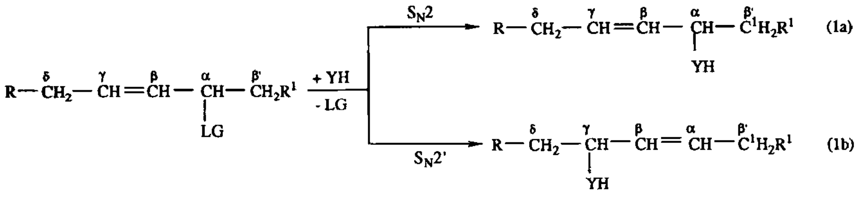
Regioselectivity in the Gas-Phase Nucleophilic Attack on O-Protonated 3-Methyl-2-cyclohexen-1-ol and 1-Methyl-2-cyclohexen-1-ol**

Emanuela Dezi, Antonietta Lombardozzi, Gabriele Renzi, Adriano Pizzabiocca, and Maurizio Speranza*

Abstract: Our radiolytic study of the occurrence in the gas phase of concerted S_N2' reactions on several open-chain allylic oxonium ions generated in the gas phase from the attack of gaseous GA^+ acids ($GA^+ = C_nH_5^+$ ($n = 1$, 2), $iC_3H_7^+$, and $(CH_3)_2F^+$) on suitable substrates is now continued with cyclic allylic alcohols, such as 3-methyl-2-cyclohexen-1-ol (**1**) and 1-methyl-2-cyclohexen-1-ol (**2**), with both MeOH and NMe_3 as neutral nucleophiles. With MeOH as the nucleophile, the substitution reaction exclusively takes place on **1** as the starting compound, whereas when the substrate is **2** it is accompanied by extensive elimination. With NMe_3, only the elimination reaction is observed in the same systems. The analysis of the isomeric distribution of the substitution and elimination products allows definition of the corresponding reaction patterns. As for open-chain oxonium ions, the nucleophilic attack on O-protonated **1** and **2** is preceded by significant intramolecular interconversion. Partial unimolecular dissociation of the same ionic intermediates also takes place. After careful evaluation of the extent of these side processes, it is demonstrated that the O-protonated **1** undergoes the concerted S_N2 process with MeOH almost exclusively ($\geq 99\%$). With O-protonated **2**, however, the concerted S_N2' pathway (84–95%) prevails over the classical S_N2 one (6–17%). Concomitant [1,2] (E2) and [1,4] elimination (E2′) pathways involve attack of the selected nucleophiles on the oxonium ions from **1** and **2**. Their relative extent (E2′/E2:1.78–1.96 (**1**); 1.43–1.70 (**2**)) appears only slightly dependent on the nature of the ionic substrate, the nucleophile (whether MeOH or NMe_3), and the leaving group (whether H_2O or MeOH). The effects of both intrinsic structural factors and experimental conditions in determining the S_N2'/S_N2 and E2′/E2 branchings in the selected oxonium ions is discussed and compared with related gas-phase data.

Keywords
cyclohexenols · elimination reactions · gas-phase chemistry · mechanistic studies · nucleophilic substitutions

Introduction



The first inquiry into the regioselectivity of gas-phase acid-catalyzed nucleophilic attack on some allylic compounds, that is, isomeric 2-buten-1-ols and 1-buten-3-ol, has been reported in the preceding paper in this issue.[1] In these systems, the gas-phase nucleophilic substitution proceeds by a concerted S_N2' pathway [Eq. (1 b)] in competition with the classical S_N2 one [Eq. (1 a)]. Their extent is insensitive to the presence of a methyl substituent at the reaction center, as demonstrated by the comparable efficiency of the S_N2' and the S_N2 paths in O-protonated *trans*-2-buten-1-ol ($57 \pm 2\%$ S_N2'; $43 \pm 2\%$ S_N2) and O-protonated 1-buten-3-ol ($54 \pm 2\%$ S_N2'; $46 \pm 2\%$ S_N2) by MeOH. In contrast, structural effects on the shape and the energy of the π* antibonding orbital of the O-protonated allylic substrate may appreciably affect the regiochemistry of the gas-phase nucleophilic substitution. Indeed, in O-protonated *cis*-2-buten-1-ol, where structural (and, thus, orbital) distortion is more pronounced than in the *trans* isomer, the concerted S_N2 mechanism ($66 \pm 2\%$) prevails over the S_N2' one ($34 \pm 2\%$). In general, the substitution reactions are accompanied in these systems by less efficient elimination processes (up to 19% relative to substitution), especially when a powerful base, such as NMe_3, is added to the reaction mixture. The only elimination product from isomeric 2-buten-1-ols and 1-buten-3-ol is obviously 1,3-butadiene, whose formation in-

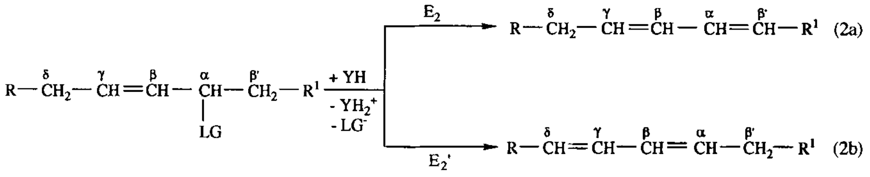
---

[*] Prof. M. Speranza
Dipartimento di Studi di Chimica e Tecnologia
delle Sostanze Biologicamente Attive
Università degli Studi di Roma "La Sapienza"
P.le A. Moro 5, 00185 Rome (Italy)
Fax: Int. code + (6)499-13888
e-mail: chimfar@itcaspur.caspur

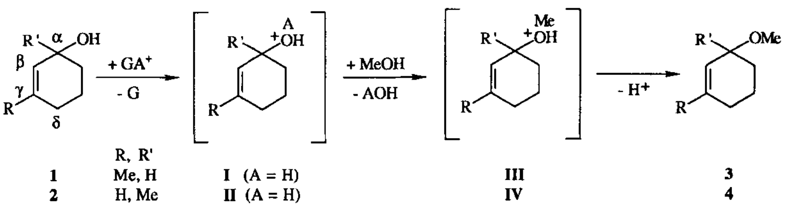
Dr. E. Dezi, Dr. A. Lombardozzi, Prof. G. Renzi, Prof. A. Pizzabiocca
Dipartimento di Scienze Chimiche, Università di Camerino
Fax: Int. code + (737)40321
Via S. Agostino 1, 62032 Camerino (MC) (Italy)

[**] Gas-Phase Acid-Induced Nucleophilic Displacement Reactions, Part 11. Part 10: G. Renzi, A. Lombardozzi, E. Dezi, A. Pizzabiocca, M. Speranza, preceding paper in this issue.

volves necessarily a [1,4] mechanism in the first two substrates (a E2′ process) [Eq. (2a)] and a [1,2] one in the latter (a E2 process) [Eq. (2b)].

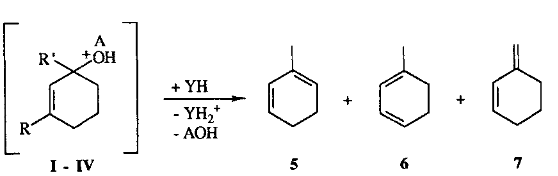


To gather more evidence about the concerted S_N2' reaction in the gas phase and to delineate the precise circumstances influencing its occurrence in competition with the classical bimolecular S_N2 and unimolecular S_N1/S_N1' pathways, the investigation is now extended to the determination of the regiochemistry of gas-phase acid-induced nucleophilic substitution by YH = MeOH on methylcyclohexenols **1** and **2**, wherein the C_α and C_γ substitution centers present one or two alkyl substituents [Eq. (3)]. From a comparison with the results of the preceding paper, it is hoped to ascertain whether the increased number of alkyl groups at the reaction site affects S_N2'/S_N2 branching in bimolecular substitution and its extent relative to conceivable unimolecular processes.



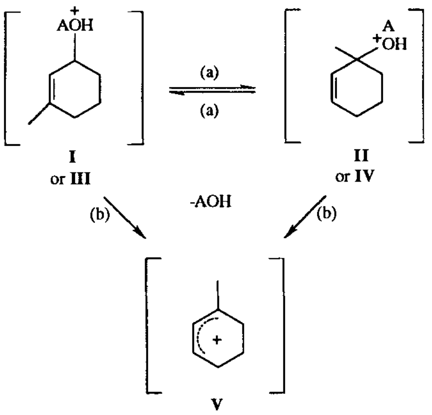
(3)

A further problem tackled in the present investigation is the extent and the mechanism of the gas-phase elimination reaction accompanying acid-induced nucleophilic substitution on methylcyclohexenols **1** and **2**. In particular, the study is addressed to the evaluation of the intrinsic structural factors determining the occurrence and the regiochemistry of the acid-induced elimination process (4) in oxonium ions **I** and **II** in the gas phase, where solvation and ion-pairing effects normally complicating similar processes in solution are excluded.[2]



(4)

The same experimental procedure illustrated in the previous study is adopted here.[1] It is based upon preparation of stationary concentrations of gaseous acids ($GA^+ = C_nH_5^+$ (n = 1, 2) and $(CH_3)_2F^+$) from the γ-radiolysis of the corresponding neutral precursors (CH_4 and CH_3F, respectively). Attack of GA^+ ions on the oxygen atom of the allylic alcohols **1** and **2** is expected to generate the corresponding oxonium ions **I** and **II**, which may undergo several gas-phase processes, including isomerization [Eq. (5a)] and unimolecular dissociation [Eq. (5b)], as well as attack by the present nucleophiles (YH = MeOH or NMe_3) [Eqs. (3), (4)]. Neutralization of the ensuing intermediates by proton transfer to a suitable acceptor yields the corresponding neutral products **3**–**7**, whose isomeric distribution reflects that of their ionic precursors and, thus, may allow assessment of the regiochemistry of both the substitution [Eq. (3)] and elimination pathways [Eq. (4)].



(5)

Experimental Section

Materials: Methane, methyl fluoride, oxygen, and trimethylamine were purchased from Matheson, with a stated purity of at least 99.9 mol%, and were used without further purification. 3-Methyl-2-cyclohexen-1-ol (**1**) was obtained as a research-grade chemical from Aldrich. 1-Methyl-2-cyclohexen-1-ol (**2**) [3], 3-methoxy-1-methyl-1-cyclohexene (**3**) [4], 3-methoxy-3-methyl-1-cyclohexene (**4**) [4], 2-methyl-1,3-cyclohexadiene (**5**) [5], 1-methyl-1,3-cyclohexadiene (**6**) [6], and 3-methylenecyclohexene (**7**) [7] were prepared according to established procedures. The crude products from the syntheses 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-DCMS; the operation was repeated until analytical GLC of the purified samples failed to detect traces of unwanted impurities. The final purity exceeded 99.95%. The identity of the alcohols **1** and **2**, ethers **3** and **4**, and dienes **5**–**7** was confirmed by NMR and mass spectrometry.

Procedure: The gaseous samples were prepared by the same procedure illustrated in the preceding paper [1]. 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 irradiated mixtures were analyzed by GLC with a Hewlett–Packard 5890 series II gas chromatograph equipped with a flame ionization detector. The products were identified by comparison of their retention volumes with those of authentic standards on the following columns: i) a 30 m long, 0.32 mm i.d. Supelcowax 10 fused silica capillary column, operated at temperatures ranging from 30 to 180 °C, 5 °C min^{-1}; ii) a 50 m long, 0.32 mm i.d. crosslinked methyl silicone HP ultra-performance capillary column, operated at temperatures ranging from 25 to 160 °C, 5 °C min^{-1}. The identity of the products was further confirmed by GLC-MS with a Hewlett–Packard 5971 A mass-selective GLC detector. The yields of the products were deduced from the areas of the corresponding eluted peaks by the internal standard calibration method.

Results

Gas-phase attack of GA^+ acids on allylic alcohols **1** and **2** in the presence of the nucleophile YH = NMe_3 invariably yielded the isomeric dienes **5** and **6**, in proportions depending upon the specific alcohol used. No detectable formation of the exocyclic isomer **7** was observed (absolute yield <0.2% under all conditions). In the presence of YH = MeOH, the gas-phase GA^+ attack on **1** and **2** led to formation of isomeric allylic ethers **3** and **4**. With **2** only, formation of these products was accompanied by minor quantities of isomeric dienes **5** and **6**.

