of about 5%. [c] Absolute yields estimated from the percentage ratio of the combined $G_{(M)}$ values of products and the literature $G_{(GA^+)}$ values (ref. [8]). [d] With $H_2{}^{18}O$ (^{18}O content >97%), no incorporation of the ^{18}O label was observed. [e] 3 Torr of NMe_3 added to the gaseous mixture. [f] With $H_2{}^{18}O$ (^{18}O content >97%), over 70% incorporation of the ^{18}O label was observed in allylic alcohol **3**.

2 Torr of H_2O induces its isomerization exclusively to **3** to a very limited extent, which slightly increases with the strength of the gaseous acid employed (3% with $C_nH_5^+$ ($n = 1, 2$), 1% with $iC_3H_7^+$). Similarly, protonation of **3** yielded comparably low amounts of its isomer **1** (5% with $C_nH_5^+$ ($n = 1, 2$), 2% with $iC_3H_7^+$), whereas protonation of **2** produced slightly higher yields of both **1** and **3** (**1**: 8.3% with $C_nH_5^+$ ($n = 1, 2$), 3.5% with $iC_3H_7^+$; **3**: 3.7% with $C_nH_5^+$ ($n = 1, 2$), 1.1% with $iC_3H_7^+$). When the reactions were carried out in the presence of approximately 2 Torr of $H_2{}^{18}O$ (^{18}O content >97%) instead of H_2O no detectable excess of the ^{18}O label above the natural abundance was observed in the same rearranged products.

Inspection of the results of the experiments of group (ii) revealed that the nature and extent of the isomerization pattern triggered by the gas-phase $C_nH_5^+$-protonation ($n = 1, 2$) of ethers **4**–**6** (entries 7–15) was fully comparable with that observed with alcohols **1**–**3**. Thus, **4** produced low yields of **6** (7%) exclusively and **6** gave rise only to **4** (5%), while **5** slightly isomerized to both **4** (2.1%) and **6** (1.1%). The extent of isomerization increased appreciably when the system pressure was decreased from 760 to 100 Torr. An apparently different **4**–**6** isomeric distribution was obtained by O-methylation of alcohols **1**–**3** by $(CH_3)_2F^+$ ions (entries 16–21) since, in these experiments, the major products were invariably the methyl ether corresponding to the starting alcohol (**4** (68–72%, from **1**); **5** (74–85%, from **2**); **6** (82–94%, from **3**)). However, if the analysis was restricted to the other isomeric ethers, the experiments demonstrated that their composition and absolute yields nearly coincided with those measured from the $C_nH_5^+$-protonation ($n = 1, 2$) of ethers **4**–**6**. Thus, the predominant isomer of **4** formed from methylation of **1** by $(CH_3)_2F^+$ was **6** (7% (entry 16), compared with 7% absolute isomerization yield of **6** in the $C_nH_5^+$-protonation ($n = 1, 2$) of ether **4** (entry 8)). In the same way, the only isomer of **6** from methylation of **3** by $(CH_3)_2F^+$ was ether **4** (2% (entry 18) compared with 5% of **4** from $C_nH_5^+$-protonation ($n = 1, 2$) of ether **6** (entry 14)). Finally, both **4** and **6** arose from methylation of **2** by $(CH_3)_2F^+$ (2.3% **4** and 1.6% **6** (entry 17), compared with 2.1% of **4** and 1.1% of **6** from $C_nH_5^+$-protonation ($n = 1, 2$) of ether **5** (entry 11)). Decreasing the pressure of the gaseous mixtures from 760 to 100 Torr increased the rearrangement of the ethers

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formed by methylation of **1–3** by $(CH_3)_2F^+$ to an extent which was fully comparable to that observed in the $C_nH_5^+$-protonation ($n = 1$, 2) of ethers **4–6** by lowering the bulk gas pressure to the same level.

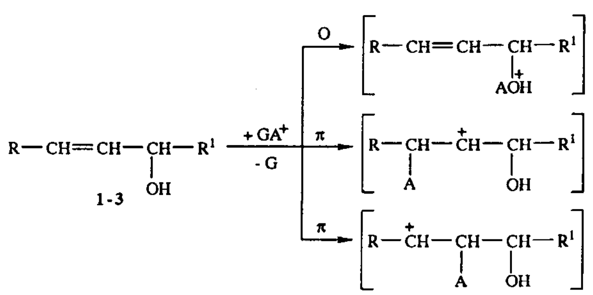
The results of the experiments of group (iii) (entries 22–27 of Table 1) refer to the regiochemistry of the attack of the selected nucleophile YH (H_2O or MeOH) on free 1-methylallyl cation **VII** generated in the gas phase by $C_nH_5^+$-protonation ($n = 1$, 2) of 1,3-butadiene (**7**). Accordingly, both nucleophiles added to **VII** to form the corresponding products, that is, alcohols **1–3** (YH = H_2O) or ethers **4–6** (YH = MeOH), in considerable amounts. However, while the attack of **VII** on H_2O yielded exclusively alcohol **3**, addition of **VII** to MeOH gave rise to all isomeric ethers **4–6** (**4**: 32–38%, **5**: 10–15%, **6**: 52–53%). As expected, alcohol **3** from addition of **VII** to $H_2{}^{18}O$ (^{18}O content > 97%) displayed significant ^{18}O incorporation (> 70%).

