Do Gas-phase Reactions between Alcohols and Protonated Alcohols proceed through S_N2 Transition States? An *Ab Initio* Study

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Ab initio calculations (GAUSSIAN 82, SCF 4-31G) indicate that methanol can react with protonated methanol to form two initial intermediates. The minor route produces a species where the methanol oxygen is hydrogen-bonded to the methyl hydrogen atoms of $Me\overset{+}{O}H_2$; the major route involves formation of a hydrogen bond between the methanol oxygen and an oxonium hydrogen to produce an unsymmetrical bismethanolhydrogen(1+) ion. Both initial intermediates react further to form the dimethyl oxonium ion plus water: the former reaction proceeds efficiently through an S_N2 transition state, the latter by a less efficient process involving the same S_N2 transition state.

The gas-phase positive ion chemistry of alcohols was one of the first areas to be extensively studied by ion cyclotron resonance (i.c.r.) and high-ressure mass spectrometry.[1–6] It was proposed[4] that the reaction between an alcohol (*e.g.* methanol) and its protonated form produced both stable and decomposing forms of a bismethanolhydrogen(1+) ion (a), the decomposing form of which eliminates water to produce a protonated ether (d) (Scheme).

The reaction between methanol and protonated methanol can be considered a prototypical nucleophilic substitution (displacement), and the following questions need to be answered:

(i) Are routes A and B (Scheme) followed and if so in what relative proportions?

(ii) If both routes are followed, can product ion (d) be formed both through (a) and *directly* through S_N2 transition state (c)?

(iii) If the vibrationally excited ion (a) is produced in significant amounts, does it produce the product (d) through a high-energy S_Ni transition state [*e.g.* (b)] or does (a) rearrange (in some as yet undefined manner) to the S_N2 transition state (c)?

Recent experimental work has provided information concerning these questions. Kleingeld and Nibbering[7] have studied the methanol system using Fourier transform i.c.r. spectrometry. In the reaction between $Me^{16}OH$ and $Me^{18}\overset{+}{O}H_2$, two product ions $Me^{16}\overset{+}{O}(H)Me$ and $Me^{18}\overset{+}{O}(H)Me$ were formed in the ratio 2.8:1, during a 64 ms reaction time in the i.c.r. cell. It was concluded that at least a portion of $Me^{16}\overset{+}{O}(H)Me$ is formed by the S_N2 reaction (1). Morton and co-workers have reported[8] evidence for an S_N2 reaction in an electron bombardment flow study of the butan-2-ol system. When optically active butan-2-ol is used, the configuration of neutral s-butyl ether [formed following deprotonation of the product corresponding to (d)] indicates *inversion* at the reacting carbon centre.

$$Me^{16}OH + Me^{18}\overset{+}{O}H_2 \longrightarrow Me^{16}\overset{+}{O}(H)Me + H_2{}^{18}O \quad (1)$$

Collision-induced mass-analysed ion kinetic energy (c.i.d. m.i.k.e.) spectra of the bismethanolhydrogen ion (a) show loss of water [to form (d)] to be a major process,[9] and infrared laser excitation coupled with i.c.r. has shown this loss of water to be the decomposition of lowest activation energy for this system.[10]

