

## Direct Evidence of Neighbouring Group Participation in the Gas Phase

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**Summary** The nature and the isomeric distribution of the neutral products, obtained from the gas-phase attack of radiolytically formed Brønsted acids on selected vicinal halogeno-alcohols, provide direct evidence of an extensive gas-phase neighbouring group participation process involving the intermediacy of an *O*-protonated alkene oxide.

THE understanding of the structure-reactivity relationship in solvolytic displacement reactions is usually impeded by the presence of the solvent and counterion, both being of critical importance because of the possibility of ion-pairing in the solvated intermediates and, therefore, affecting the stabilization energy of the transition state of the rate-determining-step, and the isomeric distribution of the final products.<sup>1</sup> In particular, the study of solvolytic displacement processes involving neighbouring group participation is often complicated by nucleophilic solvent assistance to the leaving group, which, in some cases, throws doubt on the recognition of anchimerically assisted substitution reactions.<sup>1,2</sup>

Of particular interest are ion-cyclotron-resonance (ICR) mass-spectrometric experiments designed to investigate gas-phase nucleophilic substitutions,<sup>3-5</sup> which provide indirect support for the existence of neighbouring group effects, paralleling those observed in analogous solvolytic processes; however, direct evidence for gas-phase  $S_N1$

reactions is required in order to evaluate their intrinsic features without interference from solvation and ion-pairing effects invariably encountered in solution studies. These conditions have been attained in the gas-phase radiolytic<sup>6</sup> protonation of vicinal halogeno-alcohols, at pressures ensuring efficient collisional deactivation of the ionic intermediates, where the occurrence of intramolecular nucleophilic substitution reactions and their stereochemical features can be directly corroborated by analysis of the neutral end products.<sup>7</sup> The protonation of  $\beta$ -halogeno-substituted alcohols (RCHX-CHOHR, with X = F, Cl, Br, and R = H, Me) was carried out by irradiating (<sup>60</sup>Co source; room temperature) a gaseous system containing CH<sub>4</sub> (760 Torr), in the presence of traces (2-4 Torr) of the alcohol, a thermal radical scavenger (O<sub>2</sub>), and a gaseous base, when required. The neutral products were identified by comparison of their retention volumes, on at least three different g.l.c. columns, with those of authentic samples, and their yields were determined from the areas of the corresponding elution peaks, using individual calibration factors. Radiolysis of CH<sub>4</sub> generates strong gaseous Brønsted acids (C<sub>n</sub>H<sub>5</sub><sup>+</sup>, with *n* = 1,2), in known yields, that are thermally equilibrated by unreactive collisions with the parent molecule before attacking the substituted alcohols.

The ambident nature of the selected substrates has been stressed by Caserio *et al.*,<sup>4</sup> where the ratio of the ionic intensities (R.I.) of the dehydrohalogenated (MH<sup>+</sup> - HX)

TABLE. Products and yields from the gas-phase attack of  $C_nH_5^+$  ( $n = 1,2$ ) on halogeno-alcohols.

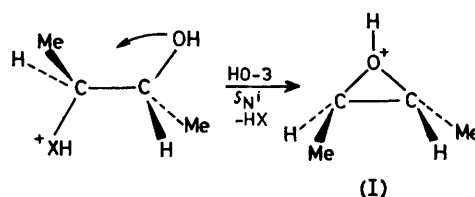
| System composition <sup>a</sup> |    |                 | $G(M)^b$ values          |   |                   |                         |  |        | % Total absolute yields <sup>c</sup> | % R.I.(HX) <sup>d</sup> |
|---------------------------------|----|-----------------|--------------------------|---|-------------------|-------------------------|--|--------|--------------------------------------|-------------------------|
| P[RH(X)C-CH(OH)R]/Torr          | X  | R               | P(H <sub>2</sub> O)/Torr | RHC $\overline{O}$ CHR<br><i>trans</i> <i>cis</i> |                   | RCH <sub>2</sub> -C(O)R | R(OH)CH-CH(OH)R<br><i>meso</i> ( $\pm$ ) |        |                                      |                         |
| 3-2                             | F  | H               | —                        | n.d. <sup>e</sup>                                 |                   | 1.007                   | n.d. <sup>e</sup>                        |        | 35.96                                | 38                      |
| 3-4                             | F  | H               | 1.4                      | 0.140   |                   | 1.119                   | 0.168                                    |        | 50.96                                | —                       |
| 3-4                             | F  | H               | 3.4                      | 0.042   |                   | 0.603                   | 0.243                                    |        | 31.71                                | —                       |
| 2-5                             | Cl | H               | —                        | 0.078   |                   | 0.412                   | n.d.                                     |        | 17.50                                | 16                      |
| 3-9                             | Cl | H               | 1.6                      | 0.052   |                   | 0.508                   | 0.069                                    |        | 22.46                                | —                       |
| 2-7                             | Br | H               | —                        | n.d. <sup>e</sup>                                 |                   | n.d. <sup>e</sup>       | n.d. <sup>e</sup>                        |        | —                                    | 12                      |
| 2-3                             | Br | H               | 1.0                      | n.d. <sup>e</sup>                                 |                   | n.d. <sup>e</sup>       | 0.250                                    |        | 8.93                                 | —                       |
| 2-0                             | Cl | Me <sup>f</sup> | 1.9                      | 0.424   | 0.051             | 1.100                   | 0.036                                    | 0.0024 | 57.62                                | —                       |
| 2-0                             | Br | Me <sup>f</sup> | 1.8                      | n.d. <sup>e</sup>                                 | n.d. <sup>e</sup> | 0.366                   | 0.019                                    | 0.0016 | 13.81                                | —                       |