Both the experimental conditions and the corresponding substitution and elimination products are presented in detail in Table 1. The absolute yields of the radiolytic products are given

Table 1. Product yields from the gas-phase attack of GA^+ acids on allylic alcohols **1** and **2**.

Entry	System composition [a]				Product yields, $G_{(M)}$ (%) [b]				Total absolute
No.	Substrate (p/Torr)	Bulk gas (p/Torr)	YH (p/Torr)	GA^+	**3**	**4**	**5**	**6**	yield (%) [c]
1	**1** (0.5)	CH_4 (760)	NMe_3 (2)	$C_nH_5^+$			0.29 (63)	0.17 (37)	16
2	**1** (0.5)	CH_4 (760)	NMe_3 (5)	$C_nH_5^+$			0.16 (64)	0.09 (36)	9
3	**1** (0.5)	CH_4 (100)	NMe_3 (2)	$C_nH_5^+$			0.53 (62)	0.32 (38)	30
4	**1** (0.5)	CH_4 (100)	NMe_3 (5)	$C_nH_5^+$			0.25 (62)	0.15 (35)	14
5	**1** (0.5)	CH_4 (760)	MeOH (2)	$C_nH_5^+$	0.36 (98)	0.00_6 (2)	–	–	13
6	**1** (0.5)	CH_4 (760)	MeOH (5)	$C_nH_5^+$	0.41 (98)	0.00_7 (2)	–	–	15
7	**1** (0.5)	CH_4 (100)	MeOH (2)	$C_nH_5^+$	1.10 (99)	0.00_8 (1)	–	–	40
8	**1** (0.5)	CH_4 (100)	MeOH (5)	$C_nH_5^+$	1.62 (99)	0.00_8 (1)	–	–	58
9	**1** (0.5)	CH_4 (760)	MeOH (5) [d]	$C_nH_5^+$	0.03 (98)	0.00_1 (2)	–	–	1
10	**1** (0.5)	CH_3F (760)	–	Me_2F^+	0.15 (6)	0.00_1 (0.04)	1.72 (66)	0.74 (28)	77
11	**1** (0.5)	CH_3F (760)	NMe_3 (2)	Me_2F^+	0.10 (18)	0.00_1 (0.2)	0.28 (52)	0.16 (30)	16
12	**1** (0.5)	CH_3F (760)	NMe_3 (5)	Me_2F^+	0.07 (29)	0.00_2 (0.8)	0.11 (45)	0.06 (25)	7
13	**1** (0.5)	CH_3F (100)	NMe_3 (2)	Me_2F^+	0.02 (3)	0.00_2 (0.2)	0.47 (60)	0.29 (37)	23
14	**1** (0.5)	CH_3F (100)	NMe_3 (5)	Me_2F^+	0.01 (3)	0.00_2 (0.6)	0.21 (61)	0.12 (35)	10
15	**2** (0.5)	CH_4 (760)	NMe_3 (2)	$C_nH_5^+$			0.20 (39)	0.31 (61)	18
16	**2** (0.5)	CH_4 (760)	NMe_3 (5)	$C_nH_5^+$			0.09 (39)	0.14 (61)	8
17	**2** (0.5)	CH_4 (100)	NMe_3 (2)	$C_nH_5^+$			0.43 (47)	0.49 (53)	33
18	**2** (0.5)	CH_4 (100)	NMe_3 (5)	$C_nH_5^+$			0.15 (45)	0.18 (55)	12
19	**2** (0.5)	CH_4 (760)	MeOH (2)	$C_nH_5^+$	0.35 (40)	0.06 (7)	0.18 (20)	0.29 (33)	31
20	**2** (0.5)	CH_4 (760)	MeOH (5)	$C_nH_5^+$	0.41 (43)	0.08 (8)	0.16 (17)	0.31 (32)	34
21	**2** (0.5)	CH_4 (100)	MeOH (2)	$C_nH_5^+$	1.10 (57)	0.09 (5)	0.31 (16)	0.42 (22)	69
22	**2** (0.5)	CH_4 (100)	MeOH (5)	$C_nH_5^+$	1.61 (66)	0.09 (4)	0.34 (14)	0.39 (16)	87
23	**2** (0.5)	CH_4 (760)	MeOH (5) [d]	$C_nH_5^+$	0.06 (22)	0.00_7 (3)	0.08 (30)	0.12 (45)	9
24	**2** (0.5)	CH_3F (760)	–	Me_2F^+	0.03 (1)	0.23 (8)	0.98 (35)	1.56 (56)	82
25	**2** (0.5)	CH_3F (760)	NMe_3 (2)	Me_2F^+	0.00_8 (2)	0.12 (20)	0.17 (29)	0.29 (49)	17
26	**2** (0.5)	CH_3F (760)	NMe_3 (5)	Me_2F^+	0.00_7 (2)	0.08 (22)	0.10 (28)	0.17 (48)	10
27	**2** (0.5)	CH_3F (100)	NMe_3 (2)	Me_2F^+	0.00_9 (1)	0.10 (12)	0.28 (35)	0.41 (51)	23
28	**2** (0.5)	CH_3F (100)	NMe_3 (5)	Me_2F^+	0.00_2 (0.5)	0.07 (17)	0.14 (34)	0.20 (48)	12

[a] Racemic mixtures of 1 and 2 were used. O_2: 4 Torr. Radiation dose 2×10^4 Gy (dose rate: 1×10^4 Gy h^{-1}). [b] $G_{(M)}$ as the number of molecules M produced per 100 eV of absorbed energy. Percentage values as the ratios between the $G_{(M)}$ of each product and the combined $G_{(M)}$ values of all products identified. The bars denote that the absolute yield of the corresponding products is below the detection limit, about 0.2%. Each value is the average of several determinations, with an uncertainty level around 5%. [c] Absolute yields estimated from the percentage ratio between the combined $G_{(M)}$ values of products and the literature $G_{(GA^+)}$ values (ref. [8]). [d] 3 Torr of NMe_3 added to the gaseous mixture.

as the percentage ratio of their combined $G_{(M)}$ values, expressed as the number of molecules M produced per 100 eV of energy absorbed by the gaseous mixture, to the $G_{(GA^+)}$ of their acid precursors.[8] The product yields and distributions were measured under different experimental conditions at a constant temperature of 37.5 °C and for a total dose of 2×10^4 Gy (dose rate: 1×10^4 Gy h^{-1}). The ionic origin of the radiolytic products was ensured by the presence in all mixtures of O_2 (4 Torr), an effective radical scavenger, and by the pronounced decrease of the absolute yield of the products (73–93%) observed on introduction into the mixture of approximately 4 mol% of NMe_3, an effective interceptor of all cationic species, including the GA^+ acids.

Concerning the elimination products **5** and **6**, entries 1–4 point to the predominance of diene **5** (62–64%) from $C_nH_5^+$-protonation (n = 1, 2) of alcohol **1** in the presence of NMe_3, whilst diene **6** was preferentially formed from alcohol **2** under the same conditions (53–61%) (entries 15–18). The same pattern was observed for $(CH_3)_2F^+$ as the gaseous acid instead of $C_nH_5^+$ (**5**:**6** = 1.2–1.9 from **1** (entries 11–14); 0.6–0.7 from **2** (entries 25–28)). When NMe_3 was replaced by the same concentration of MeOH, $C_nH_5^+$-protonation of alcohol **2** (entries 19–23) yielded dienes **5** and **6** in proportions (0.5 to 0.9) close to those measured in the experiments with YH = NMe_3 (entries 15–18 and 25–28).

Concerning the substitution products **3** and **4**, entries 5–9 indicate that $C_nH_5^+$-protonation (n = 1, 2) of **1** in the presence of variable concentrations of MeOH yielded almost exclusively ether **3** (>98%). Predominance of this product was also observed after $C_nH_5^+$-protonation of **2** in the presence of MeOH (entries 19–23), although attenuated by the formation of appreciable yields of its isomer **4** (5–16% relative to **3**).

Ethers **3** and **4** were also generated from direct attack of $(CH_3)_2F^+$ ions on allylic alcohols **1** and **2** (entries 10–14 and 24–28). Here, the ether derived directly from the starting alcohol formed predominantly, together with minor amounts of the other isomer in yields that increased when the bulk gas pressure was decreased (up to 17% of **4** from **1** and 8% of **3** from **2**).

To ascertain whether ionic intermediates other than **I** and **II** could be responsible of the formation of the radiolytic products of Table 1, free allylic cations such as **V** [Eq. (5)] were generated in the gas phase by $C_nH_5^+$-protonation (n = 1, 2) of **5**–**7** in exactly the same reaction media employed in the experiments in Table 1. The behavior of the carbocations thus formed towards the nucleophile YH = NMe_3 or MeOH was examined (the relevant results are given in Table 2). They were found to transfer protons to NMe_3 readily. Deprotonation of the allylic ions from **5** yielded essentially diene **6** (81–92%) together with minor amounts of the exocyclic diene **7** (8–19%) (entries 9–12 of Table 2). The same yields of **7** (9–13%) accompanied the formation of diene **5** (87–91%) from NMe_3-deprotonation of the allylic cations from **6** (entries 5–8 of Table 2). Finally, both dienes **5** and **6** were generated in comparable yields (46–57% of **5**; 43–54% of **6**) from proton transfer from the allylic ions from **7** to NMe_3 (entries 1–4 of Table 2). Combination of these results reveals a distribution of isomeric products **5**–**7** (44–55% of **5**; 42–51% of **6**; 3–6% of **7**) that is relatively unaffected by the nature of the starting substrate. A most plausible reason for

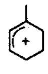
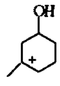
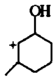
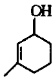
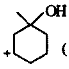
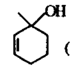
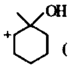
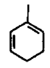
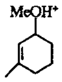
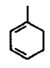
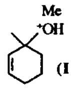
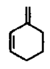
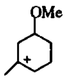
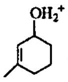
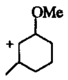
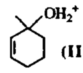
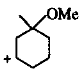
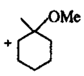
Table 2. Product yields from the gas-phase attack of $C_nH_5^+$ (n = 1, 2) acids on dienes **5**–**7**.

Entry No.	System composition [a] Substrate (p/Torr)	pCH$_4$/ Torr	YH (p/Torr)	Product yields, $G_{(M)}$ (%) [b] **3**	**4**	**5**	**6**	**7**	Total absolute yield (%) [c]
1	**7** (0.5)	760	NMe$_3$ (2)			0.06_5 (46)	0.07_5 (54)		5
2	**7** (0.5)	760	NMe$_3$ (5)			0.03_7 (48)	0.04_0 (52)		3
3	**7** (0.5)	100	NMe$_3$ (2)			0.065 (56)	0.50 (44)		41
4	**7** (0.4)	100	NMe$_3$ (5)			0.29 (57)	0.22 (43)		18
5	**6** (0.5)	760	NMe$_3$ (2)			0.21 (91)		0.01_9 (9)	8
6	**6** (0.4)	760	NMe$_3$ (5)			0.11_6 (91)		0.01_9 (9)	4
7	**6** (0.4)	100	NMe$_3$ (2)			0.52 (87)		0.08 (13)	21
8	**6** (0.5)	100	NMe$_3$ (5)			0.30 (90)		0.03_5 (10)	12
9	**5** (0.5)	760	NMe$_3$ (2)				0.24 (92)	0.02_2 (8)	9
10	**5** (0.5)	760	NMe$_3$ (5)				0.10_6 (90)	0.01_2 (10)	4
11	**5** (0.5)	100	NMe$_3$ (2)				0.48 (84)	0.09 (16)	20
12	**5** (0.5)	100	NMe$_3$ (5)				0.23 (81)	0.05_6 (19)	10
13	**5** (0.5)	760	MeOH (2)	0.35 (96)	0.01_5 (4)		–	–	13
14	**5** (0.5)	760	MeOH (5)	0.26 (93)	0.02_0 (7)		–	–	10
15	**5** (0.5)	100	MeOH (2)	1.57 (96)	0.06 (4)		–	–	58
16	**5** (0.5)	100	MeOH (5)	1.35 (94)	0.08 (6)		–	–	51
17	**5** (0.5)	760	MeOH (5) [d]	0.06_9 (89)	0.01_9 (11)		–	–	3

[a] See footnote [a] of Table 1. [b] See footnote [b] of Table 1. [c] See footnote [c] of Table 1. [d] See footnote [d] of Table 1.

this constancy can be found in the generation of a unique cyclohexenyl cation structure (**V**) from the gas-phase $C_nH_5^+$-protonation of **5**–**7**, although alternative explanations, such as that involving the fortuitous occurrence of the same isomeric distribution of different cyclohexenyl ions from **5**–**7**, though unlikely, cannot be excluded a priori. Within the first hypothesis, the results of entries 13–16 of Table 2 refer to the isomeric distribution of ethers **3** and **4** from the addition of MeOH to the cyclohexenyl cation **V**. Accordingly, the formation of ether **3** by far predominates over that of its isomer **4** under all conditions (**3**:**4** = 13–26). No detectable formation of dienes **6** and **7** was observed in these systems.