The results of the experiments in group (iv) indicate that $C_nH_5^+$-protonation ($n = 1$, 2) of **1–3** in the presence of approximately 0.6 Torr of MeOH led to high yields of all isomeric ethers **4–6** (31–36% at 760 Torr; 64–67% at 100 Torr), irrespective of the starting allylic alcohol (entries 28–36). Their distribution was strongly affected by the nature of the alcoholic substrate. Thus, at 760 Torr, $C_nH_5^+$-protonation ($n = 1$, 2) of **1** yielded both **6** (64%) and **4** (35%), as well as traces of **5** (0.3%). Under the same conditions, alcohol **2** yielded ethers **5** (51%) and **6** (40%), together with minor amounts of **4** (9%). Alcohol **3** instead gave rise to **4** (42%) and **6** (58%) only. Addition of 3 Torr of a powerful base, such as NMe_3, to the gaseous mixture, while strongly decreasing the absolute yields of ethers **4–6** (6–9%), did not substantially modify their isomeric distribution. In these systems, 1,3-butadiene was also recovered in appreciable yields (up to ca. 19% of the overall absolute yield of ethers).

Discussion

Gas-phase GA$^+$ attack on allylic alcohols: The conditions typical of the present experiments, in particular the low concentrations of alcohols **1–3** (< 0.6 mol%) diluted with a large excess of the bulk gas (CH_4, C_3H_8, or CH_3F), exclude direct radiolysis of the alcoholic substrate as a significant route to the products of Table 1. The presence of an efficient thermal radical scavenger, O_2, in about tenfold excess over the substrate inhibited possible free-radical pathways to products in favor of the competing ionic ones, whose large predominance was demonstrated by the marked effect of an ion trap such as NMe_3 on the overall product yield.

The gaseous acids ($GA^+ = C_nH_5^+$ ($n = 1$, 2), $iC_3H_7^+$, and $(CH_3)_2F^+$), formed in known yields by γ-radiolysis of the bulk gas (CH_4, C_3H_8, and CH_3F, respectively), were thermalized by many unreactive collisions with their parent molecules before attacking the nucleophiles present in the mixture, including the allylic alcohols **1–3**. Two nucleophilic centers are present in the latter compounds, namely the oxygen atom and the π bond, both susceptible to attack by a proton or an alkyl cation from GA$^+$, if thermochemically allowed [Eq. (8)].



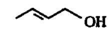
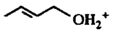
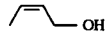
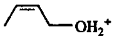
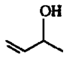
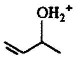
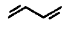
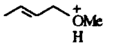
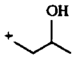
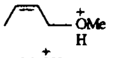
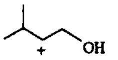
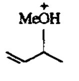
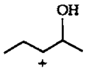
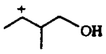
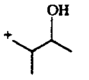
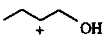
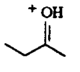
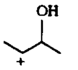
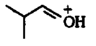
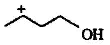
I-III (A = H)
IV-VI (A = Me) (8a)

VIII (R = Me; R^1 = H; A = H) (8b)
IX (R = H; R^1 = Me ; A = H)
X (R = Me; R^1 = H ; A = Me)
XI (R = H; R^1 = Me ; A = Me)

XII (R = Me; R^1 = H; A = H) (8c)
XIII (R = H; R^1 = Me ; A = H)
XIV (R = Me; R^1 = H ; A = Me)
XV (R = H; R^1 = Me ; A = Me)

A major difficulty in determining the thermochemistry of the gas-phase reactions (8) arises from the lack of experimental thermochemical data for the involved ionic species **IV–VI** and **VIII–XV**. However, the application of well-established estimation procedures (outlined in the footnotes of Table 2) led to their approximate formation enthalpies, as reported in Table 2. On these grounds, reactions (8a–c) were calculated to be thermochemically allowed, except perhaps the $iC_3H_7^+$-protonation of the π bond of **3** (Table 3). Among them, the gas-phase attack of GA$^+$ on the O atom of the allylic alcohol [Eq. (8a)] appeared to prevail kinetically over attack at the π bond [Eqs. (8b,c)], as testified by the absence of carbonylic compounds such as butanone and butyraldehyde among the radiolytic products in Table 1. Their O-protonated precursors were, in fact, the stable

Table 2. Thermochemical data (kcal mol^{-1}) (estimated values in italics).

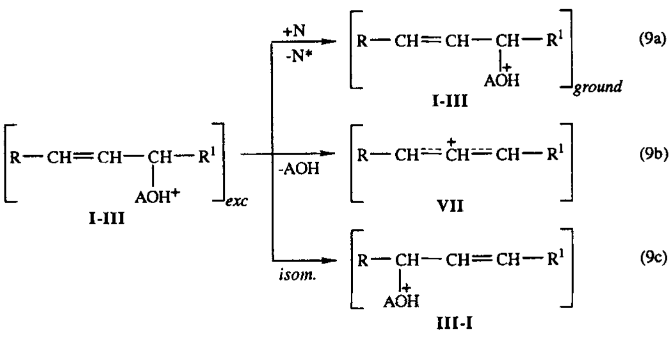
Species	ΔH_f°	Source	Species	ΔH_f°	Source
CH_4	-17.8	[a]	CH_5^+	216	[a]
C_2H_4	12.5	[a]	$C_2H_5^+$	215.6	[a]
C_3H_6	4.8	[a]	i-$C_3H_7^+$	190.9	[a]
CH_3F	-59	[a]	$(CH_3)_2F^+$	147	[a]
 (**1**)	-37	[a]	 (**I**)	*137*	[d]
 (**2**)	*-36*	[b]	 (**II**)	*138*	[d]
 (**3**)	-38	[a]	 (**III**)	*132*	[e]
 (**7**)	26.3	[c]	 (**IV**)	*133*	[f]
 (**XIII**)	*165*	[e]	 (**V**)	*134*	[f]
 (**X**)	*151*	[d]	 (**VI**)	*130*	[f]
 (**XI**)	*147*	[d]	 (***exo*-VII**)	202	[a]
 (**XIV**)	*144*	[d]	 (***endo*-VII**)	205	[g]
 (**XV**)	*160*	[d]	 (**VIII**)	*156*	[e]
	109	[a]	 (**IX**)	*152*	[e]
	121	[a]	 (**XII**)	*149*	[e]

