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AN IMPROVED METHOD FOR THE SYNTHESIS OF ACYLAMINO ACIDS THROUGH 2,4-DISUBSTITUTED 2-IMIDAZOLIN-5-ONES.

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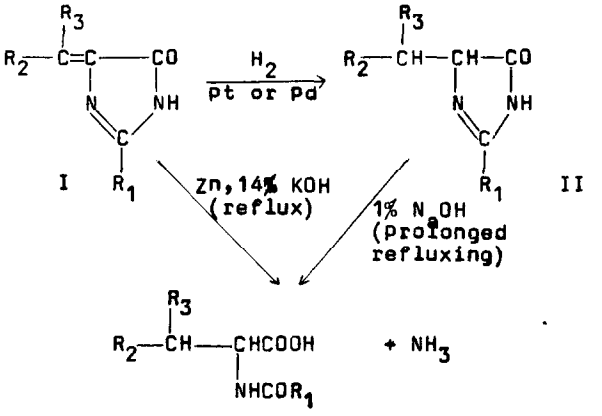
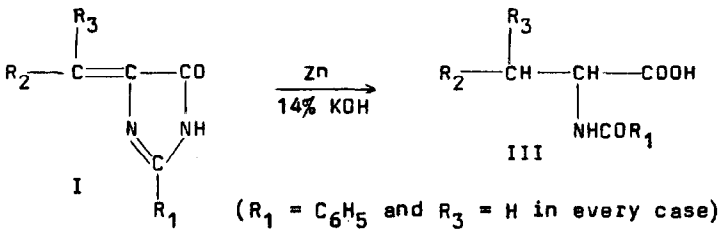
Acylamino acids are largely used for the resolution of amino acids[1] and for the synthesis of peptides.[2] Although there are several methods for the synthesis of amino acids only a few of them afford acylamino acids directly.[3,4] Kidwai and Devasia[4] prepared acylamino acids (III) in good yields by the catalytic hydrogenation of unsaturated 2,4-disubstituted 2-imidazolin-5-ones(I) to the corresponding saturated 2-imidazolin-5-ones(II) followed by the hydrolysis of the latter with 1% sodium hydroxide solution. The present work describes a practical and one-step synthesis of acylamino acids (III) by the simultaneous reduction and hydrolysis of the unsaturated 2-imidazolin-5-ones (I) with a mixture of zinc dust and potassium hydroxide solution.



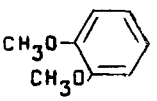
III

The table shows the acylamino acids (all benzoylamino acids) prepared by the present method. The required unsaturated 2-imidazolin-5-ones (I) were prepared by the methods (A and B) of Kidwai and Devasia[4]. The last three unsaturated 2-imidazolin-5-ones in the table were prepared for the first time by employing their methods. In every case 2 g. of the crude unsaturated 2-imidazolin-5-one was refluxed with a mixture of 5g. of zinc dust and 50 ml. of 14% aqueous potassium hydroxide solution for 1 hr. The reaction mixture was shaken const-

antly for the first few minutes and then occasionally. There was copious evolution of ammonia. The unreacted zinc dust was removed and the reacted zinc was precipitated by passing carbon dioxide through the solution. After filtration the solution was shaken twice with 50-ml. portions of ethyl acetate. On acidification of the aqueous layer with concentrated hydrochloric acid (about 12ml.) the acylamino acid precipitated. After keeping overnight the product was filtered and washed thoroughly with water and ether and crystallised from glacial acetic acid. The identity of the compound was established by mixed m.p. determination with authentic sample.



(R_1 = C_6H_5 and R_3 = H in every case)

R_2	Compound I			Compound III	
	Method of Synthesis	m.p., °C[a,b]	Yield, %	m.p., °C[b]	Yield, %
C_6H_5	A	281-282	74	188-189	67
p-$CH_3OC_6H_4$	B	300-301	71	178-179	56
	A	269-270	93	185.5-186.5	41[c]
	B		42		
p-$CH_3C_6H_4$	A	312-313	73	179.5-180.5	56[c]
	B		81		
o-ClC_6H_4	A	267-268	29	190-191	53
	B		19		

[a]Crystallised from amyl acetate in all cases [b]Melting points are corrected
[c]Compounds reported for the first time.

The present method for the synthesis of acylamino acids is a significant improvement over the the existing method. The advantages of the method include operational simplicity, low cost of reagents and higher yields. Works are under way to extend this method of synthesis to a large number of acylamino acids.

References:

1. J.P.Greenstein and M.Winitz, "Chemistry of the Amino Acids", John Wiley and Sons, Inc. New York London Sydney, 1961, Vol.I,Ch.9.Resolution of the Amino Acids.
2. J.P.Greenstein and M.Winitz, ibid, Vol.II, pp.804-808.
3. J.P.Greenstein and M.Winitz, Ibid., Vol.I,Ch.8. Synthesis of α-Amino Acids.
4. A.R.Kidwai and G.M.Devasia, J.Org.Chem.,27, 4527 (1962).