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CARBON VERSUS OXYGEN ALKYLATION OF GASEOUS NUCLEOPHILES

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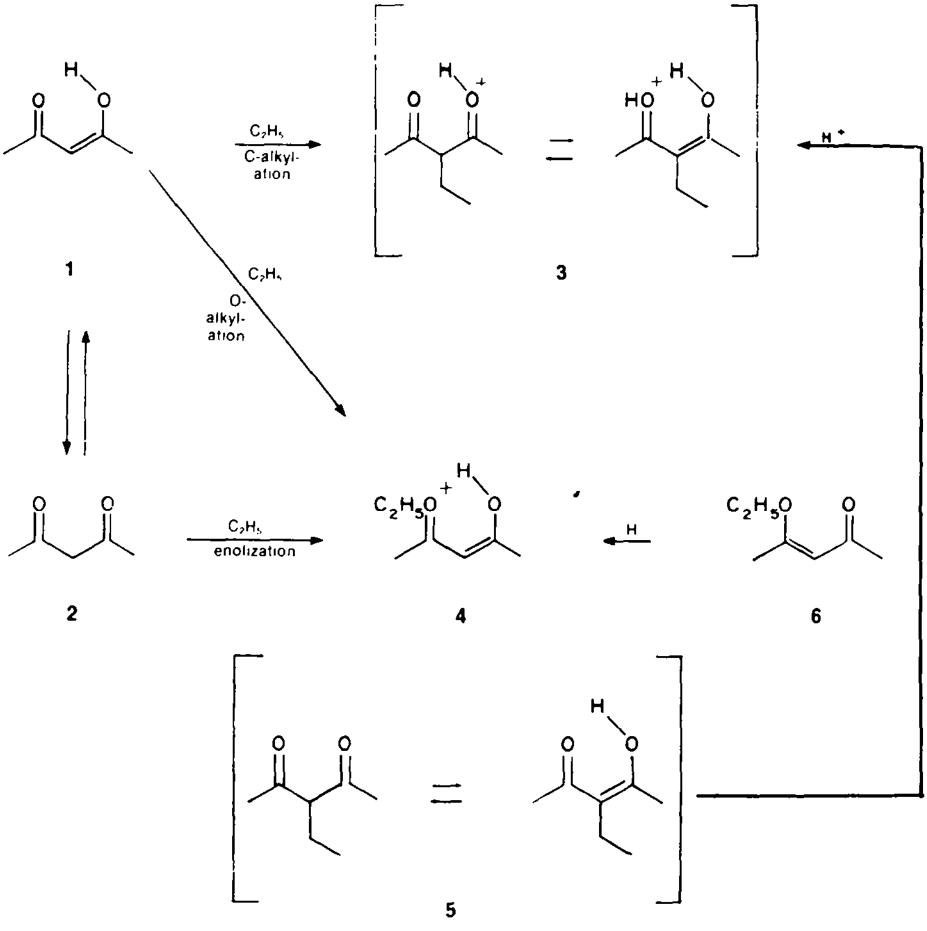
Abstract—The reaction of gaseous ethyl cations with the ambident nucleophile 2,4-pentanedione produces o-alkylation, in agreement with the "hard and soft" acid-base principle.

Recent investigations of gas-phase ionic reactions using ion cyclotron resonance[1,2] or chemical-ionization (CI) mass spectrometry[3-6] have shown encouraging correspondence between these results and the much more extensive body of data on condensed-phase reactions. Here we extend studies of ionic alkylations in the gas phase[1-4] to those involving ambident nucleophiles.[7] Such condensed phase reactions have provided definitive tests of the "hard and soft acids and bases" (HSAB) principle,[8,9] which predicts that hard acids (strong electrophiles) prefer to combine with hard bases (strong nucleophiles), and soft acids prefer to combine with soft bases. The reactivity of gaseous protons, a very "hard" acid, does not always follow these predictions; CI cross-sections for *initial* o- and N-protonation are comparable in some aminoalcohols.[5] CI protonation of olefinic methyl esters occurs at the C=C bond (a "soft" nucleophilic center) as well as at oxygen.[6] We chose to explore this further with gaseous ethyl alkylations, as the "hardness" of $C_2H_5^+$ for solution alkylation varies with its leaving group; acetophenone gives O/C alkylation ratios of 0.1 and 4.9 with ethyl iodides and triethyloxonium fluoroborate,[10] respectively, indicating that the $C_2H_5^+$ is more "naked" with the latter leaving group. We show here (Scheme) that alkylation of 2,4-pentanedione with "naked" $C_2H_5^+$ ions is predominantly (>95%) on the "hard" oxygen (not the "soft" carbon) nucleophilic center, as predicted by HSAB.



