Acid Catalyzed Aldol Condensation in the Gas Phase

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The gas phase reaction of acetaldehyde with a Brønsted acid in a chemical ionization source yields protonated crotonaldehyde, as shown by its collisional activation mass spectrum. This is thus analogous to the well known aldol condensation in solution, in which the initial aldol adduct loses water to yield crotonaldehyde. The possibility of a common mechanism for the gas phase and solution reactions is discussed.

A variety of recent studies have shown encouraging parallels between well known ionic reactions in solution and their gaseous counterparts studied by ion cyclotron resonance[1,2] and chemical ionization (CI)[3,4] mass spectrometry. Examples of such similar behavior include classic reactions such as nucleophilic substitution,[1] the Michael addition,[2] Fisher indole synthesis[3] and pinacol rearrangement.[3,4] We report here evidence for an acid catalyzed aldol addition/condensation[5] in the gas phase.

Under CI conditions (methane reagent gas) acetaldehyde (**1**) gives the mass spectrum shown in Table 1. The protonated molecular ion *a* (m/z 45) is the most intense peak, while the ion of highest mass (m/z 89) corresponds to $[2M+H]^+$. The latter could be the proton bound dimer *b* (Scheme 1) or the protonated product *c* expected from aldol addition of the enol **2** to *a*.[5] A common further reaction of neutral aldol addition products is dehydration,[5] which for **1** would produce crotonaldehyde (**3**); for CI conditions this would correspond to the $[2M+H-H_2O]^+$ ion at m/z 71 of structure *e*.

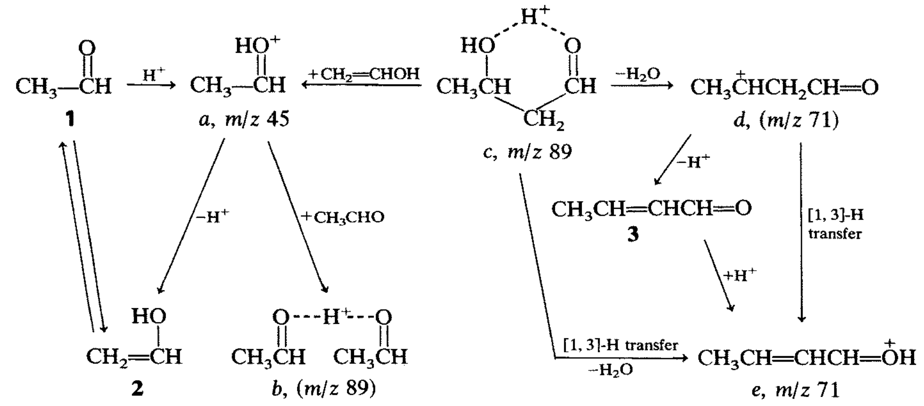
Table 1. Chemical ionization spectrum of acetaldehyde

m/z	Abundance[a]	m/z	Abundance[a]
45	2400	69	2.8
57	7.5	70	2.8
58	4.3	71	10
59	27	87	2.1
60	6.8	89	2.1
61	35		

[a] % total ion abundance for ions above m/z 45

To determine the structure of this m/z 71 ion, its collisional activation (CA) mass spectrum[6] was measured (Table 2) and compared with that of m/z 71 ions formed by the CI protonation of crotonaldehyde. These CA spectra are identical within experimental error, consistent with the postulated initial aldol addition forming *c*. A mechanistic rationalization of the water loss from *c* is also shown in Scheme 1. Hydrogen loss from the α-position is required for the formation of *e*; this could occur by α-H transfer to the hydroxyl group in *c* followed by H_2O loss yielding *e*, or H_2O loss yielding *d* with α-H transfer to its carbonyl group, but either of these reactions should have high critical energies as they involve symmetry-forbidden 1,3-hydrogen rearrangements. Under the CI conditions, there is a high probability that *d* could lose the α-hydrogen as a proton to form crotonaldehyde, which would reprotonate to form the more stable isomer *e*, the structure expected from the CA data.

A referee has questioned the postulation of the enol **2** as one of the reacting species because its concentration in equilibrium with **1** should be extremely low; **2** is less stable than **1** by 49 kJ mol^{-1}.[7] However, this criticism should also be applicable to the accepted



Scheme 1

CCC-0030-493X/81/0016-0381$01.00

Table 2. Collisional activation spectra of isomeric $[C_4H_7O]^+$ ions[a]

m/z	Precursor		m/z	Precursor	
	CH_3CHO	$CH_3CH{=}CHCHO$		CH_3CHO	$CH_3CH{=}CHCHO$
12	0.7	0.6	42	3.9	3.4
13	0.4	0.5	43	16	11
14	0.8	0.8	44	0.8	0.6
15	2.0	1.8	49	1.1	1.0
25	1.1	1.4	50	3.1	3.3
26	3.5	3.6	51	3.8	3.4
27	12	12	52	0.5	0.5
28	1.4	1.3	53	8.7	12
29	7.4	7.8	55	3.5	3.4
31	4.9	5.4	56	0.6	0.4
36	0.8	0.8	66	0.5	0.4
37	3.1	3.9	67	0.5	0.4
38	4.3	4.3	68	0.5	0.5
39	15	16	69	9.8	9.9
40	1.4	1.3	70	7.6	3.7
41	12	11			

[a] Relative intensities as % of total ion abundance except *m/z* 43, 53 and 70, which can be formed by metastable ion decomposition.[6]

mechanism for the solution phase aldol reaction, which also postulates the addition of **2** to *a*.[5] When ionized, the enol is actually more stable than its keto counterpart;[8] charge exchange could increase the concentration of reactant **2**, or the reaction could also involve formation of *c* through ionized **2** or the dimer *b*. Studies which could provide further clarification include the effect of adding labeled **1** molecules or **2** ions to the reaction and structural identities of other product ions.

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 °C (CI, CH_4 reagent gas), ion kinetic energy 10 keV, and He pressure in the collision region allowing 25% transmittance of the precursor ions.[9] The CA spectra were averages of several runs.

Acetaldehyde and crotonaldehyde were obtained commercially and distilled immediately before use. The electron ionization mass spectrum of acetaldehyde showed no ions (<0.1%) above *m/z* 46.

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