[a] S. G. Lias, J. E. Bartmess, J. F. Liebmann, J. L. Holmes, R. D. Levin, W. G. Mallard, *J. Phys. Chem. Ref. Data* **1988**, *17*, Suppl. 1. [b] Estimated by $\Delta\Delta H_f^\circ = \Delta H_f^\circ$ (*cis*) – ΔH_f° (*trans*) = 1 kcal mol^{-1} for but-2-ene (cf. [a] and the calculation method reported in [d]). [c] D. R. Strull, E. F Westrum, Jr., G. C. Sinke, *The Chemical Thermodynamics of Organic Compounds*, Wiley, New York, **1969**. [d] Estimated by the method illustrated in R. D. Bowen, D. H. Williams, *J. Am. Chem. Soc.* **1977**, *99*, 6822. [e] R. D. Bowen, D. H. Williams, *J. Am. Chem. Soc.* **1978**, *100*, 7454. [f] Estimated by ΔPA = PA (methyl ether) – PA (alcohol) = 10 kcal mol^{-1} (PA = proton affinity) from [g] and R. D. Bowen, D. H. Williams, G. Hvistendahl, J. R. Kalman, *Org. Mass Spectrom.* **1978**, *13*, 721. [g] Estimated by the calculated $\Delta\Delta H_f^\circ = \Delta H_f^\circ$ (*endo*) – ΔH_f° (*exo*) = 3 kcal mol^{-1} (H. Mayr, W. Förner, P. v. R. Schleyer, *J. Am. Chem. Soc.* **1979**, *101*, 6032.

Table 3. Reaction enthalpies ($kcal\,mol^{-1}$).

Equation	Ionic reactant	(A)	ΔH° (substrate)		
8a	CH_5^+	(H)	−60 (1)	−60 (2)	−64 (3)
	$C_2H_5^+$	(H)	−29 (1)	−29 (2)	−33 (3)
	$iC_3H_7^+$	(H)	−12 (1)	−12 (2)	−16 (3)
	$(CH_3)_2F^+$	(Me)	−36 (1)	−36 (2)	−38 (3)
8b	CH_5^+	(H)	−41 (1)	−42 (2)	−44 (3)
	$C_2H_5^+$	(H)	−10 (1)	−11 (2)	−13 (3)
	$iC_3H_7^+$	(H)	+ 7 (1)	+ 6 (2)	+ 4 (3)
	$(CH_3)_2F^+$	(Me)	−18 (1)	−19 (2)	−21 (3)
8c	CH_5^+	(H)	−48 (1)	−49 (2)	−31 (3)
	$C_2H_5^+$	(H)	−17 (1)	−18 (2)	0 (3)
	$iC_3H_7^+$	(H)	0 (1)	− 1 (2)	+17 (3)
	$(CH_3)_2F^+$	(Me)	−25 (1)	−26 (2)	− 8 (3)
	exo-**VII**		− 7 (H_2O, yielding **I**) −12 (H_2O, yielding **III**) −21 (MeOH, yielding **IV**) −24 (MeOH, yielding **VI**)		
	endo-**VII**		− 9 (H_2O, yielding **II**) −15 (H_2O, yielding **III**) −23 (MeOH, yielding **V**) −27 (MeOH, yielding **VI**)		

structures to which the conceivable intermediates **VIII–XV** are known to isomerize without any significant activation barrier.[9] Therefore, the GA^+ acids selectively attack the n-electrons of **1–3** yielding the corresponding oxonium intermediates **I–III** (A = H) or **IV–VI** (A = Me), excited by the exothermicity of their formation process [Eq. (8a)], increasing in the order: $iC_3H_7^+ < C_2H_5^+ < (CH_3)_2F^+ < CH_5^+$ (Table 3). Owing to their excess energy, the excited onium intermediates **I–III** (A = H) or **IV–VI** (A = Me) may undergo extensive interconversion to their isomeric structures [Eq. (9c)], for example, **I**↔**II**↔**III**, or unimolecular fragmentation to the corresponding 1-methylallyl cation **VII** [Eq. (9b)], for example **II** → *endo*-**VII**, **I** and **III** → *exo*-**VII**, in competition with their collisional quenching with the bulk gas molecules N [Eq. (9a)].



Thus, in principle, the radiolytic products of entries 28–36 of Table 1 may originate from different reaction pathways, that is, from nucleophilic attack of MeOH on either the isomeric allylic ions **VII** and/or the isomeric oxonium ions **I–III**. In the latter case only, their formation proceeds by a rate-limiting step that involves departure of the leaving group (H_2O) through the action of the nucleophile MeOH and, therefore, can be marked as concerted S_N2 or S_N2' processes. Thence, it follows that attribution of kinetic and mechanistic significance to the results of entries 28–36 of Table 1 is critically determined by the unequivocal identification of the reactive intermediates involved in the substitution process.

