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THE BEHAVIOUR OF UNSATURATED 1,2-HYDROXYIMINOKETONES WITH TRIFLUOROACETIC ACID

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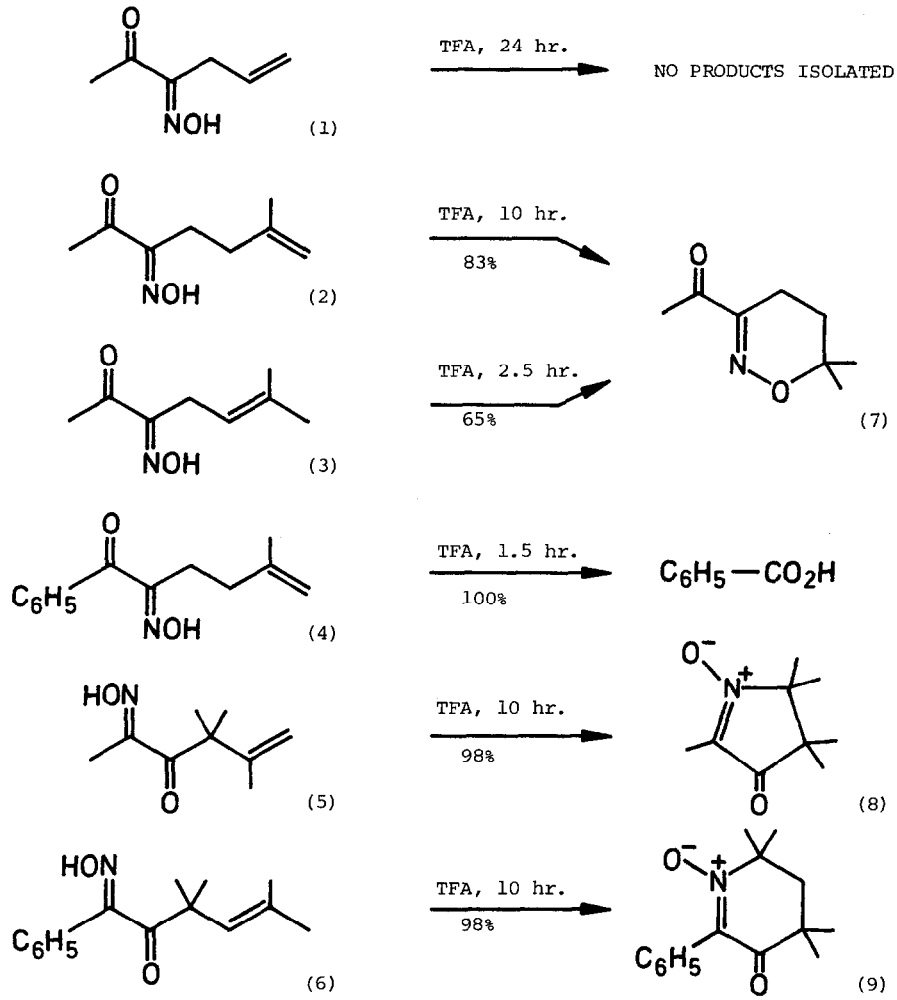
Abstract : (E)-1,2-Hydroxyiminoketones containing an appropriately positioned and substituted olefinic group afford high yields of various 5- and 6-membered heterocyclic systems when reacted with trifluoroacetic acid. Under the same conditions inappropriately substituted unsaturated 1,2-hydroxyiminoketones fragment by means of the second order Beckmann process.

Hydrolysis of 1,2-hydroxyiminoketones using mineral acid is a classical and widely used method[1] for the preparation of the corresponding 1,2-diketones. However, in the course of earlier work on the photochemical behaviour[2] of unsaturated 1,2-diketones we found this procedure to be somewhat erratic in the synthesis of such materials, and consequently other more reliable methods were generally employed. We now present preliminary results showing that the behaviour of unsaturated 1,2-hydroxyiminoketones with acid is more involved than previously realised.