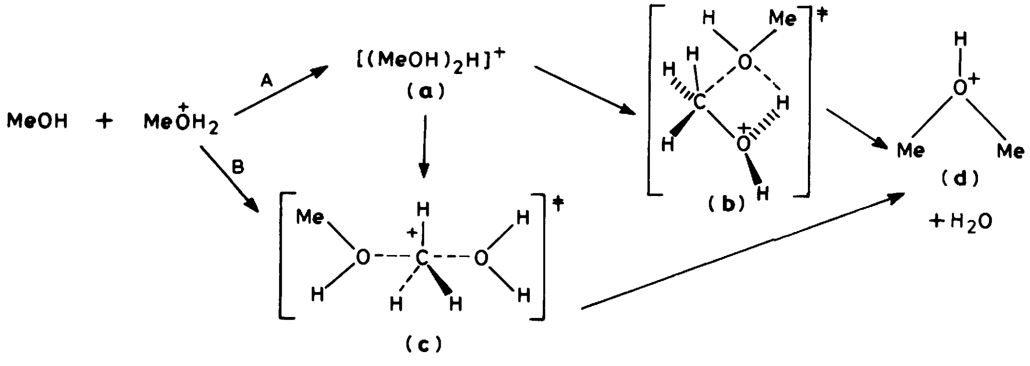
Since (d) can be produced from vibrationally excited (a), Morton's results[8] cast doubt on the intermediacy of S_Ni species [*e.g.* (b)], since such an intermediate should lead to retention of configuration in the butan-2-ol system. Three explanations present themselves to explain reaction through (a) with inversion of configuration:

(i) Vibrationally excited (a) rearranges by some low-energy pathway to (c).

(ii) Vibrationally excited (a) reverts to reactants which then undergo the normal S_N2 process through (c).

(iii) An S_N2 reaction (2) may occur between an alcohol and a bisalcoholhydrogen ion. Of these suggestions, only the first can pertain in a c.i.d. m.i.k.e.s. experiment: in contrast all need to be considered for i.c.r. experiments.

$$ROH + [(ROH)_2H]^+ \longrightarrow R_2\overset{+}{O}H + [H_2O + ROH] \quad (2)$$



Scheme.

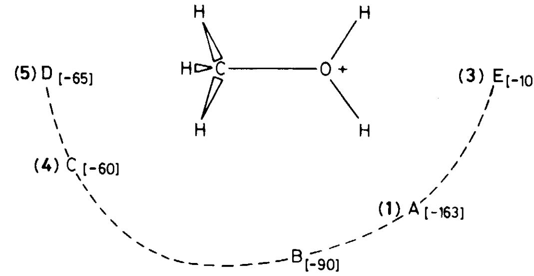


Figure 1. Movement of MeOH around $\mathrm{Me\overset{+}{O}H_2}$ (4-31G level). Numbers in parentheses refer to the structures in Figure 2 or 3. Numbers in square brackets refer to energies (kJ mol^{-1}) at that point

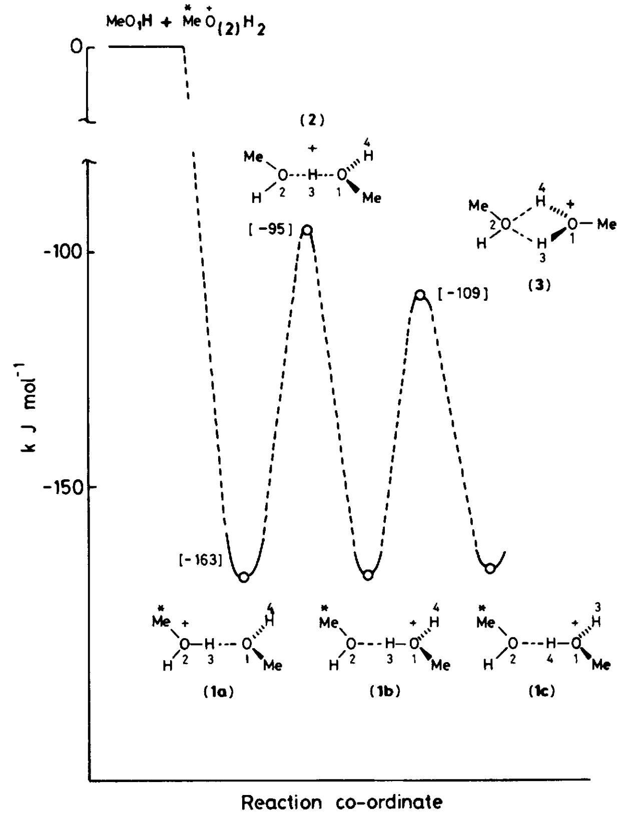


Figure 2. Calculated (4-31G) reaction routes for oxygen and hydrogen equilibration of [$\mathrm{Me\overset{+}{O}H_2}$ --- HOMe]. Circled points are fully optimised geometries. Bond lengths and other distances (Å) are as follows: (**1a**) O(2)–H(3) 1.15, O(1) --- H(3) 1.22; (**2**) O(2) --- H(3) and O(1) --- H(3) 1.18; (3) O(2) --- H(3) and O(2) --- H(4) 2.05

