

INTERMOLECULAR REACTIONS OF ENAMINO KETONES SALTS : FORMATION OF AROMATIC COMPOUNDS

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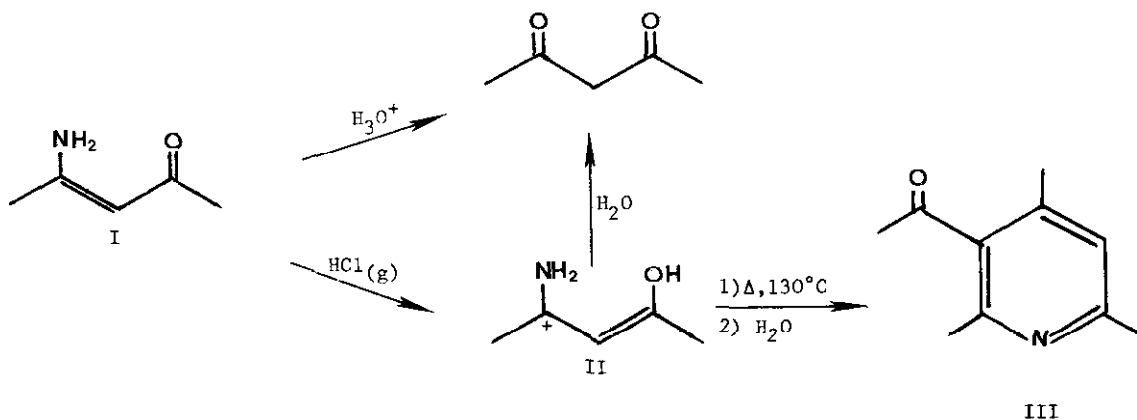
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We have recently pointed out that enamino derivatives of β -tetraketones react with gaseous HCl in an aprotic medium to yield the corresponding chlorohydrates; when poured into water, these do not undergo hydrolysis, but directly supply phenols and aminophenols¹.

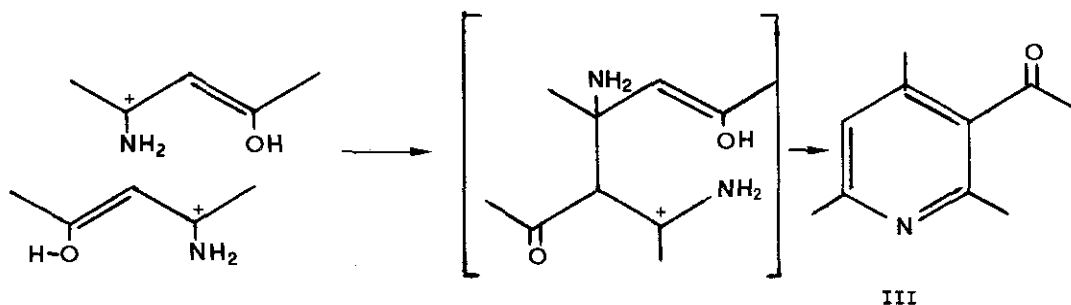
Hence, wishing to get more detailed information on the reactivity of such systems, we thought it useful to study simpler enamino derivatives of β -diketones. It is known that the enamino derivative of acetylacetone(I) on treatment with aqueous acid or through its chlorohydrate(II), obtained with gaseous HCl in ether and poured into water, gives acetylacetone in quantitative yield.

We now find that the chlorohydrate(II), heated to 130°C for 4 hrs followed by treatment with water, gives 2,4,6-trimethyl-3-acetylpyridine(III) in 90 % yield.



