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THE SYNTHESIS OF A NEW MESOIONIC AROMATIC SYSTEM AND THE MECHANISM OF DAKIN - WEST REACTION

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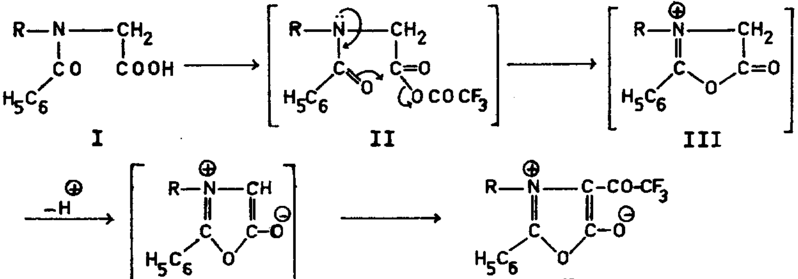
Recent publications by Huisgen et. al.[1,2,3,4]describing a new mesoionic system prompt us to put our* own findings in this field on record.

We have found, that when N-benzoylphenylglycine I (R = C_6H_5) is treated with trifluoroacetic anhydride at room temperature, there results the formation of the mesoionic system V incorporating the elements of trifluoroacetyl group, as bright yellow crystals, m.p. 195-96° in almost quantitative yield. Found C, 60.96 H, 3.47 N, 4.61 F, 16.84; $C_{17}H_{10}O_3NF_3$ requires C, 61.26 H, 3.00 N, 4.20 F, 17.11. We consider that the reaction proceeds through the mixed anhydride II to the oxazolonium cation III which on subsequent loss of a proton yields the parent mesoionic system IV.



I II III IV V

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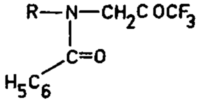
*The new mesoionic aromatic system was described by us in a paper presented at the annual meeting of the Indian Science Congress in Sept., 1963 at Delhi before the appearance of Huisgen's

Substitution reaction with trifluoracetic anhydride yields the trifluoroacetyl derivative V.

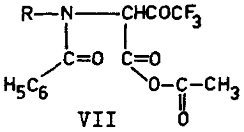
The new system incorporating the oxazole skeleton can, however, be formulated only as a completely polarized structure and is analogous to the sydnone system derived by a similar cyclodehydration of N-nitroso-N-alkylamino acids[5].

The mesoionic system V containing trifluoroacetyl group are quite stable substancesand can be readily crystallised from boiling benzene. An infrared spectrum of V ($R = C_6H_5$) reveals a doublet in the carbonyl region with bands at 5.55μ and 5.62μ. These bands can be assigned respectively to the pseudo lactone and the trifluoroacetyl carbonyl groups. Haszeldine[6] has reported a value of 5.65μ for α-fluoroketones.

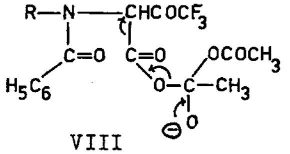
When subjected to the action of refluxing acetic anhydride, the mesoionic compound V ($R = C_6H_5$) leads to decarboxylation and the formation of N-benzoylphenylamino-trifluoroacetone VI ($R = C_6H_5$), m.p. 85° in high yield. Found C, 62.14 H, 4.16 N, 4.23 F, 18.23; $C_{16}H_{12}O_2NF_3$ requires C, 62.21 H, 3.90 N, 4.46 F, 18.56. Treatment with boiling water also results in slow evolution of carbondioxide. In the infrared the ketone VI ($R = C_6H_5$) exhibits two bands at 5.62μ and at 6.00μ in the carbonyl region which are ascribed respectively to the trifluoroacetyl and the amide linkage. The action of boiling acetic anhydride on V can be considered to lead to the mixed anhydride VII following essentially the reversal of steps (IV → II) indicated above. Further attack by an acetate ion in the manner indicated below (structure VIII) leads to decarboxylation and the formation of the ketone VI.



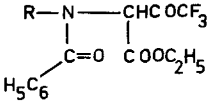
VI



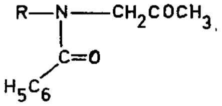
VII



VIII



IX



X

Treatment of the mesoionic compound V with ethyl alcohol brings about a very facile and quantitative opening of the mesoionic system to the corresponding β-ketoester IX which are obtainable as colourless oils and develop strong colour with alcoholic ferric chloride. The β-ketoester can be distilled almost unchanged when subjected to rapid distillation under high vacuum. Found C, 60.00 H, 4.15 N, 3.45 F, 14.87; $C_{19}H_{16}O_4NF_3$ requires C, 60.15 H, 4.22 N, 3.69 F, 15.03.

The Dakin-West[7] reaction which consists in the conversion of α-amino acid (or the corresponding α-acylamino acid) by treatment with boiling acetic anhydride (with or without the use of pyridine as a catalyst) to the corresponding α-acylaminoketone, in our opinion proceeds through the intermediate formation of the mesoionic system of the type IV. This system like sydnone has 6π electrons associated with the ring and is therefore aromatic[8]. A typical electrophilic substitution with an anhydride yields the acylated mesoionic structure analogous to V. Further reaction in boiling acetic anhydride leads to the formation of the Dakin-West type ketone VI.

The mesoionic systems V with (R = p-$CH_3C_6H_4$ and cyclohexyl) were also similarly obtained in high yields as bright yellow crystals, m.p. 247° and 194° respectively. The corresponding ketone VI (R = p-$CH_3C_6H_4$) had melting point 90°. The elemental analysis (C,H,N and F) for all these compounds was satisfactory.

When cyclisation of the acylamino acids of the type I was studied with acetic anhydride the intermediate formation of the mesoionic system corresponding to IV and V was quite evident as seen by the formation of yellow coloured solutions. However, the only isolable product in high yield was the ketone corresponding to X (R = C_6H_5; p-$CH_3C_6H_4$) having m.pts. 89° and 101° respectively. Presumably the mesoionic systems carrying the acetyl group are more sensitive and undergo cleavage more readily. It seems pertinent to point out that Huisgen et. al. (loc. cit.) who studied the cyclisations with acetic anhydride have also not reported the actual isolation or the physical constants of any of their mesoionic products. The introduction of a trifluoroacetyl group appears to confer greater stability to the mesoionic system.

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