Results and Discussion

Ab Initio Calculations on the $\mathrm{Me\overset{+}{O}H_2}$*–MeOH System.*—We have explored the reaction paths of the Scheme in terms of a series of relaxing and stable supermolecules with the force-minimisation routine of GAUSSIAN 82 (at the SCF 4-31G level).[11] Our results are summarised in Figures 1—3,* and were obtained by general procedures described elsewhere.[12] The approximations we found necessary in order that the calculations should not be too time-consuming are outlined in the following discussion.

Approach of MeOH *to* $\mathrm{Me\overset{+}{O}H_2}$: *Formation of Initial Intermediates.*—The initial orientation of methanol towards the ion determines which of two hydrogen-bonded complexes are formed, and was established by force relaxation runs as follows. Water is a good model for methanol and allows a rapid simulation of the spontaneous approach of the neutral species towards the $\mathrm{Me\overset{+}{O}H_2}$ ion from a variety of directions. This overall motion by water can be summarised as follows. Water approaches the ion directly (from the chosen starting point with oxygen at 4.0 Å from the ion's mass centre) to some 3 Å separation, whereupon it takes an abrupt turn and skirts round the ion until opposite to an oxonium hydrogen to which it then hydrogen-bonds. This expected preference for water to hydrogen-bond to the oxonium hydrogen was displayed even for very large initial angles of approach to the ion's C–O axis, *i.e.* at least as large as 120°. At much larger commencing angles, the water is adjacent to the methyl hydrogen atoms and moves directly into association with these. Methanol proves to behave similarly, as summarised in Figure 1. For example, commencing at an angle of approach of 150°, methanol, at point C, follows a curving track around the $\mathrm{Me\overset{+}{O}H_2}$ ion to the oxonium group, giving the bismethanolhydrogen ion [point A in Figure 1; (**1**) in Figure 3]. In contrast, commencing opposite the methyl group (180° to the C–O axis), methanol moves into association with the trigonal face of the methyl group, bonding weakly to all three hydrogen atoms simultaneously [point D in Figure 1; (**5**) in Figure 3]. We have not determined the exact angle of approach that acts as the boundary separating the formation of the bismethanolhydrogen ion (**1**) from that of the methyl-association complex (**5**) though we judge it to be not much greater than 150°. This suggests that the statistical formation yields will be at least 10:1 in favour of the bismethanolhydrogen ion.

An important result is that neither methanol nor water finds descending routes leading to the S_{N}i reaction [*via* transition state (b) in the Scheme]. The bismethanolhydrogen ion (**1**) can simply convert into the methyl-association complex (**5**) by the methanol orbiting round from the oxonium to the methyl group (from A to D in Figure 1), but in so doing shows no deflection towards the side face of the methyl carbon atom, and towards an association precursor for transition state (b). We have confirmed that the energy required to insert a water molecule (as a model for methanol) in this S_{N}i fashion (at a point corresponding to B in Figure 1) is large, since the transition state lies +90 kJ mol^{-1} above the reactants.

Structure of the Bismethanolhydrogen Ion.—We have 4-31G basis sets to achieve realistic computing speed since we find these bases are adequate to establish the main features of reaction potential-energy profiles.* Our calculations have correctly reproduced the known asymmetry of the bismethanolhydrogen ion. The O–H ··· H distances in crystalline [$\mathrm{(MeOH)_2H]BF_4}$ at −50 °C are reported[14] as 1.16 and 1.23 Å, respectively; *cf.* 1.15 and 1.22 Å in the present work.† In Figure 2 we address the questions (i) what barrier must be overcome in order to 'equilibrate' the two oxygen atoms of the bismethanolhydrogen ion (**1**); and (ii) do the three hydrogen atoms attached to the two oxygen atoms of (**1**) equilibrate, and if so how?