Table 3. Thermochemical data (kcal mol^{-1}) (estimated values in italics).

Species	ΔH$_f^\circ$	Source	Species	ΔH$_f^\circ$	Source
CH$_4$	-17.8	[a]			
C$_2$H$_4$	12.5	[a]	 (**V**)	*179*	[d]
CH$_3$F	-59	[a]			
CH$_5^+$	216	[a]	 (**VIII**)	*120*	[e]
C$_2$H$_5^+$	215.6	[a]			
(CH$_3$)$_2$F$^+$	147	[a]	 (**VI**)	*139*	[e]
 (**1**)	*-50*	[b]	 (**IX**)	*136*	[e]
 (**2**)	*-49*	[b]	 (**VII**)	*139*	[e]
 (**5**)	*17*	[b]	 (**III**)	*113*	[f]
 (**6**)	*17*	[b]	 (**IV**)	*107*	[f]
 (**7**)	*17*	[b]		*124*	[e]
 (**I**)	*119*	[c]		*143*	[e]
 (**II**)	*113*	[c]		*140*	[e]
				*140*	[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 the group additivity method (S. W. Benson, *Thermochemical Kinetics*, Wiley, New York, **1968**. [c] Estimated from the proton affinity (PA) limits of secondary and tertiary alcohols (197 and 204 kcal mol^{-1}, respectively) (J. Long, B. Munson, *J. Am. Chem. Soc.* **1973**, *95*, 2427). [d] Estimated from the proton affinity of **5** (ca. 204 kcal mol^{-1}) calculated by correcting the PA of 1,3-cyclohexadiene (200 kcal mol^{-1}) for the contribution of the methyl group; ΔPA = PA (3-methyl-1,3-pentadiene) – PA (1,3-pentadiene) = ca. 4 kcal mol^{-1} (footnote [a]). [e] Estimated by the method illustrated in R. D. Bowen, D. H. Williams, *J. Am. Chem. Soc.* **1977**, *99*, 6822. [f] Estimated by ΔPA = PA (methyl ether) – PA (alcohol) = 10 kcal mol^{-1} (R. D. Bowen, D. H. Williams, *J. Am. Chem. Soc.* **1978**, *100*, 7454; R. D. Bowen, D. H. Williams, G. Hvistendahl, J. R. Kalman, *Org. Mass Spectrom.* **1978**, *13*, 721). The heats of formation of neutral methyl ethers have been calculated as in footnote [b].

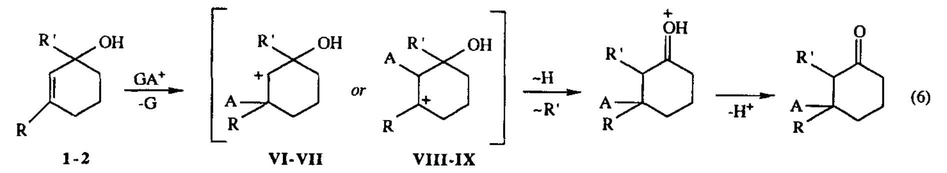
Discussion

The reaction pattern: Owing to the very limited concentration of the substrates **1** and **2** (< 0.5 mol%) and of the nucleophile(s) YH (< 4.5 mol%) in the gaseous mixtures, all the ionic species generated from attack of the GA$^+$ acids on the allylic alcohols underwent many unreactive collisions with the bulk gas prior to reaction with the neutral species present. Thus rapid thermal equilibration of the ionic intermediates occurred by removal of their excess energy arising from the exothermicity of their formation process. The thermochemistry of Equations (3)–(5) cannot be precisely evaluated because of the lack of experimental thermochemical data for the ionic intermediates **I**–**V** as well as for the neutrals **1**–**7**. However, approximate values of the enthalpies of reactions 3–5 can be inferred from the thermochemical data reported in Table 3, obtained by the widely recognized estimation procedures cited in footnotes [b–f] of the Table. From the relevant ΔH° values (Table 4), formation of the oxonium ions **I** and **II** by gas-phase $C_nH_5^+$-protonation (n = 1, 2) of alcohols **1** and **2** [first step of Eq. (3)] is markedly exothermic ($-\Delta H^\circ$ = 34–72 kcal mol^{-1}), as well as formation of oxonium ions **III** and **IV** by gas-phase methylation of the same substrates with $(CH_3)_2F^+$ ($-\Delta H^\circ$ = 43–50 kcal mol^{-1}). Proton transfer from $C_nH_5^+$ to the π bond of alcohols **1** and **2** (first step of Eq. (6)) is exothermic as well ($-\Delta H^\circ$ = 1–64 kcal mol^{-1}). In spite of this, GA$^+$ attack at the π bond of **1** and **2** is by far kinetically overwhelmed by attack at the O atom, as demonstrated by the complete absence of carbonylic products such as 2- and 3-methylcyclohexanone among the radiolytic products. Their O-protonated precursors would in fact repre-

Table 4. Reaction enthalpies (kcal mol^{-1}).

Equation	Neutral Reactant	Ionic Reactant	Products	ΔH°
3	**1**	CH_5^+	**I**	−65
	1	$C_2H_5^+$	**I**	−34
	1	$(CH_3)_2F^+$	**III**	−43
	2	CH_5^+	**II**	−72
	2	$C_2H_5^+$	**II**	−41
	2	$(CH_3)_2F^+$	**IV**	−50
6	**1**	CH_5^+	**VI**	−45
	1	$C_2H_5^+$	**VI**	−14
	2	CH_5^+	**VII**	−46
	2	$C_2H_5^+$	**VII**	−15
	1	CH_5^+	**VIII**	−64
	1	$C_2H_5^+$	**VIII**	−33
	2	CH_5^+	**IX**	−49
	2	$C_2H_5^+$	**IX**	−18
5b		**I**	**V** + H_2O	+2
		II	**V** + H_2O	+8
		III	**V** + MeOH	+12
		IV	**V** + MeOH	+18
5a		**I** (or **III**)	**II** (or **IV**)	−6
		II (or **IV**)	**I** (or **III**)	+6
3	MeOH	**I**	**III**	−16
	MeOH	**I**	**IV**	−22
	MeOH	**II**	**IV**	−16
	MeOH	**II**	**III**	−10
4	NMe_3	**I**	**5–7**	−19
	NMe_3	**II**	**5–7**	−13
	NMe_3	**III**	**5–7**	−3
	NMe_3	**IV**	**5–7**	+3
	MeOH	**I**	**5–7**	+24
	MeOH	**II**	**5–7**	+30
	MeOH	**III**	**5–7**	+40
	MeOH	**IV**	**5–7**	+46

sent the more stable structures to which carbenium ions **VI–IX** would rapidly isomerize if formed [Eq. (6)].[9]



(6)

The estimated thermochemical data of Table 4 indicate that the enthalpy of unimolecular dissociation of the oxonium ion to AOH and the allylic cation **V** [Eq. (5b)] varies significantly with the nature of the A moiety, whether H or Me, and with the structure of the oxonium ion. Thus, while unimolecular dissociation of the oxonium intermediates **III** and **IV** needs 12 and 18 kcal mol^{-1}, respectively, cleavage of the C–O bond in the O-protonated analogues requires only 2 (**I**) and 8 kcal mol^{-1} (**II**). Taking into account the favorable entropic factors, unimolecular fragmentation of oxonium intermediates **I–IV** to **V** and AOH cannot be excluded (especially for **I**), unless involving a significant activation barrier.[10] Besides fragmentation, excited oxonium ions **I–II** and **III–IV** may in principle undergo structural interconversion ($\Delta H^\circ = \pm 6$ kcal mol^{-1}) (Table 5) [Eq. (5a)].

Irrespective of the specific reaction site, whether the C_α or the C_γ of the oxonium ions **I** and **II**, nucleophilic displacement of AOH by MeOH [second step of Eq. (3)] is thermochemically allowed ($-\Delta H^\circ = 10$–22 kcal mol^{-1}) (Table 4). The NMe_3-induced elimination reactions (4) (YH = NMe_3) appear exothermic as well ($-\Delta H^\circ = 3$–19 kcal mol^{-1}), with the possible exception of that involving the oxonium ion **IV** ($\Delta H^\circ = 3$ kcal mol^{-1}). Nevertheless, taking into account the favorable entropic factors, the elimination reactions (4) (YH = NMe_3), including that involving **IV**, can be regarded as thermodynamically accessible. Another factor allowing occurrence of elimination reaction (4) may arise from conceivable clustering of the YH_2^+ fragment by the other elimination moieties (either the diene and/or the AOH leaving group) before its neutralization. In this way, the enthalpy of the NMe_3-induced elimination reactions (4) (YH = NMe_3), including that involving **IV**, may be lowered by several tens of kcalories per mol. The same considerations apply to the elimination reactions promoted by the attack of MeOH on the oxonium ions **I–IV** [Eq. (4); YH = MeOH]. Here, if the pertinent elimination enthalpies of Table 4 ($\Delta H^\circ = 24$ (**I**), 30 kcal mol^{-1} (**II**)) are corrected by the contribution of the energy released by hydrogen bonding between H_2O and $MeOH_2^+$ (ca. 30 kcal mol^{-1}), the processes are thermodynamically allowed only for **I** and **II** ($\Delta H^\circ =$ ca. -6 (**I**), 0 kcal mol^{-1} (**II**)).[11] Even considering clustering between MeOH and $MeOH_2^+$, MeOH-induced elimination on oxonium ions **III** and **IV** is thermochemically forbidden ($\Delta H^\circ =$ ca. 10–16 kcal mol^{-1}, respectively).

On purely thermochemical grounds, the substitution and elimination products of Table 1 may arise from a variety of conceivable reaction pathways. These may involve attack of the nucleophile(s) YH (MeOH and/or NMe_3), present in the gaseous mixture, on the oxonium ion (either **I** or **II**) directly obtained from O-pro-

Table 5. Maximum relative extent and regioselectivity of gas-phase elimination and substitution reactions on oxonium ions **I** and **II**.

