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A NEW METHOD FOR THE SYNTHESIS OF UNSATURATED 2,4-DISUBSTITUTED 2-IMIDAZOLIN-5-ONES[1].

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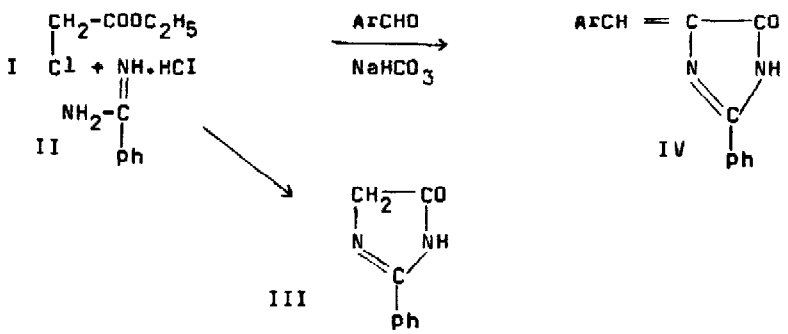
Unsaturated 2,4-disubstituted 2-imidazolin-5-ones(IV) which are the nitrogen analogs of azlactones (IV, -O- instead of -NH-) form an important class of heterocyclic compounds because they can be converted into α-amino acids and their derivatives in good yields[2,3]. There are three general methods[2,4,5,6] for the synthesis of unsaturated 2-imidazolin-5-ones(IV), namely azlactone, amidine-glyoxal and imidic acid ester-glycine ester methods but the first two methods are not of much practical importance. Therefore it is worthwhile to develop more methods of practical importance for the synthesis of IV. The present work describes a new method of synthesis of IV which is superior to the azlactone and the amidine-glyoxal methods.

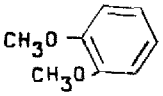
The author has observed that aromatic aldehydes condense at reflux temperature with a mixture of ethyl chloroacetate(I) and benzamidine hydrochloride(II) in the presence of sodium bicarbonate and n-propanol to give fairly good yields of the unsaturated 2-imidazolin-5-ones(IV). 2-Phenyl-2-imidazolin-5-one(III) with an active methylene group may be formed as intermediate as in the cases of amidine-glyoxal and imidic acid ester-glycine ester methods[4,5] and the aromatic aldehydes condense with it to form IV.



The table shows the unsaturated 2-imidazolin-5-ones(IV) prepared by the new method. In every case 0.01 mole of the aromatic aldehyde was condensed with a mixture of 2.5g. of benzamidine hydrochloride dihydrate (prepared by the method of

Dox[7]), 2.5 ml. of ethyl chloroacetate in the presence of 3.38g. of sodium bicarbonate and 20 ml. of n-propanol. An intimate mixture of the solid reactants was taken in a 100-ml. round-bottomed flask with ground-glass joint. The liquid reactants and the solvent were added and the mixture was heated under reflux using an electric mantle. The flask was shaken often until boiling began and then occasionally. In the beginning there was vigorous evolution of carbon dioxide due to the reaction between sodium bicarbonate and benzamidine hydrochloride. Within 10 min. of refluxing the unsaturated 2-imidazolin-5-one began to separate as yellow crystals. After a total refluxing for 1 hr. the flask was allowed to cool and the product was filtered on a glass sintered funnel. It was first washed with 10ml. of methanol, then thrice with 10-ml. portions of water and finally with 5 ml. of methanol and dried. The product thus obtained was almost pure (recrystallisation from amyl acetate did not raise the m.p. more than 2°C in any case). The identity of the compound was established by mixed m.p. determination with authentic sample prepared by the imidic acid ester - glycine ester method[2].

Unsaturated 2-imidazolin-5-ones(IV)

Ar	m.p., D_C[a]	Yield, %
C_6H_5	282 - 283	47
p-$CH_3OC_6H_4$	301 - 302	55
	269 - 270	48
p-$CH_3C_6H_4$	312 -313	52
o-ClC_6H_4	268 - 269	30
p-$(CH_3)_2NC_6H_4$	286 - 287	51

[a] Melting points are corrected.

The new method for the synthesis of unsaturated 2-imidazolin-5-ones has certain definite advantages. (1) It is a one-step process and the operation is extremely simple. (2) The starting materials for the synthesis are easily available and very stable. (3) The products obtained are practically pure and the yields are moderately good. Attempts are underway to improve the yields further and to extend this method of synthesis to a large number of unsaturated 2-imidazolin-5-ones.

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1. This work was partially supported by the University Grants Commission, India.
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