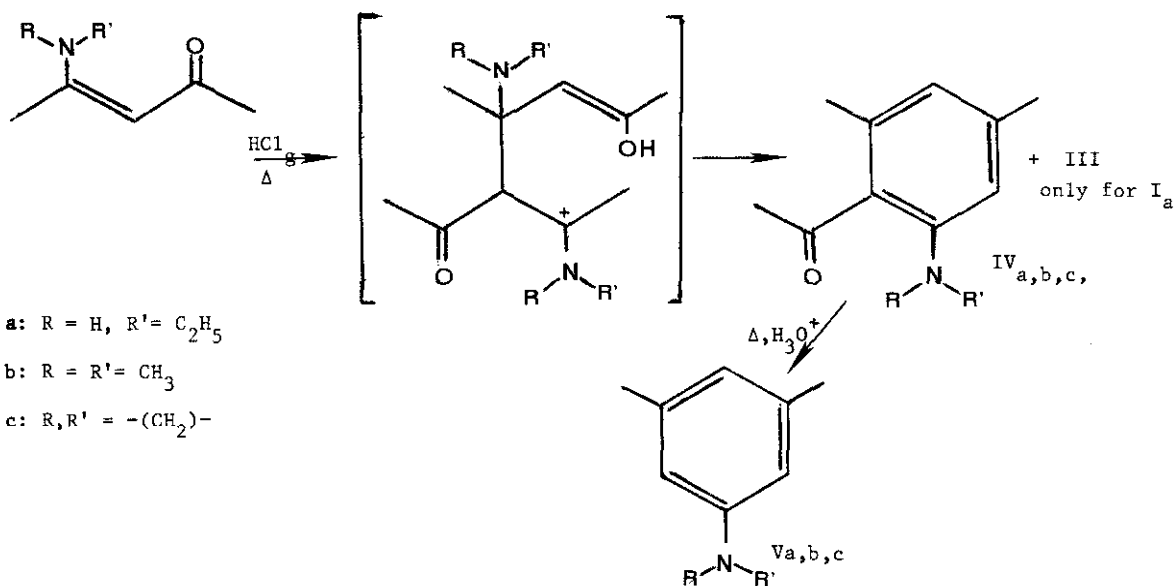
A. Dornow and H. Machens² have found that pyridine(III) may be obtained by heating acetylacetone with ammonium acetate or oxalate, or alternatively in the presence of acetylacetoneimine. Experiments carried out by us with the purpose to obtain more detailed information on the reaction, have shown the importance of the presence of a salified system of type(II). As a matter of fact, thermal treatment under controlled conditions demonstrates that the formation of the pyridine(III) by reaction of chlorohydrate(II) with variable molar ratio of acetylacetone-

imine³ (0 to 1) shows a linear dependence on the molar fraction of the chlorohydrate present. This fact suggests that quite probably the reaction caused by acetylacetone in the presence of ammonium salts takes place through the intermediate formation of a salified enamino ketone that is later transformed into the cyclic compound(III). Therefore, the following mechanism may be assumed for pyridine formation :