Elimination (Scheme 1) CH_4 (Torr)	NMe_3 (Torr)	δ^{V}	$a^{I}_{\text{elim max}}$	$b^{I}_{\text{elim max}}$	δ^{I}_{min}	δ^{I}_{max}	δ^{I}_{av}	$c^{II}_{\text{elim max}}$	$b^{II}_{\text{elim max}}$	δ^{II}
100	2	0.435	0.139	0.271	0.623	0.658	0.640 ± 0.018	0.261	0.384	0.594
760	2	0.536	0.139	0.271	0.630	0.692	0.661 ± 0.031	0.076	0.236	0.630
100	5	0.431	0.139	0.135	0.625	0.660	0.642 ± 0.018	0.183	0.267	0.588
760	5	0.519	0.139	0.135	0.640	0.684	0.662 ± 0.022	0.072	0.189	0.630

Substitution (Scheme 2) CH_4 (Torr)	MeOH (Torr)	α^{V}	$a^{I}_{\text{subs max}}$	$b^{I}_{\text{subs max}}$	α^{I}_{min}	α^{I}_{max}	α^{I}_{av}	$c^{II}_{\text{subs max}}$	$b^{II}_{\text{subs max}}$	α^{II}_{min}	α^{II}_{max}	α^{II}_{av}
100	2	0.038	0.092	0.184	0.993	1.000	0.996 ± 0.004	0.177	0.268	0.076	0.091	0.083 ± 0.008
760	2	0.041	0.092	0.184	0.984	0.997	0.990 ± 0.007	0.050	0.159	0.146	0.166	0.156 ± 0.010
100	5	0.056	0.092	0.089	0.995	1.000	0.997 ± 0.003	0.121	0.181	0.053	0.060	0.056 ± 0.004
760	5	0.071	0.092	0.089	0.983	0.998	0.990 ± 0.008	0.047	0.126	0.163	0.176	0.169 ± 0.007

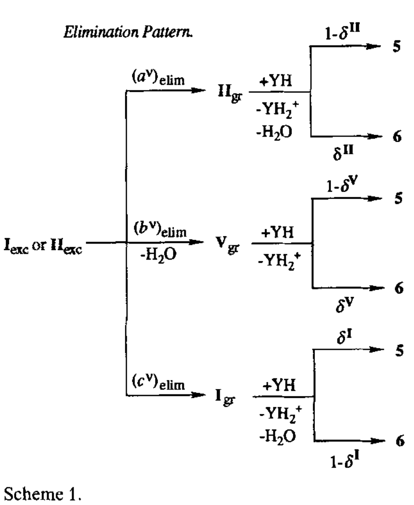
0947-6539/96/0203-0327 $ 15.00+.25/0

tonation of the starting cyclohexenol. The YH attack may be preceded by partial isomerization of the starting oxonium ion (**I**↔**II**) as well as its fragmentation to allylic ion **V**. Both the isomers **I** and **II**, as well as the allylic ion **V**, may react with YH, yielding the same substitution (the oxonium ions **III** and **IV**) and elimination products (the dienes **5** and **6**). In principle, the substituted intermediates (either **III** or **IV**) may also undergo partial isomerization (**III**↔**IV**) and fragmentation to allylic ion **V** prior to neutralization.

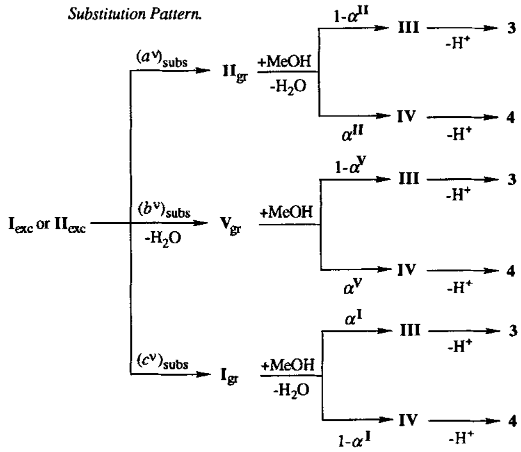
Among the above possibilities, those involving extensive **III**↔**IV** interconversion as well as unimolecular dissociation of **IV** to **V** and MeOH can be safely excluded on the grounds of the following considerations. According to entries 13–16 of Table 2, the allylic ion **V** added to MeOH yielding predominantly ether **3** (93–96%), together with very minor amounts of its isomer **4** (4–7%). A similar product pattern was observed in methylation of **1** by $(CH_3)_2F^+$ (**3** (99%), **4** (1%); entry 10 of Table 1). In contrast, methylation of **2** by $(CH_3)_2F^+$ yielded predominantly ether **4** (88%), together with minor amounts of **3** (12%) (entry 24 of Table 1). This demonstrates the reluctance of oxonium ions **III** and **IV** to interconvert and of isomer **IV** to fragment to **V** under the conditions used.

Once both **IV** → **III** isomerization and **IV** → **V** fragmentation are excluded, the formation of ether **3** from $C_nH_5^+$-induced substitution (n = 1, 2) on **2** by MeOH (entries 19–23 of Table 1) can be accounted for by either fast **II** → **I** isomerization before nucleophilic attack of MeOH or, alternatively, predominant attack of the nucleophile at the C_γ center of **II** (a S_N2' process). Concomitant abundant formation of dienes **5** and **6** (30–53%), which were instead completely absent from $C_nH_5^+$-protonation of **1** in the presence of MeOH (entries 5–9 of Table 1), leads us to rule out the first hypothesis in favor of the latter. Even admitting the release of a $MeOH_2^+$–MeOH proton-bound dimer, MeOH-induced elimination on **III** is endothermic (ΔH° = 10 kcal mol^{-1}) and, thus, insignificant under any conditions (entries 5–9 of Table 1). Hence, occurrence under the similar conditions of MeOH-induced elimination on **IV**, which is even more endothermic (ΔH° = 16 kcal mol^{-1}), can be excluded a fortiori. It follows that the formation of dienes **5** and **6** in entries 19–23 of Table 1 must arise predominantly, if not exclusively, from MeOH-induced elimination of H_2O from the oxonium ion **II**, probably permitted by the release of a $MeOH_2^+$–H_2O cluster from the elimination product.

The above considerations point to the general reaction patterns for the gas-phase $C_nH_5^+$-induced elimination and substitution reactions on allylic alcohols **1** and **2** by YH (= NMe_3, MeOH) as outlined in Schemes 1 and 2.



Scheme 1.



Scheme 2.

In analogy with the indications given in the preceding paper,[1] the reaction networks are characterized by the partial isomerization and fragmentation of the O-protonated starting substrate (first step of the networks of Schemes 1 and 2), yielding a variable distribution of the thermally equilibrated oxonium ions **I** and **II** as well as the free allylic cation **V**. The terms a^v, b^v, and c^v (with $a^v + b^v + c^v = 1$) appearing in the first step of Schemes 1 and 2 represent the relative extent of formation of ions **II**, **V**, and **I**, respectively, for any given excited oxonium ion **I** and **II** from Equation (19–23). In the presence of YH, ions **II**, **V**, and **I** undergo rate-determining elimination to dienes **5** and **6** (Scheme 1) and/or substitution to oxonium ions **III** and **IV** (YH = MeOH) (Scheme 2), followed by their rapid neutralization by proton transfer to a suitable base.[12]

Orientation of the gas-phase YH attack: Discussion of the mechanistic details of the YH-induced elimination [whether E2 or E2′, Eqs. (2a,b)] and substitution reactions (whether S_N2/S_N2' [Eqs. (1a,b)] or S_N1/S_N1') requires preliminary evaluation of the a^v, b^v, and c^v terms of Schemes 1 and 2.

Under conditions allowing more or less extensive **I**–**II** interconversion as well as fragmentation to **V**, the value of the a^v, b^v, and c^v terms of Schemes 1 and 2 strongly depends upon several factors, such as i) the nature of the primary oxonium ion, either **I** or **II**, excited by the exothermicity of its formation process; ii) its quenching efficiency, which is influenced by the nature and the pressure of the bulk gas; iii) the rate constants of the competing isomerization (k_i) and fragmentation processes (k_f); and iv) the time-lag between the formation of the primary excited oxonium ion and its reaction (or those of its progeny) with YH. For a given starting allylic alcohol (v = **I** or **II**) in CH_4 at a specific pressure, the values of the a^v, b^v, and c^v terms of Schemes 1 and 2 depend exclusively upon factor (iv) and, therefore, upon the nature and the concentration of the YH nucleophile. The time interval between the initial formation of the excited oxonium ion and its first collision with YH can be estimated from the collision rate between the ion and the nucleophile calculated according to Su and Chesnavich's trajectory calculation method.[13] Accordingly, for both **I** and **II** isomers, this time-lag amounts to 8.5×10^{-9} and 3.4×10^{-9} s at MeOH partial pressures of 2 and 5 Torr, respectively, and to 13.2×10^{-9} and 5.3×10^{-9} s at a NMe_3 partial pressure of 2 and 5 Torr, respectively. By virtue of their different lifetimes in the presence of the same concentration of YH = MeOH or NMe_3, different sets of a^v, b^v, and c^v values would be expected, one for the elimination (Scheme 1) and the other for the substitution network (Scheme 2). At the same YH concentration, a relationship can be established between the two sets of values on the grounds of the following considerations. In the extreme case wherein the only process active in Schemes 1 and 2, besides quenching of the starting excited oxonium ion (e.g., c^v for **I**), is unimolecular fragmentation ($a^v = 0$), the relative concentration of the ion **V** immediately before it is trapped by the nucleophile YH (i.e., $b^v = 1 - c^v$) can be expressed by Equation (7). When YH = NMe_3, namely for the elimination (Scheme 1), Equation (7) becomes Equation (8), where k_f is the oxonium ion fragmentation rate constant and t is the calculated ion lifetime in the corresponding NMe_3 concentration. When YH = MeOH, namely for the substitution (Scheme 2), Equation (7) becomes Equation (9), where τ is the difference in oxonium ion lifetime between YH = NMe_3 to YH = MeOH. Combination of Equations (8) and (9) leads to relationship (10), linking the two sets of b^v parameters of Schemes 1 and 2.

$$\begin{aligned} b^v &= 1 - c^v = 1 - c^{\circ v}\exp(-k_f t) \\ &= 1 - \exp(-k_f t)\ (\text{since } c^{\circ v} = 1) \end{aligned} \tag{7}$$

$$b^v_{\text{elim}} = 1 - \exp(-k_f t) \tag{8}$$

$$b^v_{\text{subs}} = 1 - \exp(-k_f(t - \tau)) \tag{9}$$

$$b^v_{\text{elim}} = 1 - \exp(-k_f\tau) + b^v_{\text{subs}}\exp(-k_f\tau) \tag{10}$$

A similar expression is obtained by considering the other extreme case, wherein the only process active in Schemes 1 and 2, besides quenching of the starting excited oxonium ion (e.g., c^v for **I**), is unimolecular isomerization ($b^v = 0$). In this case, the relationship linking the two sets of a^v parameters of Schemes 1 and 2 is given by Equation (11), where k_i is the oxonium ion isomerization rate constant.

$$a^v_{\text{elim}} = 1 - \exp(-k_i\tau) + a^v_{\text{subs}}\exp(-k_i\tau) \tag{11}$$

The general procedure adopted to obtain the elimination (δ^v) and substitution (α^v) regioselectivity factors of Schemes 1 and 2 from the experimental results of Tables 1 and 2 involves expression of the isomeric distribution of the elimination (dienes **5** and **6**) and substitution products (ethers **3** and **4**) from the radiolytic experiments in terms of the parameters of Scheme 1 and 2, and definition of the minimum and maximum relative extent of isomerization (either a^v or c^v) and fragmentation (b^v) of a given primary excited oxonium ion v (either **I** or **II**) under specific experimental conditions.