Nature of the substitution intermediates: As pointed out in the introduction, positive demonstration of a genuine S_N2' mechanism in allylic substrates is made extremely difficult in solution by the incursion of a number of complicating phenomena. These may involve solvent-, counterion-, and nucleophile-assisted heterolysis of the allylic compound in the solvent cage with formation of ion pairs, which may either collapse with the nucleophile or recombine with the leaving moiety to yield an isomerized allylic compound before substitution by the nucleophile [Eqs. (2–6)].[3, 4]

In the gas phase, mechanistic analysis is greatly facilitated by the absence of solvation and ion-pairing phenomena and by the capability of the radiolytic methodology to generate different intermediates by different approaches, such as **I–III** or **VII**, held responsible for the formation of the substituted products, and to investigate their behavior in the same gaseous medium. For instance, free 1-methylallyl cation **VII** is conveniently prepared in the gas phase by $C_nH_5^+$-protonation ($n = 1, 2$) of 1,3-butadiene (**7**) ($-\Delta H^\circ = 58$ ($n = 1$), 27 ($n = 2$) $kcal\,mol^{-1}$). In 100–760 Torr of CH_4, ion **VII** adds to H_2O yielding exclusively **3** in sizable amounts (over 83%) (entries 23 and 24 of Table 1). In the same medium, addition of ion **VII** to MeOH yields all isomeric ethers **4–6** (**4**: 32–38%, **5**: 10–15%, **6**: 52–53%) (entries 26 and 27 of Table 1). In compliance with the Hammond postulate, the higher regioselectivity of **VII** towards H_2O is attributed to the lower exothermicity of the addition process ($-\Delta H^\circ = 7$–$15\ kcal\,mol^{-1}$), relative to that involving MeOH ($-\Delta H^\circ = 21$–$27\ kcal\,mol^{-1}$) (Table 3).

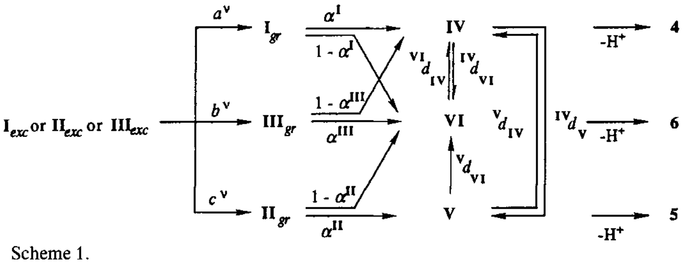
Comparison of these results with those of entries 1–6 of Table 1 provides the first piece of evidence against the intermediacy of allylic ions **VII** in the substitution process [Eq. (9b)]. In fact, were free ions **VII** abundantly generated by $C_nH_5^+$-protonation ($n = 1, 2$) of **1–3**, they would attack H_2O producing *exclusively* high yields of alcohol **3** (entries 22–24). Extensive **1** → **3** and **2** → **3** isomerization would be observed from **1** and **2**, respectively, whereas protonation of the starting alcohol **3** would have *no visible effects*. In fact, at 760 Torr, $C_nH_5^+$-protonation ($n = 1, 2$) of **3** led to *limited, but easily detectable amounts* of **1** (5%, compared with the 0.2% sensitivity limit of the analytical methodology used (Table 1, entry 3)). The same reaction with **1** yielded comparatively low quantities of **3** (3%, entry 1), whereas **2** gave rise to appreciable yields of both **1** (8.3%) and **3** (3.7%, entry 2), in proportions opposite to those expected on the grounds of the relative stability of their oxonium ion precursors **I** and **III** (Table 2). Furthermore, replacement of $C_nH_5^+$ with the milder $iC_3H_7^+$ ion as the acid catalyst not only reduced significantly the yield of the isomerized products (by over 60%), as predicted, but also their distribution (cf., e.g., entries 2 and 5), in contrast to what was expected for free allylic ions **VII**. In addition, while the free ions **VII** added to $H_2{}^{18}O$ to yield large amounts of ^{18}O-labeled **3** (^{18}O-content >70%), $C_nH_5^+$-protonation ($n = 1, 2$) of **1–3** in the presence of the same concentration of $H_2{}^{18}O$ led to small yields of isomeric alcohols with no detectable excess of the ^{18}O label above the natural abundance.

A similar picture emerges from comparison of the relative distribution of isomeric methoxybutenes **4–6** (**4**: 32–38%, **5**: 10–15%, **6**: 52–53%) from attack of allylic ions **VII** on MeOH (entries 26 and 27 of Table 1) with that from $C_nH_5^+$-protonation ($n = 1, 2$) of **4–6** (e.g., **4**: 63–67%, **6**: 33–37% from protonation of **5**) (entries 7–15 of Table 1).

An additional piece of evidence against significant unimolecular dissociation of oxonium ions **I–III** to free allylic ions **VII** [Eq. (9b)] arises from comparison of the product distribution of entries 26 and 27 (**4**:**5**:**6** = (0.62–0.70):(0.20–0.28):1.00) with the corresponding results of entries 16–21 concerning methylated oxonium ions **IV**–**VI**. When generated in the gas phase by methylation of **1**–**3** by $(CH_3)_2F^+$, the corresponding methylated oxonium ion (**IV** or **V** or **VI**) yielded all isomeric methoxybutenes **4**–**6**, but in proportions markedly dependent upon the nature of the starting allylic alcohol: **4**:**5**:**6** = (2.41–2.84):(0.08–0.14):1.00 (from **1**); (1.36–1.60):(6.64–14.8):1.00 (from **2**); (6.67–22.2):(<0.006):1.00 (from **3**). Besides excluding facile dissociation of oxonium ions **I**–**III** and **IV**–**VI** to the free ion **VII**, product distributions which differ by such large amounts speak against extensive **IV**↔**V**↔**VI** interconversion prior to their neutralization to ethers **4**–**6** [Eq. (9b)]. It follows that the free ion **VII** plays a negligible role, if any, in determining the isomeric distribution of the substitution products in entries 28–36 of Table 1. Rather, this reflects the specific regioselectivity of the MeOH-induced displacement in the primary oxonium ions **I**–**III**, possibly altered by partial isomerization of ions **I**–**III** [Eq. (9c)], before YH attack, or their substitution derivatives **IV**–**VI**, before neutralization. The extent of these partial isomerizations reflects the structure and the excess energy of the oxonium intermediate and hence it increased for any given starting alcohol with the strength of the gaseous acid GA^+ and with decreasing pressure of the gaseous mixture.