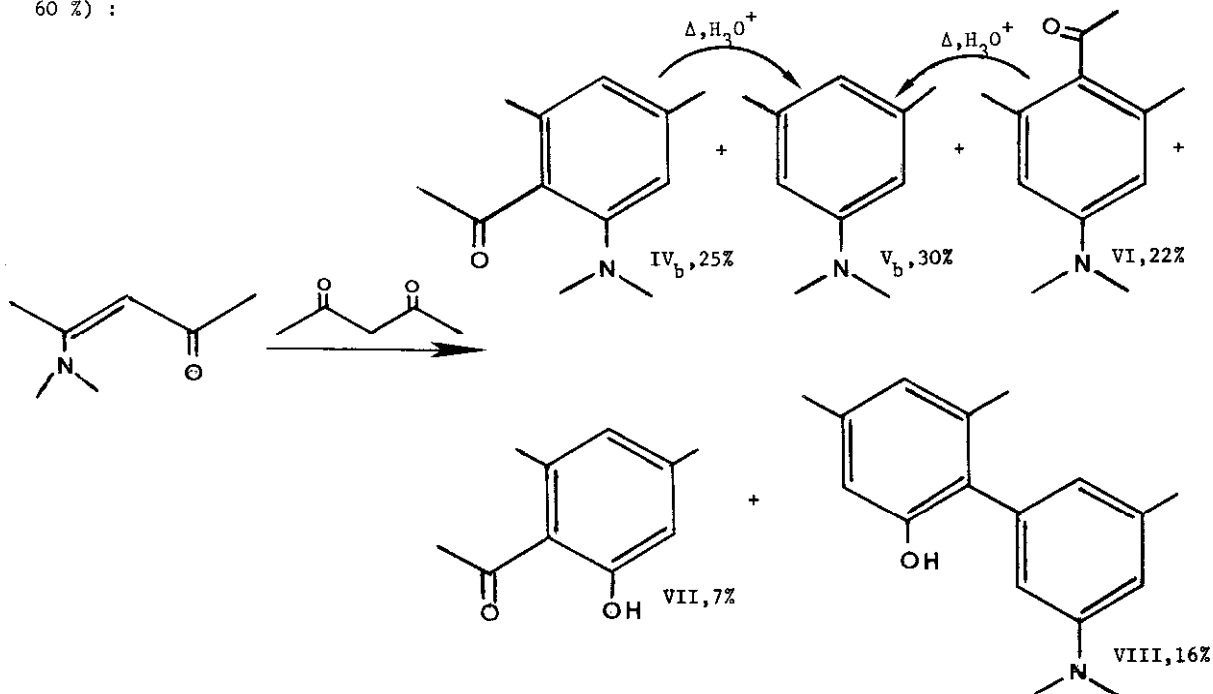
where the salified enamino acts both as an electrophile and a nucleophile.

Surprisingly replacement of hydrogens of the enamino group by alkyl substituents causes a different behaviour of the second reaction step with formation of differently structured compounds. In fact, by heating to 120°C under anhydrous conditions the chlorohydrate of (I_a) gives the substituted aniline(IV_a)⁴ along with small amounts of pyridine (III)⁵. When both hydrogens of the enamino group are replaced by alkyl substituents (I_{b,c}), satisfactory yields of anilines (IV_{b,c})⁴ are obtained together with variable amounts of the corresponding deacetylated compounds (V_{b,c})⁴, in yields of 40 - 50 %⁶.



The ratio of IV/V varies as a function of the reaction temperature and time : (IV) is quantitatively transformed into (V) by heating in an acid environment.

We have also examined the reaction of the enamino ketone (I_b) ($R = R' = CH_3$) in the presence of acetylacetone, by maintaining the reaction mass at $120^\circ C$ for three days. Three further compounds⁷ (VI), (VII) and (VIII) were isolated along with (IV_b) and (V_b) (yield 60 %) :



The structure of (VI) was deduced by its conversion into (V_b) on heating in an acid medium.

The structure of (VIII), which is presumably derived from the condensation of three molecules of (I_b), was determined by chemical analysis, Mass and N.M.R. spectra :

MS m/e : 255 (M^+ , 100); 254 (40); 240 (32); 211 (18); 196 (11); 195 (10); 149 (17).

N.M.R. ($CDCl_3$) δ ppm : 6.65 (s, 2H, $H_{(2)}$ and $H_{(4)}$); 6.58 (m, 1H, $H'_{(2)}$), t by decoupling at 2.32); 6.43 (m, 2H, $H'_{(4)}$ and $H'_{(6)}$), two t by decoupling at 2.32); 2.95 (s, 6H, $N(CH_3)_2$); 2.34 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 2.09 (s, 3H, CH_3).

The N.M.R. spectrum of trichlorocarbamate derivative of (VIII) shows : ($CDCl_3$) δ ppm :

7.20 (s, 1H, $H_{(2)}$); 6.85 (s, 1H, $H_{(4)}$); 6.58 (m, 1H, $H'_{(2)}$); 6.43 (m, 2H, $H'_{(4)}$ and $H'_{(6)}$); 2.95 (s, 6H, $N(CH_3)_2$); 2.34 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 2.16 (s, 3H, CH_3).