In the framework of the elimination pattern of Scheme 1, the relative distribution of isomeric dienes **5** and **6**, that is, **5**/(**5** + **6**) and **6**/(**5** + **6**), respectively, from $C_nH_5^+$-protonation (n = 1, 2) of alcohols **1** and **2** in the presence of YH can be expressed by Equations (12) and (13).

$$\mathbf{5}/(\mathbf{5}+\mathbf{6}) = a^v_{\text{elim}}(1 - \delta^{\text{II}}) + b^v_{\text{elim}}(1 - \delta^{\text{V}}) + c^v_{\text{elim}}\delta^{\text{I}} \tag{12}$$

$$\mathbf{6}/(\mathbf{5}+\mathbf{6}) = a^v_{\text{elim}}\delta^{\text{II}} + b^v_{\text{elim}}\delta^{\text{V}} + c^v_{\text{elim}}(1 - \delta^{\text{I}}) \tag{13}$$

When the fact that $c^v_{\text{elim}} = 1 - a^v_{\text{elim}} - b^v_{\text{elim}}$ is considered, these equations reduce to Equation (14).

$$\begin{aligned} b^v_{\text{elim}} &= a^v_{\text{elim}}(\delta^{\text{I}} + \delta^{\text{II}} - 1)/(1 - \delta^{\text{I}} - \delta^{\text{V}}) \\ &\quad + \{[\mathbf{5}/(\mathbf{5}+\mathbf{6})] - \delta^{\text{I}}\}/(1 - \delta^{\text{I}} - \delta^{\text{V}}) \end{aligned} \tag{14}$$

In the same way, according to the substitution network of Scheme 2, the fractions of isomeric ethers **3** and **4**, that is, **3**/(**3** + **4**) and **4**/(**3** + **4**), respectively, obtained from $C_nH_5^+$-induced nucleophilic displacement by MeOH on alcohols **1** and **2** can be expressed as Equations (15) and (16).

$$\mathbf{3}/(\mathbf{3}+\mathbf{4}) = a^v_{\text{subs}}(1 - \alpha^{\text{II}}) + b^v_{\text{subs}}(1 - \alpha^{\text{V}}) + c^v_{\text{subs}}\alpha^{\text{I}} \tag{15}$$

$$\mathbf{4}/(\mathbf{3}+\mathbf{4}) = a^v_{\text{subs}}\alpha^{\text{II}} + b^v_{\text{subs}}\alpha^{\text{V}} + c^v_{\text{subs}}(1 - \alpha^{\text{I}}) \tag{16}$$

When the fact that $c^v_{\text{subs}} = 1 - a^v_{\text{subs}} - b^v_{\text{subs}}$ is taken in to account, these become Equation (17).

$$\begin{aligned} b^v_{\text{subs}} &= a^v_{\text{subs}}(\alpha^{\text{I}} + \alpha^{\text{II}} - 1)/(1 - \alpha^{\text{I}} - \alpha^{\text{V}}) \\ &\quad + \{[\mathbf{3}/(\mathbf{3}+\mathbf{4})] - \alpha^{\text{I}}\}/(1 - \alpha^{\text{I}} - \alpha^{\text{V}}) \end{aligned} \tag{17}$$

By introducing the **3**/(**3** + **4**) substitution ratio, the α^{II} regioselectivity factor taken from Table 1, and the α^{V} factor taken from Table 2 into Equation (17), a general equation containing the unknowns α^{I}, a^v_{subs}, and b^v_{subs} is obtained, corresponding to a family of straight lines in a $x = a^v_{\text{subs}}/y = b^v_{\text{subs}}$ graph. Only those straight lines for which a^v_{subs} and b^v_{subs} range from zero, which corresponds to the minimum value of α^{I} ($\alpha^{\text{I}}_{\text{min}}$), to their maximum value ($a^v_{\text{subs max}}$ and $b^v_{\text{subs max}}$), which corresponds to the maximum value of α^{I} ($\alpha^{\text{I}}_{\text{max}}$), are physically meaningful and are used to calculate the substitution regioselectivity factor ($\alpha^{\text{I}}_{\text{av}}$) as the average of $\alpha^{\text{I}}_{\text{min}}$ and $\alpha^{\text{I}}_{\text{max}}$. The same procedure is repeated with the elimination results by means of Equation (14). Of course, the ranges of physically acceptable values of a^v_{elim} and b^v_{elim}, $0 < a^v < a^v_{\text{elim max}}$ and $0 < b^v < b^v_{\text{elim max}}$, must satisfy the relationships (10) and (11) using the relevant $a^v_{\text{subs max}}$ and $b^v_{\text{subs max}}$ parameters. Within these ranges, substitution of the **5**/(**5** + **6**) elimination ratio, the δ^{II} regioselectivity factor deduced from Table 1, and the δ^{V} factor obtained from Table 2 into Equation (12) leads to the elimination regioselectivity factor $\delta^{\text{I}}_{\text{av}}$ obtained from the average between the minimum ($\delta^{\text{I}}_{\text{min}}$) and the maximum value ($\delta^{\text{I}}_{\text{max}}$) of δ^{I}.

The most convenient way to treat the data of Tables 1 and 2 in the light of the above general procedure consists in considering first the experiments carried out on **I** at 100 Torr of CH_4 and in the presence of 2 Torr of YH, namely under conditions allowing most extensive fragmentation b^v_{max} and isomerization a^v_{max} of the oxonium ion. Then the analysis is extended to the systems at 760 Torr and in the presence of 5 Torr of YH, wherein the maximum extent of fragmentation b^v_{max} and isomerization a^v_{max} of the relevant oxonium ion cannot exceed that estimated at 100 Torr of CH_4 and in the presence of 2 Torr of YH.

Nucleophilic substitution on I by MeOH (2 Torr): For the systems containing **1** as the starting alcohol (v = **I**) in 100 Torr of CH_4 and in the presence of YH = MeOH (2 Torr) (entry 7 of Table 1), the α^{V} factor is 0.038 as reported in entry 15 of Table 2. As discussed in the previous section, the yield factor of ether **4** from entry 21 of Table 1 provides the value of the α^{II} term directly ($\alpha^{\text{II}} = 0.076$). By introducing $\alpha^{\text{V}} = 0.038$, $\alpha^{\text{II}} = 0.076$, and **3**/(**3** + **4**) = 0.993 from entry 7 of Table 1 into Equation (17) the parametric linear Equation (18) is obtained, which corresponds to a bundle of straight lines, some of them shown in Figure 1 for several different values of the α^{I} parameter. The α^{I} value ranges from the minimum value of 0.993 ($\alpha^{\text{I}}_{\text{min}}$), obtained by assuming

$$\begin{aligned} b^{\text{I}}_{\text{subs}} &= a^{\text{I}}_{\text{subs}}(\alpha^{\text{I}} - 0.924)/(0.962 - \alpha^{\text{I}}) \\ &\quad + (0.993 - \alpha^{\text{I}})/(0.962 - \alpha^{\text{I}}) \end{aligned} \tag{18}$$

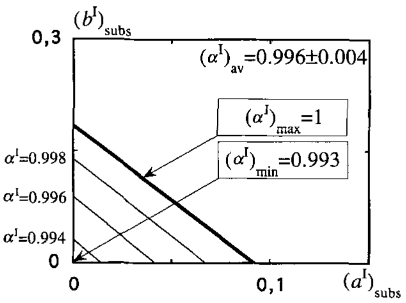


Fig. 1. Regioselectivity boundaries [Eq. (17)] for the nucleophilic displacement on **I** by MeOH (2 Torr) at 100 Torr of CH_4.

$a^I_{subs} = b^I_{subs} = 0$ and thus $c^I_{subs} = 1$, to a maximum value of 1 (α^I_{max}) represented by the points on the thick straight line in Figure 1, whose intercepts with the axes corresponds to $a^I_{subs\,max} = 0.092$ ($b^I_{subs} = 0$) and $b^I_{subs\,max} = 0.184$ ($a^I_{subs} = 0$). From the average between α^I_{min} and α^I_{max}, the substitution regioselectivity factor $\alpha^I_{av} = 0.996 \pm 0.004$ is obtained.

By applying the same procedure to the systems containing **1** as the starting alcohol (v = **I**) in 760 Torr of CH_4 and in the presence of YH = MeOH (2 Torr) (entry 5 of Table 1), with $\alpha^V = 0.041$ (entry 13 of Table 2), $\alpha^{II} = 0.146$ (entry 19 of Table 1), and **3**/(**3** + **4**) = 0.984 from entry 5 of Table 1, an equation analogous to (18) is obtained, which is represented by the bundle of straight lines of Figure 2.

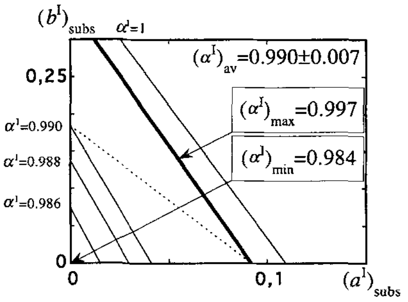


Fig. 2. Regioselectivity boundaries [Eq. (17)] for the nucleophilic displacement on **I** by MeOH (2 Torr) at 760 Torr of CH_4.

The lower limit of these lines corresponds again to the condition $a^I_{subs} = b^I_{subs} = 0$ and thus $c^I_{subs} = 1$ ($\alpha^I_{min} = 0.984$), whereas the upper limit can be calculated by considering that, at 760 Torr, the maximum extent of isomerization $a^I_{subs\,max}$ and fragmentation $b^I_{subs\,max}$ of **I** cannot exceed the corresponding values measured at 100 Torr (see point (ii) above), namely $a^I_{subs\,max} = 0.092$ and $b^I_{subs\,max} = 0.184$ (the broken line of Fig. 2). Accordingly, the maximum value of the α^I factor ($\alpha^I_{max} = 0.997$) is represented by the thick straight line in Figure 2, corresponding to $a^I_{subs\,max} = 0.092$ and $b^I_{subs} = 0$. Therefore, for these systems, $\alpha^I_{av} = 0.990 \pm 0.007$.

Elimination reaction on I by NMe_3 (2 Torr): For the systems containing **1** as the starting alcohol (v = **I**) in 100 Torr of CH_4 and in the presence of YH = NMe_3 (2 Torr) (entry 3 of Table 1), the δ^V term amounts to 0.435 (entry 3 of Table 2). Concerning δ^{II}, we can assume for a moment that the regioselectivity of NMe_3-induced elimination on oxonium ions of Equation (4) is essentially unaffected by the nature of the leaving moiety AOH. Later on (see **E2 versus E2′ elimination on allylic alcohols 1 and 2**), this assumption will be proved to be fully acceptable. Along this line, $\delta^{II} = 0.594$ (entry 27 of Table 1). By substituting these values, as well as the **5**/(**5** + **6**) = 0.623 from entry 3 of Table 1, into Equation (14), the parametric linear Equation (19) is obtained, which corresponds to the bundle of straight lines

$$b^I_{elim} = a^I_{elim}(\delta^I - 0.406)/(0.565 - \delta^I) + (0.623 - \delta^I)/(0.565 - \delta^I) \qquad (19)$$

reported in Figure 3. As pointed out before for MeOH-substitution on **I**, the lower extreme of these lines corresponds to the origin of a^I_{elim} and b^I_{elim} axes, where $a^I_{elim} = b^I_{elim} = 0$ and thus $c^I_{elim} = 1$ ($\delta^I_{min} = 0.623$). The upper extreme can be obtained by considering that replacement of MeOH with the same concentration of NMe_3 appreciably affects the extent of isomerization and fragmentation of **I** (see point (iv) above), as shown by Equations (10) and (11). Accordingly, their maximum extent can be calculated from the corresponding $a^I_{subs\,max} = 0.092$ and $b^I_{subs\,max} = 0.184$ and the relative $k_{f\,max}$ and $k_{i\,max}$ maximum rate constants. These latter can be obtained from the corresponding values $b^I_{subs\,max} = 0.184$ and $a^I_{subs\,max} = 0.092$ by the general rate expression for unimolecular reactions (e.g., $b^I_{max} = 1 - \exp(-(k_{f\,max}t))$ and the ion lifetimes t estimated in MeOH. In this way, the values $a^I_{elim\,max} = 0.139$ and $b^I_{elim\,max} = 0.271$ are obtained (the broken line of Fig. 3). Accordingly, the maximum value of the δ^I factor ($\delta^I_{max} = 0.658$) is represented by the thick straight line in Figure 3, corresponding to $a^I_{elim\,max} = 0.139$ and $b^I_{elim} = 0$. From the average of δ^I_{min} and δ^I_{max}, the elimination regioselectivity factor $\delta^I_{av} = 0.640 \pm 0.018$ is calculated.

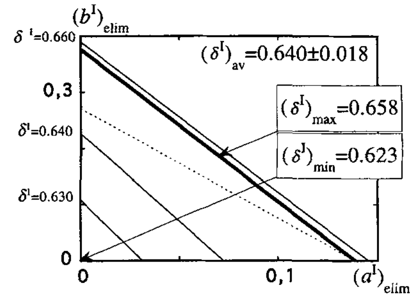


Fig. 3. Regioselectivity boundaries [Eq. (14)] for the elimination reaction on **I** induced by NMe_3 (2 Torr) at 100 Torr of CH_4.