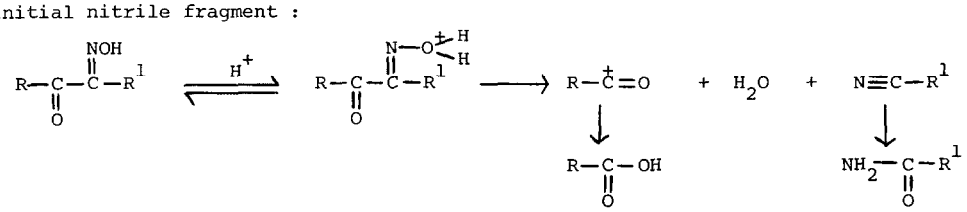
The 1,2-hydroxyiminoketones (1-6) reported here were all synthesised using standard methods. Compounds (1-2) were obtained by treatment of an alkaline solution of the appropriate β-keto acid carboxylate with sodium nitrite[3], whereas (3-6) were formed from the corresponding unsaturated ketone using an alkyl nitrite under basic conditions[4]. All six compounds[5] had the *(E)*-configuration on the basis of their complexation with copper(II) acetate[6], the strong bathochromic shift of λ_{max} on moving to high pH[7], and the chemical shift value of their hydroxyimino proton in dimethylsulphoxide solution[8].

GENERAL REACTION PROCEDURE :

Stoppered solutions of the unsaturated *(E)*-1,2-hydroxyiminoketones (1-6) in neat trifluoroacetic acid (TFA) (0.10 g solute/1 mL solvent) were allowed to stand in a desiccator at room temperature. At regular intervals an aliquot (1 mL) was withdrawn and worked up as follows. Trifluoroacetic acid was evaporated under reduced pressure without heating, water was added to the residue, and organic material extracted using 40-60° petroleum (5 x 15 mL). The combined extracts were washed with water (3 x 5 mL, or till neutral), dried (Na_2SO_4), and the solvent evaporated from the filtrate to give the product. This was then analysed using t.l.c. ($SiO_2/CHCl_3$) and spectroscopic methods. The aliquot affording the highest yield of product determined the time used for preparative scale reactions. These utilised 1-2 g of the solute in TFA (10 mL), and were worked up in the same manner. The reaction times for (1-3) were more critical than those for (4-6) whose products are more stable to acid conditions.



Treatment of 1,2-hydroxyiminoketone (1) with TFA resulted in slow but complete destruction of the starting material and no products were isolated from the reaction. Compound (4) underwent rapid decomposition but gave a quantitative yield of benzoic acid. It has been recognised for many years that while *(Z)*-1,2-hydroxyiminoketones undergo 'normal' Beckmann rearrangement, the more common *(E)*-isomers undergo fragmentation by a process termed the 'abnormal' or 'second order' Beckmann rearrangement[9]. Under the vigorous conditions originally used (e.g. heating with 85% sulphuric acid) the products isolated were a carboxylic acid and an amide, but later workers[10] realised that the latter product resulted from hydrolysis of an initial nitrile fragment :



Since it is well known that trifluoroacetic acid causes second order Beckmann rearrangement of *(E)*-1,2-hydroxyiminoketones to yield carboxylic acid and nitrile fragments[11], it appears that (1) and (4) underwent the anticipated decomposition by this pathway. Under the experimental conditions used here, the only product expected to be isolated would be the involatile and water insoluble benzoic acid fragment from (4).

In contrast to the above behaviour, the remaining four 1,2-hydroxyiminoketones showed quite different reactivity. Each underwent clean reaction resulting in a single heterocyclic product in good to excellent yield. Both (2) and (3) formed the same material which was obtained as a slightly yellowish oil and identified as 3-acetyl-6,6-dimethyl-5,6-dihydro-4*H*-1,2-oxazine (7):

EI m/z$^+$: Found $(M)^+$ = 155.0946 . $(C_8H_{13}NO_2)^+$ requires 155.0941 .

CI m/z$^+$: Found $(M+1)^+$ = 156.1024 . $(C_8H_{14}NO_2)^+$ requires 156.1019 .

ν_{max} (film): 2975s, 1685s, 1580m, 1435m, 1355s, 1280m, 1155m, 965s cm^{-1}.

