Evidence for a Concerted S_N2' Mechanism in the Gas-Phase Acid-induced Nucleophilic Substitutions on Allylic Substrates

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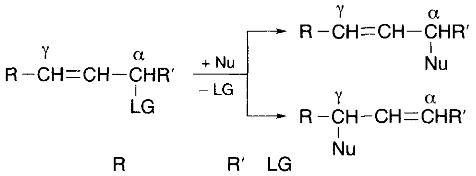
Gas phase nucleophilic substitution on oxygen-protonated but-1-en-3-ol and *trans*-but-2-en-1-ol by methanol proceeds *via* the concerted S_N2' mechanism in competition with the classical S_N2 mechanism.

Nucleophilic attack on an allylic substrate bearing an α-leaving group (LG in eqn. 1) can occur at both the Cα [S_N2, eqn. (1a)] and the Cγ centres [S_N2', eqn. (1b)] with concerted or stepwise departure of the leaving group LG. Alternatively, rate-determining dissociation of LG may precede attachment of the nucleophile at either the Cα (S_N1) or the Cγ sites (S_N1').[1] In general, concerted S_N2' reactions in solution are expected to be best favoured on α-substituted allylic substrates[2d,3] when using neutral nucleophiles in apolar, aprotic solvents.[4] However, demonstration of the concerted S_N2' mechanism is seldom clear,[2] since formation of the rearranged product [eqn. (1b)] may be often accounted for by the nucleophile-assisted heterolysis of the allylic substrate to an intermediate ion pair (an S_N1' mechanism) as well.[2a,5]



(1a)

(1b)

	R	R'	LG
1	Me (*trans*)	H	OH
2	H	Me	OH
3	Me (*trans*)	H	OMe
4	H	Me	OMe
5	Me (*trans*)	H	OH_2^+
6	H	Me	OH_2^+

Here we report a preliminary investigation of nucleophilic substitutions in allylic substrates, such as alcohols **1** and **2**, under extreme conditions expected to favour the occurrence of S_N2' reactions, namely in the gas phase and using MeOH as the neutral nucleophile. Alcohols **1** and **2** were submitted to protonation by $C_nH_5^+$ (n = 1,2) ions, generated in the gas phase by γ-radiolysis (^{60}Co source, room temp.) of CH_4 (760 Torr), in the presence of small concentrations of MeOH as the nucleophile, and O_2 as a thermal radical scavenger. The high-pressure conditions adopted ensure efficient collisional deactivation of the ionic species involved, whose structure and isomeric composition can be derived from analysis of their neutral substitution derivatives.

The experimental results are reported in Table 1. Efficient formation of both ethers **3** and **4** (total absolute yield 30–37%, entries i and ii),† irrespective of the starting allylic alcohol, demonstrates that nucleophilic attack of MeOH indeed takes place at both the Cα and the Cγ centres of the ionic intermediate(s) involved in eqn. (1).

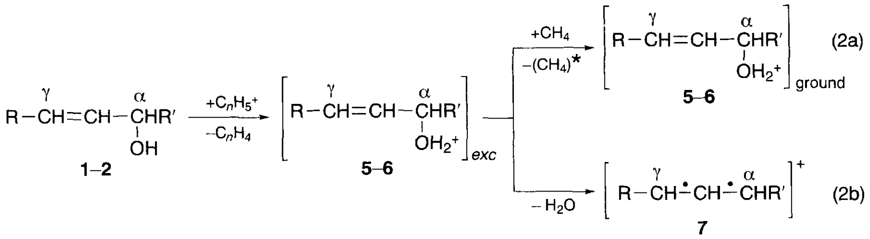
Concerning the nature of these intermediates, it should be considered that oxonium ions **5** and **6**, formed respectively from $C_nH_5^+$ (n = 1,2) protonation of **1** and **2**, are generated with an excess internal energy arising from the exothermicity of their formation processes [$-\Delta H°$(kJ mol^{-1}) = 251 (**1**; n = 1); 125 (**1**; n = 2); 268 (**2**; n = 1); 142 (**2**; n = 2)].[6,7] It follows that, in principle, excited oxonium ions **5** and **6** may undergo unimolecular dissociation to the allyl cation **7** and H_2O [eqn. (2b); $\Delta H°$(kJ mol^{-1}) = 29 (**5**); 50 (**6**)],[6,7] unless stabilised by multiple unreactive collisions with the bath CH_4 gas (2.5×10^{10} collisions per second) [eqn. (2a)].

Thus, the formation of similar proportions of ethereal products **3** and **4** from both **1** and **2** may in principle be accounted for by either unimolecular S_N1 and S_N1' mechanisms involving the allyl cation **7** (R, R' = Me, H) and/or bimolecular S_N2 and S_N2' mechanisms involving the oxonium ions **5** and **6**. Discrimination between these routes is possible on the grounds of the results reported in entries iii–vii of Table 1. Accordingly, when free allyl cation **7** (R,R' = Me,H) is generated in the gas phase by direct $C_nH_5^+$ (n = 1,2) protonation of buta-1,3-diene **8** in the presence of H_2O (2.0 Torr; entry v), it produces *exclusively* but-1-en-3-ol **2** in high absolute yield (83%). The product displays a significant ^{18}O-atom incorporation (>70%) when the reaction involves $H_2{}^{18}O$ (^{18}O >97%). This indicates that the encounter complex between ion **7** and H_2O evolves