By applying the same procedure to the systems containing **1** as the starting alcohol (v = **I**) in 760 Torr of CH_4 and in the presence of YH = NMe_3 (2 Torr) (entry 1 of Table 1), $\delta^V = 0.536$ (entry 1 of Table 2) and $\delta^{II} = 0.630$ (entry 25 of Table 1) give an equation analogous to (19), which is represented by the bundle of straight lines of Figure 4. The lower

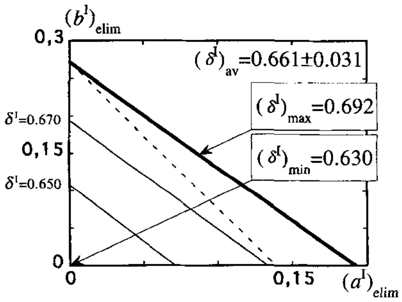


Fig. 4. Regioselectivity boundaries [Eq. (14)] for the elimination reaction on **I** induced by NMe_3 (2 Torr) at 760 Torr of CH_4.

boundary of these lines refers to $a^{I}_{elim} = b^{I}_{elim} = 0$ and thus $c^{I}_{elim} = 1$ ($\delta^{I}_{min} = 0.630$), whereas the upper boundary corresponds to $a^{I}_{elim\,max} = 0.139$ and $b^{I}_{elim\,max} = 0.271$ (the broken line of Fig. 4) (see point (iv) above). Accordingly, the maximum value of the δ^{I} factor ($\delta^{I}_{max} = 0.692$) is represented by the thick straight line in Figure 4, corresponding to $b^{I}_{elim\,max} = 0.271$ and $a^{I}_{elim} = 0$. Therefore, for these systems, $\delta^{I}_{av} = 0.661 \pm 0.031$.

Nucleophilic substitution on I by MeOH (5 Torr): The entire procedure is repeated for the systems containing **1** in the presence of 5 Torr of YH = MeOH or NMe_3. In 100 Torr of CH_4 with YH = MeOH (entry 8 of Table 1), the α^{V} factor amounts to 0.056 as reported in entry 16 of Table 2. The α^{II} factor is equal to 0.053 (entry 22 of Table 1). By introducing these values and $3/(3+4) = 0.995$ from entry 8 of Table 1 into Equation (17), an equation analogous to (18) is obtained corresponding to the bundle of straight lines of Figure 5. Accordingly, the α^{I} value ranges from $\alpha^{I}_{min} = 0.995$, if $a^{I}_{subs} = b^{I}_{subs} = 0$ and thus $c^{I}_{subs} = 1$, to $\alpha^{I}_{max} = 1$ ($a^{I}_{subs\,max} = 0.094$, $b^{I}_{subs} = 0$ and $b^{I}_{subs\,max} = 0.089$, $a^{I}_{subs} = 0$), represented by the points on the thick straight line in Figure 5. In this context, it should be pointed out that in the presence of 5 Torr of MeOH, the maximum extent of isomerization $a^{I}_{subs\,max}$ of **I** cannot exceed the corresponding value measured at 100 Torr in the presence of 2 Torr of MeOH (point (iv) above), namely $a^{I}_{subs\,max} = 0.092$. Even if the $a^{I}_{subs\,max}$ limit is reduced from 0.094 to 0.092 ($b^{I}_{subs} = 0$), the α^{I}_{max} remains essentially equal to 1. Thus, $\alpha^{I}_{av} = 0.997 \pm 0.003$. Use of the same upper boundaries ($a^{I}_{subs\,max} = 0.092$, $b^{I}_{subs} = 0$ and $b^{I}_{subs\,max} = 0.089$, $a^{I}_{subs} = 0$) for the systems containing **1** in 760 Torr of CH_4 with YH = MeOH (5 Torr) (entry 6 of Table 1) yields a result of $\alpha^{I}_{av} = 0.990 \pm 0.008$ (Fig. 6) from $\alpha^{V} = 0.071$ (entry 14 of Table 2), $\alpha^{II} = 0.163$ (entry 20 of Table 1), and $3/(3+4) = 0.983$ (entry 6 of Table 1).

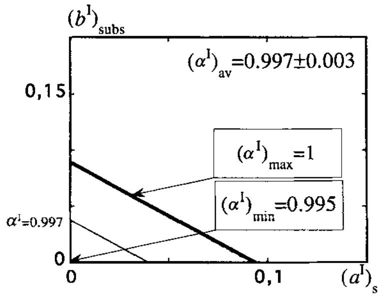


Fig. 5. Regioselectivity boundaries [Eq. (17)] for the nucleophilic displacement on **I** by MeOH (5 Torr) at 100 Torr of CH_4.

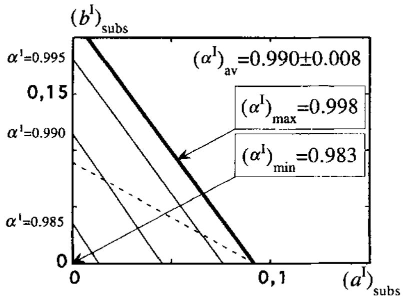


Fig. 6. Regioselectivity boundaries [Eq. (17)] for the nucleophilic displacement on **I** by MeOH (5 Torr) at 760 Torr of CH_4.

Elimination reaction on I by NMe_3 (5 Torr): As pointed out before, the upper extent of isomerization ($a^{I}_{elim\,max}$) and fragmentation ($b^{I}_{elim\,max}$) of **I** in the experiments in CH_4 with YH = NMe_3 (5 Torr) can be obtained by applying Equations (10) and (11). By introducing the corresponding values $a^{I}_{subs\,max} = 0.092$ and $b^{I}_{subs\,max} = 0.089$ and the estimated $k_{f\,max}$ and $k_{i\,max}$ maximum rate constants, upper limits of $a^{I}_{elim\,max} = 0.139$ and $b^{I}_{elim\,max} = 0.135$ are obtained. Within these limits, the results from the elimination experiments on **1** in 100 Torr of CH_4 with YH = NMe_3 (5 Torr) (entry 4 of Table 1) lead to $\delta^{I}_{av} = 0.642 \pm 0.018$ (Fig. 7), whereas those relative to the systems in 760 Torr of CH_4 with YH = NMe_3 (5 Torr) (entry 2 of Table 1) yield $\delta^{I}_{av} = 0.662 \pm 0.022$ (Fig. 8). As expected, increasing the concentration of the nucleophile YH from 2 to 5 Torr does not affect the substitution α^{I}_{av} and elimination δ^{I}_{av} regioselectivity factors. They also seem essentially insensitive to variations in the bulk gas pressure from 100 to 760 Torr.

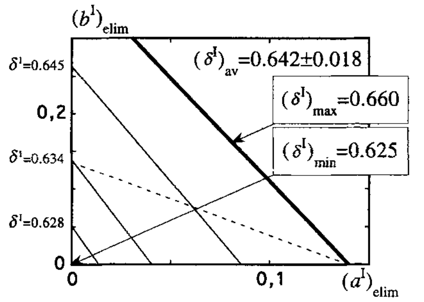


Fig. 7. Regioselectivity boundaries [Eq. (14)] for the elimination reaction on **I** induced by NMe_3 (5 Torr) at 100 Torr of CH_4.

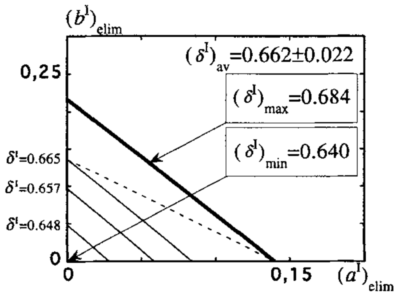


Fig. 8. Regioselectivity boundaries [Eq. (14)] for the elimination reaction on **I** induced by NMe_3 (5 Torr) at 760 Torr of CH_4.

Elimination reaction on II by NMe_3 (2 Torr): With **2** as the starting alcohol (v = **II**), Equations (14) and (17) become (20) for elimination by YH = MeOH and NMe_3, and (21) for nucleophilic substitution by MeOH, respectively.

$$\begin{aligned} b^{II}_{elim} &= c^{II}_{elim}(1 - \delta^{I} - \delta^{II})/(\delta^{II} - \delta^{V}) \\ &\quad + \{\delta^{II} - [\mathbf{6}/(\mathbf{5}+\mathbf{6})]\}/(\delta^{II} - \delta^{V}) \end{aligned} \tag{20}$$

$$\begin{aligned} b^{II}_{subs} &= c^{II}_{subs}(1 - \alpha^{I} - \alpha^{II})/(\alpha^{II} - \alpha^{V}) \\ &\quad + \{\alpha^{II} - [\mathbf{4}/(\mathbf{3}+\mathbf{4})]\}/(\alpha^{II} - \alpha^{V}) \end{aligned} \tag{21}$$

In the elimination reactions on **II** induced by NMe_3 (2 Torr) in 100 Torr of CH_4 (entry 17 of Table 1), the same δ^{V} and δ^{II} values employed in the elimination reaction on **1** are used: $\delta^{V} = 0.435$ (entry 3 of Table 2); $\delta^{II} = 0.594$ (entry 27 of

Table 1). As estimated above from the corresponding systems, $\delta^{\mathrm{I}} = \delta^{\mathrm{I}}_{\mathrm{av}} = 0.640 \pm 0.018$. Substitution of these values, together with the yield factor **6**/(**5** + **6**) = 0.533 from entry 17 of Table 1 into Equation (20) gives Equation (22).

$$b^{\mathrm{II}}_{\mathrm{elim}} = -1.472\, c^{\mathrm{II}}_{\mathrm{elim}} + 0.384 \qquad (22)$$

Accordingly, the maximum extents of isomerization $c^{\mathrm{II}}_{\mathrm{elim\,max}}$ (when $b^{\mathrm{II}}_{\mathrm{elim}} = 0$) and fragmentation $b^{\mathrm{II}}_{\mathrm{elim\,max}}$ of **II** (when $c^{\mathrm{II}}_{\mathrm{elim}} = 0$) at 100 Torr amount to 0.261 and 0.384, respectively. Consistently lower values for the maximum extent of isomerization, $c^{\mathrm{II}}_{\mathrm{elim\,max}} = 0.076$, and fragmentation, $b^{\mathrm{II}}_{\mathrm{elim\,max}} = 0.236$, are obtained at 760 Torr of $\mathrm{CH_4}$ with $\mathrm{NMe_3}$ (2 Torr) (entry 15 of Table 1), with $\delta^{\mathrm{V}} = 0.536$ (entry 1 of Table 2), $\delta^{\mathrm{II}} = 0.630$ (entry 25 of Table 1), and $\delta^{\mathrm{I}} = \delta^{\mathrm{I}}_{\mathrm{av}} = 0.661 \pm 0.031$.