Discrimination between the inter- or intramolecular character of rearrangement of oxonium ions **I**–**III** is permitted by analysis of the results of Table 1, in particular the limited yields of isomeric alcohols from $C_nH_5^+$-protonation ($n = 1, 2$) of **1**–**3** (<12%) (entries 1–3), despite the high concentration of added H_2O (ca. 2 Torr) and the lack of detectable incorporation of the ^{18}O label when H_2O is replaced by $H_2{}^{18}O$. These results indicate that rearrangement in oxonium ion **I**–**III** [Eq. (7); YH = AOH = H_2O] proceeds essentially by consecutive [1,3] intramolecular shifts of the AOH (A = H) leaving moiety [Eq. (9c)]. That this conclusion is extensible to the case where A = Me was demonstrated by the isomeric product pattern from entries 16–21, which can only be accounted for by consecutive [1,3] intramolecular shifts of the AOH (A = Me) group in the excited oxonium ions **IV**–**VI**. According to the available experimental evidence, unimolecular dissociation of **I**–**III** (and **IV**–**VI**) to free allylic ions **VII** [Eq. (9b)] is negligible under the conditions used. This excludes any significant contribution of unimolecular mechanisms to allylic nucleophilic displacements in **1**–**3** in the gaseous irradiated mixtures.

Substitution pattern and orientation: The conclusions reached in the previous section point to a general reaction pattern for the gas-phase GA^+-promoted nucleophilic substitution on allylic alcohols **1**–**3** by YH = MeOH as outlined in Scheme 1. In the first step of Scheme 1, the a^v, b^v, and c^v terms (with $a^v + b^v + c^v = 1$) represent the interconversion factors for any given excited oxonium ion **I**–**III** [Eqs. (9a,c)]. Their values can be inferred from entries 1–3 of Table 1. Thus, for ion **I** (v = **I**) at 760 Torr CH_4, b^I is given by the absolute yield factor of **3** (0.034, approximated to 0.03 in entry 1), while c^I is equal to zero, owing to the complete absence of isomer **2** among the products. As a consequence, a^I ($= 1 - b^I - c^I$) amounts to 0.966. In the same way, for ion **II**, a^{II} is inferred from the absolute yield factor of **1** ($= 0.69 \times 0.12 = 0.083$) and b^{II} from the absolute yield factor of **3** ($= 0.31 \times 0.12 = 0.037$) (entry 2). Therefore, $c^{II} = 0.880$. For ion **III**, $a^{III} = 0.046$ (absolute yield factor of **1**, approximated to 0.05 in entry 3 of Table 1) and $c^{III} = 0$ and, therefore, $b^{III} = 0.954$.



Scheme 1.

The α^I, α^{II}, and α^{III} terms in the second step of Scheme 1 refer to the regioselectivity of the nucleophilic attack of MeOH on each individual oxonium ion **I**–**III** and, with the sensible assumption of equal rates for the gas-phase capture of isomeric $(\mathbf{I})_{gr}$–$(\mathbf{III})_{gr}$ by MeOH,[10] they express the relative efficiency of MeOH-to-H_2O substitution on their C_α centers (a concerted S_N2 process). Of course, the $(1-\alpha^I)$, $(1-\alpha^{II})$, and $(1-\alpha^{III})$ terms express the relative efficiency of MeOH-to-H_2O substitution on the C_γ centers of the same oxonium ions (a concerted S_N2' process). In this context, it is reasonable to expect that the nucleophilic attack of MeOH on the C_γ of **III** leads predominantly to the *trans* isomer **4**, which is slightly more stable than the *cis* one **5**.[11]

The subsequent step of Scheme 1 concerns the structural interconversion among the substituted oxonium ions **IV**–**VI** prior to their neutralization to methoxybutenes **4**–**6**.[12] For any given oxonium ion **IV**–**VI**, the interconversion factors are denoted by the terms ^nd_m, with n indicating the starting oxonium ion and m the rearranged one. Their values under different experimental conditions can be inferred from entries 16–18 (at 760 Torr) and entries 19–21 (at 100 Torr) of Table 1. Accordingly, $^{IV}d_V = 0.02$ (760 Torr), 0.04 (100 Torr), and $^{IV}d_{VI} = 0.26$ (760 Torr), 0.28 (100 Torr) (entries 16 and 19); $^Vd_{IV} = 0.09$ (760 Torr), 0.15 (100 Torr), and $^Vd_{VI} = 0.06$ (760 Torr), 0.11 (100 Torr) (entries 17 and 20); $^{VI}d_{IV} = 0.06$ (760 Torr), 0.18 (100 Torr), while $^{VI}d_V$ is negligible under all conditions (entries 18 and 21).[13]

In the framework of the reaction pattern shown in Scheme 1, the fraction of each isomeric methoxybutene **4**–**6**, arising from $C_nH_5^+$-protonation ($n = 1, 2$) of any given allylic alcohol **1**–**3** in the presence of MeOH (entries 28–36 of Table 1) can be expressed by the following sets of equations (see Appendix).