<sup>a</sup> CH<sub>4</sub> (760 Torr) and O<sub>2</sub> (4 Torr) present in each experiment. Radiation dose: 4.8 Mrad (dose rate: 0.4 Mrad h<sup>-1</sup>). <sup>b</sup>  $G(M)$  values are the number of molecules produced per 100 eV absorbed energy. Standard deviation of data *ca.* 10%. <sup>c</sup> Total absolute yields, estimated using  $G(CH_5^+) = 1.9 \pm 0.2$  and  $G(C_2H_5^+) = 0.9 \pm 0.2$ , values measured at a somewhat different CH<sub>4</sub> pressure by P. Ausloos, S. G. Lias, and R. Gordon, Jr., *J. Chem. Phys.*, 1963, **39**, 3341. <sup>d</sup> See the text and ref. 4. <sup>e</sup> n.d. not detectable [ $G(M) < 1.0 \times 10^{-3}$ ]. <sup>f</sup> *Erythro* configuration.

ions to the dehydrated (MH<sup>+</sup> - H<sub>2</sub>O) ions increases in the order: Br (0.1) < Cl (0.2) < F (1.0). Also, as reported in the Table, the quantities R.I.(HX) =  $I(MH^+ - HX)/I(MH^+)$ , which represent the fraction of ions formed by proton transfer to the halogeno-alcohol M that dissociates by HX loss, closely parallel the absolute yields of products obtained from HX substitution in the radiolytic experiments

This further substantiates the assumption that, at least in apolar or moderately polar aprotic gaseous media, a strict correlation exists between the behaviour of the reactive ionic species at 10<sup>-6</sup> Torr (ICR) with that at 760 Torr (radiolysis).<sup>7</sup>

The data in the Table provide direct evidence that, after attack of the gaseous Brønsted acids on the halogen, extensive HO-3 type participation takes place involving the intermediacy of the *O*-protonated alkene oxide (I), which, depending on the experimental conditions and on the nature of the added base, gives rise to three different competitive processes: (i) proton transfer to the base, producing neutral alkene oxide; (ii) isomerization to the more stable *O*-protonated carbonyl compound,<sup>8</sup> (iii) intermolecular nucleophilic displacement on the *O*-protonated alkene oxide (I) by water, with formation of an *O*-protonated 1,2-glycol. When attack of the Brønsted acids does not destroy the chiral centres in the substrates, the nature and the isomeric distribution of the neutral products give strong evidence in favour of a single-step S<sub>N</sub>i reaction, with inversion of configuration. A similar bimolecular displacement process



occurs in the formation of the 1,2-glycols, whose configurational distribution confirms the intermediacy of (I) and suggests that, in general, nucleophilic substitutions in the gas phase are accompanied by Walden inversion as with S<sub>N</sub>2 processes in solution chemistry. Despite their preliminary nature, the present results provide direct evidence of the occurrence of extensive gas-phase neighbouring group participation HO-3 type processes and furnish additional information on the stereochemistry of the gas-phase nucleophilic substitution reactions, and on the strong tendency of the intermediate (I) to isomerize to the protonated carbonyl compound. However, comparison between the gas-phase and the solvolytic intramolecular substitutions requires more detailed studies, in particular direct kinetic evidence of anchimerically assisted reactions.

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<sup>4</sup> J. K. Kim, M. C. Findlay, W. C. Henderson, and M. J. Caserio, *J. Amer. Chem. Soc.*, 1973, **95**, 2184.

<sup>5</sup> T. H. Morton and J. L. Beauchamp, *J. Amer. Chem. Soc.*, 1975, **97**, 2355.

<sup>6</sup> Radiolysis of gaseous mixtures is a well established technique to generate unsolvated ionic species, at atmospheric pressure. For a review, see P. Ausloos, in 'Ion-Molecule Reactions,' ed. J. L. Franklin, Plenum, New York, 1970; P. Ausloos, S. G. Lias, and A. A. Scala, 'Ion-Molecule Reactions in the Gas Phase,' Amer. Chem. Soc., New York, 1970, p. 264; P. Ausloos, *Progr. Reaction Kinetics*, 1969, **5**, 113.

<sup>7</sup> Gas-phase intermolecular nucleophilic displacement reactions, promoted by radiolytic protonation of halogenated substrates, have been recently investigated (F. Cacace and M. Speranza, *J. Amer. Chem. Soc.*, 1976, **98**, 7299; M. Speranza and F. Cacace, *ibid.*, 1977, **99**, 3051. P. Giacomello and M. Speranza, *ibid.*, 1977, **99**, 7918.

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