Nucleophilic substitution on II by MeOH (2 Torr): The above boundaries allow one to estimate the upper extent of isomerization, ($c^{\mathrm{II}}_{\mathrm{subs\,max}}$), and fragmentation, ($b^{\mathrm{II}}_{\mathrm{subs\,max}}$), of **II** in the experiments in $\mathrm{CH_4}$ with YH = MeOH (2 Torr) by applying Equations (10) and (11). By introducing the corresponding $c^{\mathrm{II}}_{\mathrm{elim\,max}} = 0.261$ and $b^{\mathrm{II}}_{\mathrm{elim\,max}} = 0.384$ and the estimated $k_{\mathrm{f\,max}}$ and $k_{\mathrm{i\,max}}$ maximum rate constants, upper limits of $c^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.177$ and $b^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.268$ are obtained for the systems at 100 Torr of $\mathrm{CH_4}$. For those at 760 Torr of $\mathrm{CH_4}$, $c^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.050$ and $b^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.159$. These limiting values were introduced into Equation (23), obtained from rearrangement of Equation (21), to derive the value of the regioselectivity factor $\alpha^{\mathrm{II}}_{\mathrm{av}}$ and to compare it with that of the α^{II} term used in Equation (17) to estimate $\alpha^{\mathrm{I}}_{\mathrm{av}}$.

$$\alpha^{\mathrm{II}} = \{[\mathbf{4}/(\mathbf{3}+\mathbf{4})] - b^{\mathrm{II}}_{\mathrm{subs}}\alpha^{\mathrm{V}} - c^{\mathrm{II}}_{\mathrm{subs}}(1-\alpha^{\mathrm{I}})\}/(1 - b^{\mathrm{II}}_{\mathrm{subs}} - c^{\mathrm{II}}_{\mathrm{subs}}) \qquad (23)$$

Accordingly, for the systems with **2** (v = **II**) in 100 Torr of $\mathrm{CH_4}$ and in the presence of 2 Torr of MeOH, Equation (23) becomes Equation (24) if the values $\alpha^{\mathrm{V}} = 0.038$ (entry 15 of Table 2), $\alpha^{\mathrm{I}} = \alpha^{\mathrm{I}}_{\mathrm{av}} = 0.996 \pm 0.004$ (see above), and **4**/(**3** + **4**) = 0.076 (entry 21 of Table 1) are used.

$$\alpha^{\mathrm{II}} = (0.076 - 0.038\, b^{\mathrm{II}}_{\mathrm{subs}} - 0.004\, c^{\mathrm{II}}_{\mathrm{subs}})/(1 - b^{\mathrm{II}}_{\mathrm{subs}} - c^{\mathrm{II}}_{\mathrm{subs}}) \qquad (24)$$

Solving Equation (24) at the lowest ($c^{\mathrm{II}}_{\mathrm{subs}} = b^{\mathrm{II}}_{\mathrm{subs}} = 0$) and highest limits ($c^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.177$ and $b^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.268$) gives the minimum ($\alpha^{\mathrm{II}}_{\mathrm{min}} = 0.076$) and maximum value of α^{II} ($\alpha^{\mathrm{II}}_{\mathrm{max}} = 0.091$, which corresponds to $c^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.177$ and $b^{\mathrm{II}}_{\mathrm{subs}} = 0$). Thus, for these systems, $\alpha^{\mathrm{II}}_{\mathrm{av}} = 0.083 \pm 0.008$. Incidentally, this value compares well with the one deduced from the results of entry 21 of Table 1 ($\alpha^{\mathrm{II}} = 0.076$) and used before in deriving α^{I} from the corresponding systems with **1**.

At 760 Torr of $\mathrm{CH_4}$ in the presence of 2 Torr of MeOH, Equation (23) becomes Equation (25) if the values $\alpha^{\mathrm{V}} = 0.041$ (entry 13 of Table 2), $\alpha^{\mathrm{I}} = \alpha^{\mathrm{I}}_{\mathrm{av}} = 0.990 \pm 0.007$ (see above), and **4**/(**3** + **4**) = 0.146 (entry 19 of Table 1) are introduced.

$$\alpha^{\mathrm{II}} = (0.146 - 0.041\, b^{\mathrm{II}}_{\mathrm{subs}} - 0.010\, c^{\mathrm{II}}_{\mathrm{subs}})/(1 - b^{\mathrm{II}}_{\mathrm{subs}} - c^{\mathrm{II}}_{\mathrm{subs}}) \qquad (25)$$

Calculation of α^{II} in Equation (25) at the lowest ($c^{\mathrm{II}}_{\mathrm{subs}} = b^{\mathrm{II}}_{\mathrm{subs}} = 0$) and highest boundary ($c^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.050$ and $b^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.159$) gives the minimum ($\alpha^{\mathrm{II}}_{\mathrm{min}} = 0.146$) and maximum values of α^{II} ($\alpha^{\mathrm{II}}_{\mathrm{max}} = 0.166$, which corresponds to $b^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.159$ and $c^{\mathrm{II}}_{\mathrm{subs}} = 0$). Thus, for these systems, $\alpha^{\mathrm{II}}_{\mathrm{av}} = 0.156 \pm 0.010$. In this case too, the obtained $\alpha^{\mathrm{II}}_{\mathrm{av}}$ value is close to that derived from the results of entry 19 of Table 1 ($\alpha^{\mathrm{II}} = 0.146$) already used in deriving α^{I} from the corresponding systems with **1**.

Elimination reaction on II by $\mathrm{NMe_3}$ (5 Torr): The above procedure is repeated for the systems containing **2** in the presence of 5 Torr of YH = MeOH or $\mathrm{NMe_3}$. For the systems with 100 Torr of $\mathrm{CH_4}$ and in the presence of YH = $\mathrm{NMe_3}$ (5 Torr) (entry 18 of Table 1), substitution of the terms $\delta^{\mathrm{V}} = 0.431$ (entry 4 of Table 2), $\delta^{\mathrm{I}} = \delta^{\mathrm{I}}_{\mathrm{av}} = 0.642 \pm 0.018$ (see above), $\delta^{\mathrm{II}} = 0.588$ (entry 28 of Table 1), and **6**/(**5** + **6**) = 0.546 (entry 18 of Table 1) into Equation (20) gives $c^{\mathrm{II}}_{\mathrm{elim\,max}} = 0.183$ and $b^{\mathrm{II}}_{\mathrm{elim\,max}} = 0.267$. Consistently lower values for the maximum extent of isomerization, $c^{\mathrm{II}}_{\mathrm{elim\,max}} = 0.072$, and fragmentation, $b^{\mathrm{II}}_{\mathrm{elim\,max}} = 0.189$, are obtained at 760 Torr of $\mathrm{CH_4}$ with $\mathrm{NMe_3}$ (5 Torr) (entry 16 of Table 1) with the values $\delta^{\mathrm{V}} = 0.519$ (entry 2 of Table 2), $\delta^{\mathrm{I}} = \delta^{\mathrm{I}}_{\mathrm{av}} = 0.662 \pm 0.022$ (see above), $\delta^{\mathrm{II}} = 0.630$ (entry 26 of Table 1), and **6**/(**5** + **6**) = 0.609 (entry 16 of Table 1) in Equation (20).

Nucleophilic substitution on II by MeOH (5 Torr): The above boundaries are used to estimate the upper extent of isomerization ($c^{\mathrm{II}}_{\mathrm{subs\,max}}$) and fragmentation ($b^{\mathrm{II}}_{\mathrm{subs\,max}}$) of **II** in the experiments in $\mathrm{CH_4}$ with YH = MeOH (2 Torr) by applying Equations (10) and (11). The corresponding $c^{\mathrm{II}}_{\mathrm{elim\,max}} = 0.183$ and $b^{\mathrm{II}}_{\mathrm{elim\,max}} = 0.267$ and the estimated $k_{\mathrm{f\,max}}$ and $k_{\mathrm{i\,max}}$ maximum rate constants yields upper limits of $c^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.121$ and $b^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.181$ for the systems at 100 Torr of $\mathrm{CH_4}$. For those at 760 Torr of $\mathrm{CH_4}$, $c^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.047$ and $b^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.126$. These limiting values were introduced into Equation (23), which was obtained from rearrangement of Equation (21), to derive the value of the regioselectivity factor $\alpha^{\mathrm{II}}_{\mathrm{av}}$ and to compare it with that of the α^{II} term used in Equation (17) to estimate $\alpha^{\mathrm{I}}_{\mathrm{av}}$.

At 100 Torr of $\mathrm{CH_4}$ in the presence of 5 Torr of MeOH, Equation (23) becomes Equation (26) if the values $\alpha^{\mathrm{V}} = 0.056$ (entry 16 of Table 2), $\alpha^{\mathrm{I}} = \alpha^{\mathrm{I}}_{\mathrm{av}} = 0.997 \pm 0.003$ (see above), and **4**/(**3** + **4**) = 0.053 (entry 22 of Table 1) are used.

$$\alpha^{\mathrm{II}} = (0.053 - 0.056\, b^{\mathrm{II}}_{\mathrm{subs}} - 0.003\, c^{\mathrm{II}}_{\mathrm{subs}})/(1 - b^{\mathrm{II}}_{\mathrm{subs}} - c^{\mathrm{II}}_{\mathrm{subs}}) \qquad (26)$$

Solving Equation (26) at the lowest ($b^{\mathrm{II}}_{\mathrm{subs}} = c^{\mathrm{II}}_{\mathrm{subs}} = 0$) and highest limits ($c^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.121$ and $b^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.181$) gives the minimum ($\alpha^{\mathrm{II}}_{\mathrm{min}} = 0.053$) and maximum values of α^{II} ($\alpha^{\mathrm{II}}_{\mathrm{max}} = 0.060$, which corresponds to $c^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.121$ and $b^{\mathrm{II}}_{\mathrm{subs}} = 0$). Thus, for these systems, $\alpha^{\mathrm{II}}_{\mathrm{av}} = 0.056 \pm 0.004$. Again, it should be noted that this value is in good agreement with that ($\alpha^{\mathrm{II}} = 0.053$) used before in deriving α^{I} from the corresponding systems with **1**.

At 760 Torr of $\mathrm{CH_4}$ in the presence of 5 Torr of MeOH, Equation (23) becomes Equation (27) if the values $\alpha^{\mathrm{V}} = 0.071$ (entry 14 of Table 2), $\alpha^{\mathrm{I}} = \alpha^{\mathrm{I}}_{\mathrm{av}} = 0.990 \pm 0.008$ (see above), and **4**/(**3** + **4**) = 0.163 (entry 20 of Table 1) are introduced.

$$\alpha^{\mathrm{II}} = (0.163 - 0.071\, b^{\mathrm{II}}_{\mathrm{subs}} - 0.010\, c^{\mathrm{II}}_{\mathrm{subs}})/(1 - b^{\mathrm{II}}_{\mathrm{subs}} - c^{\mathrm{II}}_{\mathrm{subs}}) \qquad (27)$$

Calculation of α^{II} in Equation (27) at the lowest ($b^{\mathrm{II}}_{\mathrm{subs}} = c^{\mathrm{II}}_{\mathrm{subs}} = 0$) and highest extremes ($c^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.047$ and $b^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.126$) gives the minimum ($\alpha^{\mathrm{II}}_{\mathrm{min}} = 0.163$) and maximum values of α^{II} ($\alpha^{\mathrm{II}}_{\mathrm{max}} = 0.176$, which corresponds to $b^{\mathrm{II}}_{\mathrm{subs\,max}} = 0.126$ and $c^{\mathrm{II}}_{\mathrm{subs}} = 0$). Therefore, for these systems, $\alpha^{\mathrm{II}}_{\mathrm{av}} = 0.169 \pm 0.007$. In this case too the $\alpha^{\mathrm{II}}_{\mathrm{av}}$ value obtained agrees well with the one ($\alpha^{\mathrm{II}} = 0.163$) used before in deriving α^{I} from the corresponding systems with **1**.

As for **1**, increasing the concentration of the nucleophile YH from 2 to 5 Torr does not have much effect on the substitution ($\alpha^{\mathrm{II}}_{\mathrm{av}}$) and elimination ($\delta^{\mathrm{II}}$) regioselectivity factors in the systems with **2**. Contrary to the insensitivity to pressure variations observed for $\alpha^{\mathrm{I}}_{\mathrm{av}}$) and $\delta^{\mathrm{I}}_{\mathrm{av}}$ in the systems with **1**, the substitution ($\alpha^{\mathrm{II}}_{\mathrm{av}}$) and elimination ($\delta^{\mathrm{II}}$) regioselectivity factors measured in the runs with **2** increase appreciably with the system pressure.