$$\begin{aligned}\mathbf{4}/(\mathbf{4}+\mathbf{5}+\mathbf{6}) = (1 - {}^{IV}d_{VI} - {}^{IV}d_V)\{&a^v[\alpha^I + {}^{VI}d_{IV}(1-\alpha^I)]\\ &+ b^v[(1-\alpha^{III}) + {}^{VI}d_{IV}\alpha^{III}]\\ &+ c^v[{}^{VI}d_{IV}(1-\alpha^{II} + {}^Vd_{VI}\alpha^{II}) + {}^Vd_{IV}\alpha^{II}]\}\end{aligned} \tag{10}$$

$$\begin{aligned}\mathbf{5}/(\mathbf{4}+\mathbf{5}+\mathbf{6}) = (1 - {}^Vd_{VI} - {}^Vd_{IV})&\\ \cdot\{c^v\alpha^{II} + {}^{IV}d_V\{&a^v[\alpha^I + {}^{VI}d_{IV}(1-\alpha^I)]\\ &+ b^v[(1-\alpha^{III}) + {}^{VI}d_{IV}\alpha^{III}] + c^v[{}^{VI}d_{IV}(1-\alpha^{II})]\}\}\end{aligned} \tag{11}$$

$$\begin{aligned}\mathbf{6}/(\mathbf{4}+\mathbf{5}+\mathbf{6}) = (1 - {}^{VI}d_{IV})\{&a^v[(1-\alpha^I) + \alpha^I({}^{IV}d_{VI} + {}^{IV}d_V{}^Vd_{VI})]\\ &+ b^v[\alpha^{III} + (1-\alpha^{III})({}^{IV}d_{VI} + {}^{IV}d_V{}^Vd_{VI})]\\ &+ c^v[(1-\alpha^{II}) + \alpha^{II}({}^Vd_{VI} + {}^Vd_{IV}{}^{IV}d_{VI})]\}\end{aligned} \tag{12}$$

Nine equations are obtained (whereof only six are independent, since obviously $\mathbf{4}/(\mathbf{4}+\mathbf{5}+\mathbf{6}) + \mathbf{5}/(\mathbf{4}+\mathbf{5}+\mathbf{6}) + \mathbf{6}/(\mathbf{4}+\mathbf{5}+\mathbf{6}) = 1$) containing three unknowns, namely α^I, α^{II}, and α^{III}. By solving any system of three independent equations by the methoxybutene fractions $\mathbf{4}/(\mathbf{4}+\mathbf{5}+\mathbf{6})$, $\mathbf{5}/(\mathbf{4}+\mathbf{5}+\mathbf{6})$, and $\mathbf{6}/(\mathbf{4}+\mathbf{5}+\mathbf{6})$ as calculated from entries 31–33 of Table 1, the following values for the unknowns are obtained: $\alpha^I = 0.43 \pm 0.02$; $\alpha^{II} = 0.66 \pm 0.04$; $\alpha^{III} = 0.46 \pm 0.02$. The quoted uncertainty ranges reflect the fluctuation of the derived α^I, α^{II}, and α^{III} values with different sets of independent equations. The obtained regioselectivity factors permit evaluation of the relative extent of competing S_N2 and S_N2' pathways involved in the gas-phase nucleophilic attack of MeOH on the oxonium ion **I**–**III** in CH_4 at 760 Torr (Fig. 1).

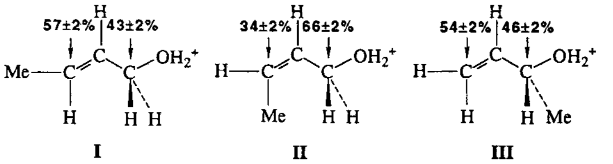


Fig. 1. Regioselectivity of the acid-catalyzed nucleophilic substitution on allylic oxonium ions **I**–**III** by MeOH in CH_4 at 760 Torr.

Analysis of Figure 1 reveals the following points:

i) In the gas phase, where solvation and ion-pairing effects are minimized, acid-promoted nucleophilic substitution by MeOH on allylic alcohols **1**–**3** proceeds by a concerted S_N2' mechanism, which competes efficiently with the classical S_N2 process. Positive recognition of the concerted S_N2' pathway was made possible in the gas phase by virtue of the specific radiolytic approach used, which allows generation of all ionic intermediates of Scheme 1 by independent procedures and investigation of their behavior towards the selected nucleophile YH in the same medium under exactly the same experimental conditions.

ii) In the presence of a neutral nucleophile, such as MeOH, the isomeric oxonium ions **I** and **III** in the gas phase exhibit almost equally extensive concerted S_N2' and S_N2 reactions, with the former (52–59 %) slightly prevailing over the latter (41–48 %). This demonstrates that, in the gas phase, both S_N2' and S_N2 substitutions are not appreciably hampered by the presence of a methyl substituent at the reaction center. It follows that the low S_N2'/S_N2 branching ratios commonly observed in solution with both unsubstituted allyl halides and crotyl halides[3–5] only in part reflect intrinsic structural and electronic factors, the major effect arising from solvation and ion-pairing phenomena;

iii) The role of intrinsic structural factors in nucleophilic substitution on allylic substrates emerges clearly from the comparison of the S_N2'/S_N2 branching ratios concerning isomeric oxonium ions **I** and **II**. In fact, the S_N2'/S_N2 branching ratio measured for the *cis* oxonium ion **II** (0.5–0.6) is markedly lower than that of the *trans* isomer **I** (1.2–1.4).

One reason for such a difference may be found in the enhanced steric strain in the *cis* isomer **II** caused by the presence of an *endo*-methyl group,[14] which may favor the distortive propensity of the π-component of **II** and, thus, the elongation of its remote C_β–C_α bond and the shortening of the adjacent C_γ–C_β one.[15] A consequence of this effect is the decreased activation enthalpy for the *endo* → *exo* stereomutation in the incipient allyl cation **VII** relative to the opposite process.[14] Another is the enhancement of the coefficient of the delocalized π* orbital at the C_α center of **II** and, therefore, of the probability of the S_N2 pathway in the S_N2'/S_N2 competition.