It is not always necessary or practical to vary systematically

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* A detailed tabulation of molecular geometries is available as Supplementary Publication No. SUP 56546 (8 pp.). For details of the Supplementary Publications Scheme, see Instructions for Authors (*J. Chem. Soc., Perkin Trans. 2*, 1986, Issue 1).

* For example, the dissociation of the ethoxide ion into dihydrogen and enolate ion shows the same distinctive two-step mechanism when computed at 4-31G or at 6-311 + + G.[13]

† On the other hand, Potier, Leclercq, and Allavena[15] find that double zeta basis sets without polarisation functions do not reproduce the asymmetry of the bisaquohydrogen ion as observed in a number of crystals.

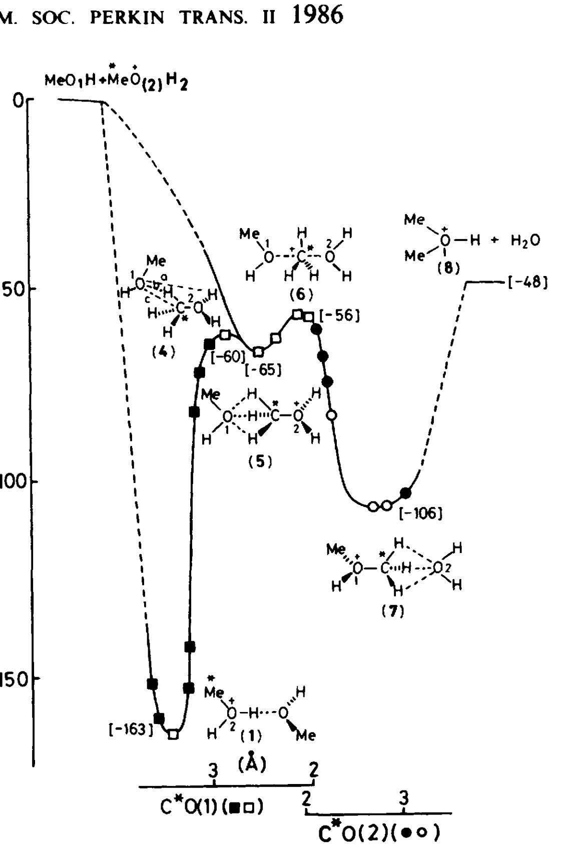


Figure 3. Calculated (4-31G) reaction routes for the formation of $Me_2\overset{+}{O}H$ from MeOH and $Me\overset{+}{O}H_2$. Open symbols (○ or □) represent fully optimised geometries. Filled symbols (● or ■) represent points derived from force relaxation runs. Bond lengths and other distances (Å) are as follows: (**1**) O(2)–H 1.15; O(1) --- H = 1.22; (**4**) a 4.44, b 2.09, c 2.86; (**5**) O(1) --- H = 2.49, O(1) --- C* 2.54, C*–O(2) 1.60; (**6**) O(1) --- C* 2.00, O(2) --- C* 2.09; (**7**) H --- O(2) 2.57, C*–O(2) 2.68, O(1)–C* 1.54; (**8**) C–O(1) 1.51, O(1)–H 0.96.

all possible co-ordinates to determine a reaction pathway, and in the simple cases mentioned above reasonable simplifications were made. First, the interconversion of (**1a**) and (**1b**) shown in Figure 2 plausibly involves the symmetrical species (**2**) as a transition state, and no other structure need be determined in order to evaluate the height of the barrier in this case. Secondly, the exchange of H-3 with H-4 [see (**1b**), Figure 2] must at some stage involve (**3**), a structure with a characteristic plane of symmetry. This lies 52 kJ mol^{-1} above (**1b**) and is a reasonable transition state. Although the barrier heights for the conversions (**1a**) $\rightleftharpoons$ (**1b**) and (**1b**) $\rightleftharpoons$ (**1c**) are relatively high (68 and 52 kJ mol^{-1}, respectively), the excess of energy of formation of (**1a**) is sufficient to overcome the barriers, provided that (**1a**) is neither collisionally nor radiatively deactivated.