S_N2 versus S_N2' substitution on allylic alcohols 1 and 2: Table 5 reports the maximum limits of the $C_nH_5^+$-induced isomerization ($a^{I}_{subs\,max}$ and $a^{I}_{elim\,max}$; $c^{II}_{subs\,max}$ and $c^{II}_{elim\,max}$) and fragmentation ($b^{I}_{subs\,max}$ and $b^{I}_{elim\,max}$; $b^{II}_{subs\,max}$ and $b^{II}_{elim\,max}$) channels of **1** and **2** in Schemes 1 and 2 (n = 1, 2) and the regioselectivity factors of the nucleophilic displacement by MeOH (α^{I}_{av} and α^{II}_{av}) and of NMe_3-induced elimination (δ^{I}_{av} and δ^{II}) on **I** and **II** at different CH_4 pressures. Analysis of Table 5 shows that gas-phase MeOH-substitution on **I** and **II** predominantly involves a bimolecular mechanism ($b^{I}_{subs\,max} = 0.184$ (MeOH, 2 Torr); 0.089 (MeOH, 5 Torr); $b^{II}_{subs\,max} = 0.268$ (CH_4, 100 Torr; MeOH, 2 Torr); 0.159 (CH_4, 760 Torr; MeOH, 2 Torr); 0.181 (CH_4, 100 Torr; MeOH, 5 Torr); 0.126 (CH_4, 760 Torr; MeOH, 5 Torr)). As shown by the regioselectivity results summarized in Figure 9, bimolecular nucleophilic displacement may follow the two competing S_N2 and S_N2' pathways. After consideration of partial **I**↔**II** interconversion prior to substitution ($a^{I}_{subs\,max} = 0.092$ and $c^{II}_{subs\,max} = 0.177$ (CH_4, 100 Torr; MeOH, 2 Torr); 0.050 (CH_4, 760 Torr; MeOH, 2 Torr); 0.121 (CH_4, 100 Torr; MeOH, 5 Torr); 0.047 (CH_4, 760 Torr; MeOH, 5 Torr)), it emerges that oxonium ion **I** follows almost exclusively the concerted S_N2 pathway (99–100%). In contrast, oxonium ion **II** tends to follow the concerted S_N2' pathway (83–94%). This suggests that, in the gas phase, the preferred site of the nucleophilic attack by a neutral nucleophile, such as MeOH, on allylic substrates may strongly depend upon the number of alkyl groups at the reaction center. While the conclusions of the preceding paper suggest that the presence of one alkyl group at either the C_α or the C_γ center of an allylic oxonium ion does not affect the corresponding MeOH diplacement rate much, the present results show that introduction of a second alkyl (or alkylene) substituent markedly decreases the efficiency of the nucleophilic attack. A plausible rationale for this effect involves a certain character of reversibility for the MeOH attack at the C_α center of **II**, as suggested by the fact that α substitution increases with the bulk gas pressure, whereas the extent of the competing elimination reactions decrease. At 760 Torr, in fact, collisional quenching of the excited encounter complex between **II** and MeOH may effectively compete with back-dissociation of the nucleophile from the encumbered C_α center of **II**, thus favoring Walden inversion of the reaction site[14] and preventing reorientation of the nucleophile from the C_α center to a neighboring ring H atom ($1 - \delta^{II} > 1 - \delta^{I}_{av}$; Table 5).

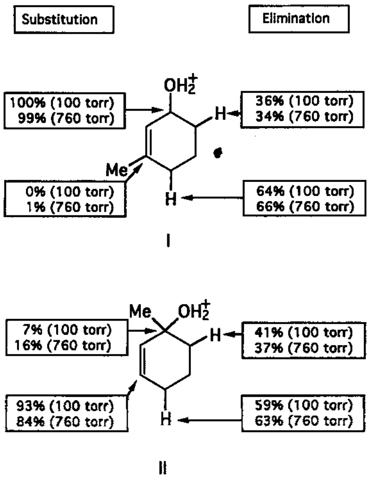


Fig. 9. Regioselectivity of the acid-catalyzed nucleophilic substitution by MeOH and elimination by NMe_3 on oxonium ions **I** and **II** in CH_4 at 100–760 Torr.

E2 versus E2′ elimination on allylic alcohols 1 and 2: As for nucleophilic substitution, the $b^{I}_{elim\,max}$ and $b^{II}_{elim\,max}$ values of Table 5 demonstrate that the gas-phase elimination on **I** and **II** involves mostly a bimolecular mechanism. After consideration of a partial **I**↔**II** interconversion before NMe_3-induced elimination (the $a^{I}_{elim\,max}$ and $c^{II}_{elim\,max}$ terms), the δ^{I}_{av} and δ^{II} regioselectivity factors of Figure 9 indicate that both oxonium ions **I** and **II** follow preferentially the concerted [1,4] elimination pathway [E2′, Eq. (2b)] (**I** 64–66%; **II** 59–63%) instead of the [1,2] one [E2, Eq. (2a)]. The E2′ mechanism appears slightly more favored in **I** than in **II** under all conditions, probably as a result of a character of partial reversibility in MeOH at the C_α center of **II** (see previous section). Besides, its extent increases with the bulk gas pressure. The similarity of the $\delta^{I}_{av} = 0.640$–0.662 of Table 5 with the **5**/(**5** + **6**) ratios (ranging between 0.618 and 0.647) reported in entries 11–14 of Table 1, relative to the NMe_3-induced elimination on **III**, indicates that the E2/E2′ branching ratio in these gaseous systems does not depend much upon the nature of the AOH leaving moiety (A = H (**I**); Me (**III**)) [Eqs. (2a,b)], although a slight preference for the E2′ mechanism can be perceived with A = H. By extension, these findings guarantee the soundness of the previous assumption about the coincidence between the NMe_3-elimination regiochemistry factor for **II** (δ^{II}) and that obtained for **IV** from the **6**/(**5** + **6**) ratios of entries 25–28 of Table 1. Besides, the E2/E2′ branching ratio in gas-phase elimination on **II** is found to be also rather insensitive to the nature of the YH nucleophile, as shown by the coincidence between the δ^{II} values of Table 5 and the **6**/(**5** + **6**) ratios (ranging between 0.534 and 0.660) reported in entries 19–22 of Table 1. In this context, it should be mentioned that the extensive MeOH-induced elimination on **II** (entries 19–22 of Table 1) necessarily involves the release of a $MeOH_2^+$–H_2O proton-bound cluster from the elimination product, which is allowed only by a concerted *syn* elimination mechanism.

Occurrence of competing E2′ and E2 mechanisms in YH-induced elimination on the selected oxonium ions finds some analogies with gas-phase elimination reactions promoted by attack of negatively charged bases on methoxycyclohexenes, investigated in a flowing afterglow apparatus.[15] In these studies, in fact, it was demonstrated that [1,4] elimination is heavily favored over [1,2] elimination when strong bases, such as OH^- and NH_2^-, are used. The [1,2] pathway instead becomes more competitive when weaker bases, such as MeO^-, are employed. The [1,4] selectivity observed with strong bases was attributed to the occurrence of a E1cB mechanism, whereas weaker bases may react only by the E2 mechanism, which however can afford both [1,2] and [1,4] products through predominant *syn* pathways. The present results fully conform to the general elimination pattern induced by weak bases, thus reinforcing and completing the view that, in similar systems, [1,4] elimination (E2′) may efficiently compete with the classical [1,2] elimination (E2), irrespective of whether the process involves neutral or negatively charged bases on positively charged or neutral substrates. Since measured in the gas phase, where the complicating effects of solvation, aggregation, and ion pairing are excluded, the relative extent of the competing E2′ and E2 mechanisms exclusively reflects the intrinsic orienting properties of the substrate towards the base.

Received: June 14, 1995 [F151]

---

[1] Part 10: G. Renzi, A. Lombardozzi, E. Dezi, A. Pizzabiocca, M. Speranza, preceding paper in this issue.

[2] a) R. J. Moss, B. Rickborn, *J. Org. Chem.* **1986**, *51*, 1992; b) D. Tobia, B. Rickborn, *ibid.* **1986**, *51*, 3849; c) R. J. Moss, R. O. White, B. Rickborn, *ibid.* **1985**, *50*, 5132; d) R. K. Hill, M. G. Bock, *J. Am. Chem. Soc.* **1978**, *100*, 637; e) E. G. Breitholle, C. H. Stammer, *J. Org. Chem.* **1974**, *39*, 1311; f) S. J. Cristol, *Acc. Chem. Res.* **1971**, *4*, 393; g) J. D. Park, R. J. McMurtry, *J. Org. Chem.* **1967**, *32*, 2397; h) S. J. Cristol, W. Barasch, C. H. Tieman, *J. Am. Chem. Soc.* **1955**, *77*, 583; i) M. Sellen, J. Backvall, P. Helquist, *J. Org. Chem.* **1991**, *56*, 835; j) M. Olwegard, P. Ahlberg, *Acta Chem. Scand.* **1990**, *44*, 642; k) C. Margot, H. Matsuda, M. Schlosser, *Tetrahedron* **1990**, *46*, 2425; l) R. P. Thummel, B. Rickborn, *J. Org. Chem.* **1972**, *37*, 4250; m) P. B. D. De La Mare, R. Koenigsberger, J. S. Lomas, *J. Chem. Soc. (B)* **1966**, 834; n) G. R.

Wenzinger, J. A. Williams, *Tetrahedron Lett.* **1973**, *24*, 2167; o) J. Baldwin, *ibid.* **1966**, 2953; p) H. D. Orloff, A. J. Kolka, *J. Am. Chem. Soc.* **1954**, *76*, 5484.

[3] K. Mori, B. G. Hazra, R. J. Pfeiffer, A. K. Gupta, B. S. Lindgren, *Tetrahedron* **1987**, *43*, 2249.

[4] U. C. Yoon, S. L. Quillen, P. S. Mariano, R. Swanson, J. L. Stavinoha, E. Bay, *J. Am. Chem. Soc.* **1983**, *105*, 1204.

[5] L. A. Paquette, F. Bellamy, G. J. Wells, C. Bohm, R. Gleiter, *J. Am. Chem. Soc.* **1981**, *103*, 7122.

[6] R. L. Cargill, A. Bradford Sears, J. Boehm, M. R. Willcott, *J. Am. Chem. Soc.* **1973**, *95*, 4346.

[7] T. L. Smithson, N. Ibrahim, H. Wleser, *Can. J. Chem* **1983**, *61*, 442.

[8] a) P. Ausloos, S. G. Lias, R. Gorden, Jr., *J. Chem. Phys.* **1963**, *39*, 3341; b) P. Ausloos, *Ion–Molecule Reactions* (Ed.: J. L. Franklin), Plenum, New York, **1970**; c) P. Ausloos, S. G. Lias, *J. Chem. Phys.* **1962**, *36*, 3163; d) S. G. Lias, P. Ausloos, *ibid.* **1962**, *37*, 877; e) I. B. Sandoval, P. Ausloos, *ibid.* **1963**, *38*, 452; f) M. Speranza, N. Pepe, R. Cipollini, *J. Chem. Soc. Perkin Trans. 2* **1979**, 1179.

[9] R. D. Bowen, D. H. Williams, *J. Am. Chem. Soc.* **1978**, *100*, 7454.

[10] Gaumann et al. (T. Gaumann, R. Houriet, D. Stahl, J. C. Tabet, N. Heinrich, H. Schwarz, *Org. Mass Spectrom.* **1983**, *18*, 215) reported generation and observation of the oxonium intermediate from protonation of 2-cyclohexen-1-ol carried out under chemical ionization conditions, namely under conditions that normally favor ion fragmentation (the dissociation energy of O-protonated 2-cyclohexen-1-ol to 2-cyclohexen-1-yl cation and H_2O, estimated according to the procedures in footnotes [b] and [c] of Table 3, amounts to only ca. 9 kcal mol^{-1}). The persistence of the stable oxonium ion at relatively low pressures, coupled with the appreciable kinetic energy release ($T_{0.5}$ (meV) = 26.8) in its metastable fragmentation, suggests that unimolecular dissociation probably involves an activation barrier.

[11] a) Y. K. Lau, S. Ikuta, P. Kebarle, *J. Am. Chem. Soc.* **1982**, *104*, 1462; b) E. P. Grimsrud, P. Kebarle, *ibid.* **1973**, *95*, 7939.

[12] In the absence of NMe_3, neutralization of the oxonium ions **III** and **IV** may occur by several pathways, including proton transfer to the starting alcohol, to the walls of the reaction vessel, or to clusters of YH molecules, either initially introduced into the gaseous mixture or generated by its radiolysis.

[13] T. Su, W. J. Chesnavich, *J. Chem. Phys.* **1982**, *76*, 5183.

[14] a) G. Angelini, M. Speranza, *J. Chem. Soc. Chem. Commun.* **1978**, 213; b) M. Speranza, G. Angelini, *J. Am. Chem. Soc.* **1980**, *102*, 3115; c) G. Angelini, M. Speranza, *ibid.* **1981**, *103*, 3792; d) G. Angelini, M. Speranza, *ibid.* **1981**, *103*, 3800.

[15] a) J. J. Rabasco, S. R. Kass, *Tetrahedron Letters* **1991**, *32*, 4077; b) J. J. Rabasco, S. R. Kass, *ibid.* **1993**, *34*, 765; c) J. J. Rabasco, S. R. Kass, *J. Org. Chem.* **1993**, *58*, 2633.