The reaction schemes not only demonstrate an interesting reactivity of enamino ketones, but also represent a starting point for the study of the intermolecular condensation of more complex enamino ketonic systems.

References and footnotes

Analytical results agree with the structures of all the products described.

1) S. Auricchio, S. Morrocchi and A. Ricca, Tetrahedron Letters 2793 (1974).

2) A. Dornow and H. Machens, B. 80, 502 (1947).

3) All yields and molar ratios of compounds obtained have been calculated by GLC with internal standard.

4) Compound (IV_a) : liquid, MS m/e : 191 (M⁺,77); 176 (100); 158 (74); 134 (16).

N.M.R. (CDCl₃) δ ppm : 6.30-6.20 (m, 2 H, arom.); 3.10 (q, 2 H, N-CH₂-); 2.45 (s, 3 H, CH₃CO); 2.35 (s, 3 H, CH₃); 2.20 (s, 3 H, CH₃); 1.20 (t, 3 H, CH₃).

Compound (IV_b) : liquid, MS m/e : 191 (M⁺,55); 176 (100); 174 (50); 161 (57); 159 (40); 148 (35). N.M.R. (CDCl₃) δ ppm : 6.60-6.80 (m, 2 H, arom.); 2.70 (s, 6 H, N(CH₃)₂); 2.45 (s, 3 H, CH₃CO); 2.3 (s, 3 H, CH₃); 2.20 (s, 3 H, CH₃).

Compound (IV_c) : liquid, MS m/e : 217 (M⁺,73); 202 (100); 200 (33); 174 (45). N.M.R. (CDCl₃) δ ppm : 6.7-6.5 (m, 2 H, arom.); 3.4-3.1 (m, 4 H, -CH₂NCH₂-); 2.50 (s, 3 H, CH₃CO); 2.32 (s, 3 H, CH₃); 2.25 (s, 3 H, CH₃); 2.1-1.8 (m, 4 H, -(CH₂)₂-).

Compound (V_b) : liquid, MS m/e : 149 (M⁺,74); 148 (100); 134 (15); 133 (19), N.M.R. (CDCl₃) δ ppm : 6.4 (s, 3 H, arom.); 2.9 (s, 6 H, N(CH₃)₂); 2.3 (s, 6 H, 2 -CH₃). Picrate : m.p. 195° C. cf ref. 6.

Compound (V_c) : liquid, MS m/e : 175 (M⁺,66); 174 (100); 132 (8); 119 (41). N.M.R. (CDCl₃) δ ppm : 6.5-6.2 (m, 3 H, arom.); 3.4-3.1 (m, 4 H, -CH₂NCH₂-); 2.3 (s, 6 H, 2 -CH₃); 2.1-2.8 (m, 4 H, C-CH₂-CH₂-C).

5) Compound (III) could be formed via a pyridinium salt.

6) O. Diels and K. Alder, B. 60, 722 (1927).

7) Compound (VI) : liquid, MS m/e : 191 (M⁺,40); 176 (100); 148 (24); 132 (11). N.M.R. (CDCl₃) δ ppm : 6.4 (s, 2 H, arom.); 2.97 (s, 6 H, N(CH₃)₂); 2.45 (s, 3 H, COCH₃); 2.3 (s, 6 H, 2 -CH₃).

Compound (VII) : see A.Heikel, Suomen. Kem. (B) 8, 33 (1935).

MS m/e : 164 (M⁺,30); 149 (100); 121 (8). N.M.R. (CDCl₃) δ ppm : 6.7-6.5 (m, 2 H, arom.); 2.61 (s, 3 H, COCH₃); 2.52 (s, 3 H, CH₃); 2.23 (s, 3 H, CH₃).