Product Formation by the S$_N$2 *Mechanism.*—Before considering the formation of products from (**1**), it is expedient to deal with the S_N2 reaction since it can be seen from Figure 3 that the two reaction routes have features in common.

The attachment of methanol to the methyl hydrogen atoms of $Me\overset{+}{O}H_2$ to produce (**5**) (Figure 3) is statistically a minor process, since methanol can only approach within an 150—210° arc of the C–O axis of the ion if it is to form the intermediate (**5**). There is a small barrier to the classical S_N2 transition state (**6**), subsequent to which (**6**) collapses to the intermediate (**7**). This intermediate, which corresponds to protonated dimethyl ether solvated with water through methyl hydrogen atoms, has excess of energy and spontaneously decomposes by elimination of water. The overall reaction is 48 kJ mol^{-1} (4-31G) exothermic.

Product Formation from the Bismethanolhydrogen Ion.—The major route of the reaction between MeOH and $Me\overset{+}{O}H_2$ leads to the bismethanolhydrogen ion (**1**) (Figure 3), and it has been shown that vibrationally excited (**1**) may decompose to the protonated dimethyl ether ion (**8**) plus water.[9,10] We calculated the enthalpy for the reaction $[(MeOH)_2H]^+ \longrightarrow Me_2\overset{+}{O}H + H_2O$ to be 115 kJ mol^{-1}; this should be compared with the value (75 kJ mol^{-1}) reported previously.[10a] This qualitative agreement is typical of the SCF 4-31G level. It is nonetheless useful in our mechanistic interpretation provided all species are subject to similar errors and the energy relativities are not affected.

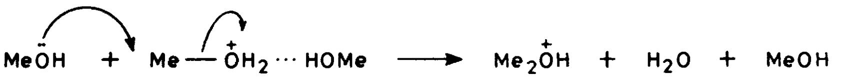
Our aims at this stage were twofold: (i) to determine whether (**1**) may form (**8**) through S_N2 transition state (**6**), and if so by what mechanism, and (ii) to determine whether an S_Ni transition state [*cf.* (b) in the Scheme] is involved in any way in the formation of (**8**) from (**1**). Results of calculations are shown in Figure 3.

Consider reaction (**1**) ⟶ (**8**) (Figure 3): MeO_1H moves around $^*Me\overset{+}{O}_2H_{(2)}$ from its initial position in (**1**) to produce a transition state (**4**) in which MeO_1H is aligned at an estimated 150° to the $^*C–O_{(2)}$ axis. This transition state, which is 103 kJ mol^{-1} above (**1**), is transformed smoothly into (**5**), the precursor of the normal S_N2 reaction already described. No evidence is obtained for an S_Ni species, and it has already been demonstrated that such a species is not formed directly in the reaction between MeOH and $Me\overset{+}{O}H_2$. Reaction (**1**) ⟶ (**8**) therefore involves 'backside' attack to produce the key S_N2 transition state (**6**). *Thus reaction with a chiral alcohol would produce inversion of configuration at the reacting carbon centre*, as observed experimentally.[8]

It is probable that reaction (**1**) ⟶ (**8**) will be slower and less efficient than the S_N2 reaction already described, since (**1**) ⟶ (**4**) has an activation energy of 103 kJ mol^{-1} whereas the comparable barrier for the S_N2 process is only 9 kJ mol^{-1} [(**5**) ⟶ (**6**)]. In addition, oxygen and hydrogen equilibration of (**1**) [(**1a**) ⟶ (**2**) and (**1b**) ⟶ (**3**), Figure 2] have activation energies of 68 and 52 kJ mol^{-1}, and these reactions should compete effectively with (**1**) ⟶ (**4**). So although previous data show that the relative efficiency of production of (**1**) and (**5**) is *ca.* 10:1, the formation of product (**8**) by the two described processes will certainly not be in this ratio, and it would not be surprising if they were similar in extent.