Table 1 Product yield and distribution from the gas phase attack of protonating and methylating ions on *trans*-but-2-en-1-ol **1**, but-1-en-3-ol **2**[a] and butadiene **8**

Entry	Substrate (p/Torr)[b]	NuH (p/Torr)[b]	Product distribution (%)[c] **1**	**2**	**3**	**4**	Absolute yield (%)[d]
i	**1** (0.44)	MeOH (0.51)		—	35	65	30
ii	**2** (0.51)	MeOH (0.51)	2		41	57	37
iii	**1** (0.52)	H_2O (1.9)[e]		100			3
iv	**2** (0.48)	H_2O (1.9)[e]	100				5
v	**8** (1.50)	H_2O (2.0)[e]	—	100			83
vi	**1** (0.45)[f]				74	26	28
vii	**2** (0.46)[f]				6	94	33

[a] The racemic mixture of **2** was used. [b] CH_4 (760 Torr) and O_2 (4 Torr) present in each experiment. Radiation dose : 1.5×10^4 Gy (dose rate : 10^4 Gy h^{-1}). [c] Percent ratio of the yield of each product to the combined yield of all products identified. The bars denote that the yield of the corresponding product is below the detection limit, *ca.* 0.2%. Each value is the average of several determinations, with an uncertainty level of *ca.* 5%. [d] Absolute yields estimated from the percent ratio between the combined G (products) value of the recovered products and the literature $G(C_nH_5^+)$ = 1.9 (n = 1); 0.9 (n = 2) (P. Ausloos, S. G. Lias and R. Gordon, Jr., *J. Chem. Phys.*, 1963, **39**, 3341); $G(Me_2F^+)$ = 3.4 (M. Speranza, N. Pepe and R. Cipollini, *J. Chem. Soc. Perkin Trans. 2*, 1979, 1179). The G(M) values are defined as the number of species M produced per 100 eV absorbed energy. [e] Replacement of natural H_2O with $H_2{}^{18}O$ (^{18}O >97%) leads to the formation of **1** (entry iii) and **2** (entry iv) with the natural $^{16}O : {}^{18}O$ isotopic ratio. In entry v, instead, alcohol **2**, with a ^{18}O content exceeding 70% is produced from **8** in the presence of $H_2{}^{18}O$ (^{18}O >97%). [f] Using MeF^+ ions from radiolysis of MeF (760 Torr). Radiation dose: 1.5×10^4 Gy (dose rate: 10^4 Gy h^{-1}).



efficiently and *exclusively* towards the formation of the stable oxonium intermediate **6**. However, when alcohol **1** (or **2**) is submitted to $C_nH_5^+$ (n = 1,2) protonation in the presence of 1.9 Torr H_2O, it produces only 3% of its isomer **2** (or **1**; 5%) (entries iii and iv). No detectable excess of the ^{18}O label over the natural abundance is observed in these products when the reactions are carried out in the presence of $H_2{}^{18}O$ ($^{18}O > 97\%$). These results demonstrate that (i) at atmospheric pressure, efficient collisional quenching of excited oxonium ions **5** and **6** from exothermic $C_nH_5^+$ (n = 1,2) protonation of alcohols **1** and **2** prevents their unimolecular dissociation to free allylic ion **7**, thus excluding the occurrence of the S_N1/S_N1' mechanism in the displacement process; (ii) the quasi-resonant, bimolecular $H_2{}^{18}O$-to-$H_2{}^{16}O$ displacement in oxonium ions **5** and **6** is very inefficient; (iii) the acid-induced **1** $\rightleftharpoons$ **2** isomerization involves the intramolecular $\alpha \rightleftharpoons \gamma$ shift of the H_2O moiety in the excited oxonium ion. It is concluded that gas phase nucleophilic substitution reactions on **1** and **2** involves the intermediacy of the stable oxonium intermediates **5** and **6**, respectively, and therefore can be best classified in the category of concerted S_N2 and S_N2' substitutions. Further convincing pieces of evidence in favour of the above conclusions arise from the results reported in entries vi and vii of Table 1, concerning O-protonated *trans*-1-methoxybut-2-ene **9** and 3-methoxybut-1-ene **10**. These ionic species have been generated in the gas phase by O-methylating **1** (or **2**) with radiolytically formed Me_2F^+ ions. The fact that the oxonium ion **9** from **1** produces eventually [**3**] : [**4**] = 2.84 : 1, whereas **10** from **2** yields [**3**] : [**4**] = 0.067 : 1, shows beyond any reasonable doubt that the gas-phase methylation of the selected allylic alcohols does not lead to formation of the allylic cation **7**, but only to a limited intramolecular isomerization of the ensuing oxonium ions, in conformity with the behaviour of oxonium ions **5** and **6**.

The present results provide direct evidence for gas phase acid-catalysed S_N2' processes on some representative allylic compounds efficiently competing with the classical S_N2 reactions. Detection of concerted S_N2' reactions is facilitated in gaseous media by the absence of solvation and ion-pairing phenomena, and by the possibility of investigating the behaviour of conceivable allylic S_N1 intermediates, such as **7**, under the same experimental conditions adopted for the substitution reactions.

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Footnote

† In spite of a specific search, no carbonylic products were detected among the radiolytic products. This indicates that the attack of $C_nH_5^+$ (n = 1,2) ions on alcohols **1** and **2** takes place exclusively at their O centre and not at the π bond (ref. 6).

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