Appendix

In Equations (10–12), the yield ratios of the ethers **4**–**6** (e.g., **4**/(**4** + **5** + **6**)) reflect those of their ionic precursors immediately before neutralization by proton transfer to a suitable base (e.g., **IV**/(**IV** + **V** + **VI**)). These are estimated by deriving the stationary concentration of each individual intermediate relative to the combined concentration of all the intermediates (**IV** + **V** + **VI** = 1) from Scheme 1 from the balance between the channels forming it and those destroying it. Thus, by neglecting the upper-order terms, the overall extent of the channels forming **IV** is expressed by the sum: $a^{v}\alpha^{I}$ (the $\mathbf{I}_{gr}$ → **IV** contribution) $+a^{v\,VI}d_{IV}(1-\alpha^{I})$ (the $\mathbf{I}_{gr}$ → **VI** → **IV** contribution) $+b^{v}(1-\alpha^{III})$ (the $\mathbf{III}_{gr}$ → **IV** contribution) $+b^{v\,VI}d_{IV}\alpha^{III}$ (the $\mathbf{III}_{gr}$ → **VI** → **IV** contribution) $+c^{v\,VI}d_{IV}(1-\alpha^{II}+{}^{V}d_{VI}\alpha^{II})$ (the $\mathbf{II}_{gr}$ → **VI** → **IV** contribution) $+c^{v\,V}d_{IV}\alpha^{II}$ (the $\mathbf{II}_{gr}$ → **V** → **IV** contribution), which leads to $a^{v}[\alpha^{I}+{}^{VI}d_{IV}(1-\alpha^{I})]+b^{v}[(1-\alpha^{III})+{}^{VI}d_{IV}\alpha^{III}]+c^{v}[{}^{VI}d_{IV}(1-\alpha^{II}+{}^{V}d_{VI}\alpha^{II})+{}^{V}d_{IV}\alpha^{II}]$. The overall extent of the channels destroying **IV** is given by the sum ${}^{IV}d_{VI}\{a^{v}[\alpha^{I}+{}^{VI}d_{IV}(1-\alpha^{I})]+b^{v}[(1-\alpha^{III})+{}^{VI}d_{IV}\alpha^{III}]+c^{v}[{}^{VI}d_{IV}(1-\alpha^{II}+{}^{V}d_{VI}\alpha^{II})+{}^{V}d_{IV}\alpha^{II}]\}$ (the **IV** → **VI** contribution) $+{}^{IV}d_{V}\{a^{v}[\alpha^{I}+{}^{VI}d_{IV}(1-\alpha^{I})]+b^{v}[(1-\alpha^{III})+{}^{VI}d_{IV}\alpha^{III}]+c^{v}[{}^{VI}d_{IV}(1-\alpha^{II}+{}^{V}d_{VI}\alpha^{II})+{}^{V}d_{IV}\alpha^{II}]\}$ (the **IV** → **V** contribution), which leads to $({}^{IV}d_{VI}+{}^{IV}d_{V})\{a^{v}[\alpha^{I}+{}^{VI}d_{IV}(1-\alpha^{I})]+b^{v}[(1-\alpha^{III})+{}^{VI}d_{IV}\alpha^{III}]+c^{v}[{}^{VI}d_{IV}(1-\alpha^{II}+{}^{V}d_{VI}\alpha^{II})+{}^{V}d_{IV}\alpha^{II}]\}$. Therefore, the stationary concentration of **IV** immediately before neutralization by proton transfer to a suitable base can be expressed by: $(1-{}^{IV}d_{VI}-{}^{IV}d_{V})\{a^{v}[\alpha^{I}+{}^{VI}d_{IV}(1-\alpha^{I})]+b^{v}[(1-\alpha^{III})+{}^{VI}d_{IV}\alpha^{III}]+c^{v}[{}^{VI}d_{IV}(1-\alpha^{II}+{}^{V}d_{VI}\alpha^{II})+{}^{V}d_{IV}\alpha^{II}]\}$. In the same way, the overall extent of the channels forming **V** is represented by the sum $a^{v\,IV}d_{V}\alpha^{I}$ (the $\mathbf{I}_{gr}$ → **IV** → **V** contribution) $+a^{v\,IV}d_{V}{}^{VI}d_{IV}(1-\alpha^{I})$ (the $\mathbf{I}_{gr}$ → **VI** → **V** contribution) $+b^{v\,IV}d_{V}(1-\alpha^{III})$ (the $\mathbf{III}_{gr}$ → **IV** → **V** contribution) $+b^{v\,IV}d_{V}{}^{VI}d_{IV}\alpha^{III}$ (the $\mathbf{III}_{gr}$ → **VI** → **V** contribution) $+c^{v}\alpha^{II}$ (the $\mathbf{II}_{gr}$ → **V** contribution) $+c^{v\,IV}d_{V}{}^{VI}d_{IV}(1-\alpha^{II})$ (the $\mathbf{II}_{gr}$ → **VI** → **V** contribution), which leads to $c^{v}\alpha^{II}+{}^{IV}d_{V}\{a^{v}[\alpha^{I}+{}^{VI}d_{IV}(1-\alpha^{I})]+b^{v}[(1-\alpha^{III})+{}^{VI}d_{IV}\alpha^{III}]+c^{v}[{}^{VI}d_{IV}(1-\alpha^{II})]\}$. The overall extent of the channels destroying **V** is given by the sum ${}^{V}d_{VI}\{c^{v}\alpha^{II}+{}^{IV}d_{V}\{a^{v}[\alpha^{I}+{}^{VI}d_{IV}(1-\alpha^{I})]+b^{v}[(1-\alpha^{III})+{}^{VI}d_{IV}\alpha^{III}]+c^{v}[{}^{VI}d_{IV}(1-\alpha^{II})]\}\}$ (the **V** → **VI** contribution) $+{}^{V}d_{IV}\{c^{v}\alpha^{II}+{}^{IV}d_{V}\{a^{v}[\alpha^{I}+{}^{VI}d_{IV}(1-\alpha^{I})]+b^{v}[(1-\alpha^{III})+{}^{VI}d_{IV}\alpha^{III}]+c^{v}[{}^{VI}d_{IV}(1-\alpha^{II})]\}\}$ (the **V** → **IV** contribution), which leads to $({}^{V}d_{VI}+{}^{V}d_{IV})\{c^{v}\alpha^{II}+{}^{IV}d_{V}\{a^{v}[\alpha^{I}+{}^{VI}d_{IV}(1-\alpha^{I})]+b^{v}[(1-\alpha^{III})+{}^{VI}d_{IV}\alpha^{III}]+c^{v}[{}^{VI}d_{IV}(1-\alpha^{II})]\}\}$. Therefore, the stationary concentration of **V** immediately before neutralization by proton transfer to a suitable base can be expressed by: $(1-{}^{V}d_{VI}-{}^{V}d_{IV})\{c^{v}\alpha^{II}+{}^{IV}d_{V}\{a^{v}[\alpha^{I}+{}^{VI}d_{IV}(1-\alpha^{I})]+b^{v}[(1-\alpha^{III})+{}^{VI}d_{IV}\alpha^{III}]+c^{v}[{}^{VI}d_{IV}(1-\alpha^{II})]\}\}$. Finally, the overall extent of the channels forming **VI** is represented by the sum: $a^{v}(1-\alpha^{I})$ (the $\mathbf{I}_{gr}$ → **VI** contribution) $+a^{v}\alpha^{I}[{}^{IV}d_{VI}+{}^{IV}d_{V}{}^{V}d_{VI}]$ (the $\mathbf{I}_{gr}$ → **IV** → **VI** contribution) $+b^{v}\alpha^{III}$ (the $\mathbf{III}_{gr}$ → **VI** contribution) $+b^{v}(1-\alpha^{III})[{}^{IV}d_{VI}+{}^{IV}d_{V}{}^{V}d_{VI}]$ (the $\mathbf{III}_{gr}$ → **IV** → **VI** contribution) $+c^{v}(1-\alpha^{II})$ (the $\mathbf{II}_{gr}$ → **VI** contribution) $+c^{v}\alpha^{II}[{}^{V}d_{VI}+{}^{V}d_{IV}{}^{IV}d_{VI}]$ (the $\mathbf{II}_{gr}$ → **V** → **VI** contribution), which leads to $a^{v}[(1-\alpha^{I})+\alpha^{I}({}^{IV}d_{VI}+{}^{IV}d_{V}{}^{V}d_{VI})]+b^{v}[\alpha^{III}+(1-\alpha^{III})({}^{IV}d_{VI}+{}^{IV}d_{V}{}^{V}d_{VI})]+c^{v}[(1-\alpha^{II})+\alpha^{II}({}^{V}d_{VI}+{}^{V}d_{IV}{}^{IV}d_{VI})]$. The extent of the only channel destroying **VI** (**VI** → **IV**) is given by ${}^{VI}d_{IV}\{a^{v}[(1-\alpha^{I})+\alpha^{I}({}^{IV}d_{VI}+{}^{IV}d_{V}{}^{V}d_{VI})]+b^{v}[\alpha^{III}+(1-\alpha^{III})({}^{IV}d_{VI}+{}^{IV}d_{V}{}^{V}d_{VI})]+c^{v}[(1-\alpha^{II})+\alpha^{II}({}^{V}d_{VI}+{}^{V}d_{IV}{}^{IV}d_{VI})]\}$. Therefore, the stationary concentration of **VI** immediately before neutralization by proton transfer to a suitable base can be expressed by $(1-{}^{VI}d_{IV})\{a^{v}[(1-\alpha^{I})+\alpha^{I}({}^{IV}d_{VI}+{}^{IV}d_{V}{}^{V}d_{VI})]+b^{v}[\alpha^{III}+(1-\alpha^{III})({}^{IV}d_{VI}+{}^{IV}d_{V}{}^{V}d_{VI})]+c^{v}[(1-\alpha^{II})+\alpha^{II}({}^{V}d_{VI}+{}^{V}d_{IV}{}^{IV}d_{VI})]\}$.