The Precursor(s) of the Product $Me\overset{+}{O}H_2$ *in I.c.r. Experiments.*—In the foregoing sections we have considered the formation of the product ion $Me_2\overset{+}{O}H$ only by the reactions between MeOH and $Me\overset{+}{O}H_2$. Yet in the introduction we suggested that there may be other modes of formation of the product ion, *e.g.* by an S_N2 reaction involving methanol and the bismethanolhydrogen ion.

In order to determine the precursor(s) of the product ion $Me_2\overset{+}{O}H$, ion cyclotron double resonance experiments were carried out with a trapped ion i.c.r. spectrometer[16] using various pressures and reaction times. At low pressures (*e.g.* 5×10^{-7} Torr of MeOH) and low reaction times (*e.g.* 1×10^{-3} s), the major precursor of $Me_2\overset{+}{O}H$ is $Me\overset{+}{O}H_2$, with a *minor* contribution from $[(MeOH)_2H]^+$ (**1**). As either the pressure or the reaction time is increased, (**1**) becomes a more important precursor. For example at 5×10^{-6} Torr and 5×10^{-2} s, ion cyclotron double resonance experiments indicate that $Me\overset{+}{O}H_2$



$$Me\overset{-}{O}H + Me-\overset{+}{O}H_2\cdots HOMe \longrightarrow Me_2\overset{+}{O}H + H_2O + MeOH \quad (3)$$

and (**1**) are both major precursors of $Me_2\overset{+}{O}H$. The ion (**1**) can of course revert to reactants (*i.e.* $Me\overset{+}{O}H_2$ and MeOH) but, at *long* reaction times and high pressures, the S_N2 reaction (2) must be taken into consideration when evaluating previous experimental results.

Conclusions.—We have gone some way to answering the questions raised initially. In summary:

(i) There are two ways in which methanol can add to protonated methanol, *viz.* a major route involving reaction at an oxonium hydrogen to form an unsymmetrical bismethanolhydrogen ion (**1**), and a minor route resulting in the formation of the intermediate (**5**), a species where methanol hydrogen-bonds to the methyl hydrogen atoms of $Me\overset{+}{O}H_2$.

(ii) The initial intermediates (**1**) and (**5**) competitively eliminate water to form the dimethyl oxonium ion (**8**). The more efficient process involves the minor intermediate (**5**), which rearranges directly to an S_N2 transition state. The second process involves migration of the methanol of (**1**) to produce ultimately the same S_N2 transition state as already mentioned. The latter process also competes with reactions which effectively equilibrate both oxygen and (certain) hydrogen atoms of the bismethanolhydrogen ion (**1**).

(iii) No evidence is available to suggest the intervention of an S_Ni transition state in $MeOH-Me\overset{+}{O}H_2$ reactions.

(iv) Under experimental i.c.r. conditions, with long reaction times and/or high cell pressures, both $Me\overset{+}{O}H_2$ and $[(MeOH)_2H]^+$ (**1**) are precursors of $Me_2\overset{+}{O}H$. Calculations of MeOH–(**1**) reaction routes have not been carried out. However it is likely that there will be at least two routes [*cf.* (i) and (ii)], one of which will be the S_N2 process (3).

Experimental

Calculations were performed with a VAX 11 computer using the standard procedures of GAUSSIAN 82 (4-31G level).[11] The i.c.r. spectra were determined with a trapped-ion instrument[16] operating at 70 eV, $\omega_c/2\pi$ = 153.7 kHz, and other experimental conditions indicated in the text.

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