λ_{max} (CH_3OH): 228 nm (ε = 4000).

^1H δ ($CDCl_3$): 2.42 (s,3H), 2.36 (t,2H,J=7.0 Hz), 1.72 (t,2H,J=7.0 Hz), 1.30 (s,6H).

^{13}C δ ($CDCl_3$): 197.2(s), 154.4(s), 75.3(s), 28.2(t), 25.5(q), 24.9(q), 16.2(t).

Compound (5) also yielded a liquid product which was assigned the structure 2,4,4,5,5-pentamethyl-1-pyrrolin-3-one 1-oxide (8):

EI m/z$^+$: Found $(M)^+$ = 169.1107 . $(C_9H_{15}NO_2)^+$ requires 169.1097 .

CI m/z$^+$: Found $(M+1)^+$ = 170.1181 . $(C_9H_{16}NO_2)^+$ requires 170.1176 .

ν_{max} (film): 2980s, 1710s, 1565s, 1415s, 1380s, 1350s, 1295m, 1160m, 1050w, 1015w, 990w cm^{-1}.

λ_{max} (CH_3OH): 273 nm (ε = 20200).

^1H δ ($CDCl_3$): 1.96 (s,3H), 1.40 (s,6H), 1.16 (s,6H).

^{13}C δ ($CDCl_3$): 203.0(s), 138.2(s), 79.6(s), 49.6(s), 23.5(q), 21.4(q), 7.5(q).

Finally, the 1,2-hydroxyiminoketone (6) was converted into a low melting solid identified as 2-phenyl-4,4,6,6-tetramethyl-5,6-dihydro-3(4*H*)-pyridinone 1-oxide (9):

(Found: C,73.38; H,7.85; N,5.66 . $C_{15}H_{19}NO_2$ requires C,73.44; H,7.81; N,5.71%).

m.p. 65-68°C (from light petroleum).

ν_{max} (KBr disc): 3020w, 2928s, 1650s, 1501m, 1283m, 995s, 701s, 630s cm^{-1}.

λ_{max} (CH_3OH): 296 nm (ε = 3800), 238 nm (ε = 3600).

^1H δ (d_6-DMSO): 7.35-7.39 (m,3H), 7.25-7.28 (m,2H), 2.27 (s,2H), 1.55 (s,6H), 1.26 (s,6H).

^{13}C δ ($CDCl_3$): 195.4(s), 142.3(s), 130.0(d), 129.6(s), 129.2(d), 127.8(d), 70.5(s), 46.3(t), 40.1(s), 29.2(q), 27.4(q).

Formation of the products (7-9) is compatible with intramolecular cyclisation in accord with Markownikoff's rule. For reagents (2) and (3) the hydroxyimino oxygen is involved producing a cyclic oxime ether derivative, while for (5) and (6) involvement of the hydroxyimino nitrogen atom leads to formation of cyclic nitrones. These isomeric functional groups can be readily distinguished from each other by various data, in particular the u.v. λ_{max} values and ^{13}C n.m.r. chemical shifts[12].

As demonstrated by the behaviour of (1), the substitution of the olefinic group of the 1,2-hydroxyiminoketone must be capable of giving a tertiary carbenium ion for

cyclisation to compete effectively with fragmentation. This is also encouraged by structures such as (4) capable of producing an aromatic substituted acylium ion fragment. Although formation of other ring sizes is possible, the most efficient examples are those leading to 5- and 6-membered heterocyclic systems.

Within these limitations, this procedure provides a simple new synthetic route which complements the current approaches to these heterocyclic structures. Most commonly, 3-acetyl-5,6-dihydro-4*H*-1,2-oxazines are prepared by cycloaddition of alkenes and 3-nitrosobut-3-en-2-one[13]; 1-pyrrolin-3-one 1-oxides by oxidation of the 1-pyrroline 1-oxide or via the 3-hydroxyimino derivative[14]; and 5,6-dihydro-3(4*H*)-pyridinone 1-oxides by acid catalysed ring expansion of 2-acyl-1-pyrroline 1-oxides[15].

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