Scheme 1.

Table 1. Collisional activation mass spectra of isomeric $C_7H_{13}O_2^+$ ions

m/z	$CH_3COCH_2COCH_3$ + $C_2H_5^+$	$C_2H_5OCH(CH_3)=CHCOCH_3$ + H^{+a}	$CH_3COCH(C_2H_5)COCH_3$ + H^{+a}
15	1	3	8
27	2	2	3
29	4	4	3
39	1	2	2
41	2	2	4
43	25	26	100
69	5	6	6
71	<1	<1	8
83	<1	<1	2
85	12	15	27
87	<1	<1	47
101	100	100	6
113	5	5	12

[a] Spectrum corrected for contributions from $C_6{}^{13}CH_{12}O_2^+$ impurity (<10%) in the precursor ions.

Chemical ionization with methane as a reagent gas was used to generate the reactant ions $C_2H_5^+$ and $C_3H_5^+$ along with the dominant CH_5^+ ion. Addition of 2,4-pentanedione to the ion source gave the protonated molecular ion at *m/z* 101 as the most abundant product. An *m/z* 129$^+$ ion of 5% intensity (relative to *m/z* 101) corresponds in mass to the product expected from alkylation with the "hard" electrophile $C_2H_5^+$; no products (< 0.5% of *m/z* 101) were observed at *m/z* 141 which would correspond to addition of $C_3H_5^+$, a "softer" alkylating agent.

C- and O-alkylation of 2,4-pentanedione should yield the products **3** and **4**, respectively (Scheme 1). These can be formed directly from the enol, **1**, which is the dominant (92%) gaseous form at 25°C,[11] while O-alkylation of the keto form **2** would give **4** after tautomerization. To characterize the structure of the $(M+C_2H_5)^+$ ion, ions which should correspond to structures **3** and **4** were made by the CI protonation of 3-ethyl-2,4-pentanedione (**5**) and of 4-ethoxy-3-pentene-2-one(**6**). Protonation of **5** should yield **3** as a mixture of enol and keto forms; a sufficient number of collisions take place under CI conditions that the enol/keto ratio should be similar to that of products from C-alkylation of **1** under CI conditions.[1,2]

The collisional activation (CA) mass spectrum [12] of the product from the ethylation of 2,4-pentadione agrees with that of reference ion **4** (Table 1) within experimental error, and is substantially different from the CA spectrum of **3**. These data indicate that < 5% of the product is the C-alkylated isomer **3**. As expected from the HSAB principle,[8,9] the "bare" ethyl cation, a "hard" acid, has alkylated the oxygen "hard base" site.

Further studies of the alkylation of hard and soft electrophiles with ambident species such as phenol, thioesters, amides, and carbamates should provide a more detailed picture of this gas phase chemistry.

EXPERIMENTAL

A triple analyzer MS/MS instrument was used which consists of an Hitachi RMH-2 double-focusing mass spectrometer as MS-I, a helium molecular beam collision system, and an electrostatic analyzer as MS-II, with ion source 150° (CI, CH_4 reagent gas) and ion kinetic energy 10 keV.[13] The CA spectra were averages of several multiscan runs; product ions formed by low energy reactions (those which can be formed by metastable ion decompositions) were not omitted from the tabulated CA spectra, as the internal energies of the precursor ions formed under CI conditions should not vary widely. 2,4-Pentanedione and 3-ethyl-2,4-pentanedione were obtained commercially. 4-Ethoxy-3-pentene-2-one was synthesized from the silver salt of 2,4-pentanedione.[14]

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