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[9] See footnote [e] of Table 2.

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[11] This assumption is strongly supported by the lack of detectable amounts of **2** from protonation of **3** by $C_nH_5^+$ (n = 1, 2) in the presence of added H_2O (entry 3 of Table 1).

[12] In the absence of NMe_3, neutralization of the oxonium intermediates **IV**–**VI** may proceed by several pathways, including proton transfer to the substrate itself, to the walls of the reaction vessel, or to clusters of YH molecules either initially added to the gaseous mixture or formed from its radiolysis.

[13] It may be argued that the reported values of the ${}^{n}d_{m}$ terms are measured from irradiated systems containing CH_3F as the bulk gas (entries 16–21 of Table 1), while the reaction pattern of Scheme 1 deals with substitution reactions performed in CH_4 as the bulk gas. However, as mentioned in the Results section, the experiments demonstrate that the composition and absolute yields of isomeric ethers obtained in CH_3F, for example **5** and **6** from methylation of **1** by $(CH_3)_2F^+$, are fully comparable to those measured in CH_4 from the $C_nH_5^+$-protonation (n = 1, 2) of the ether analogue **4**. This indicates that the extent of **IV**–**VI** interconversion in the gas phase is not affected much either by the nature of the specific process used for generating the oxonium ions or by the nature of the bulk gas. Accordingly, it is reasonable that the ${}^{n}d_{m}$ terms measured in CH_3F can be extended safely to the systems with CH_4.

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