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A NOVEL ELIMINATION-ADDITION REACTION OF A DIACYLATED HYDROXYLAMINE

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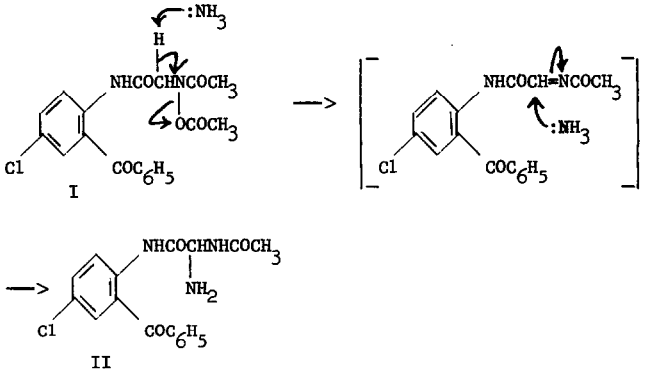
A novel elimination of acetic acid from an O,N-diacetylated N-alkylhydroxylamine with subsequent addition of ammonia to the resultant C=N bond has been observed. 2-(N-Acetoxyacetamido)-2'-benzoyl-4'-chloroacetanilide (I), upon treatment with ammonia in ethanol, afforded 2-acetamido-2-amino-2'-benzoyl-4'-chloroacetanilide (II) (m.p. 140-142°)* as shown below.



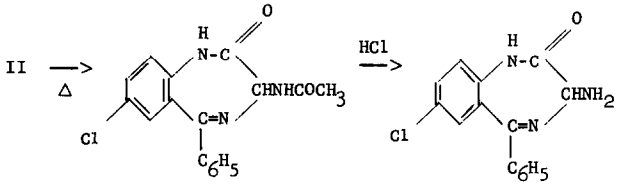
II

*All of the compounds reported herein are supported by satisfactory microanalytical values. Tetramethylsilane was the internal reference for the n.m.r. spectra.

Presumably, an attack by ammonia on the α-methylene group abstracts a proton leading to the elimination of the acetate anion from the neighboring nitrogen atom. Ammonia then adds to the resulting highly polarized carbon-nitrogen double bond to afford II.

The structure of II has been established by infrared [λ_{max}^{KBr} 2.99, 3.07, 3.11 (NH, NH_2); 5.85 and 6.11 μ (broad) (CO)] and n.m.r. spectra ($CDCl_3$) [CH_3, δ 2.04 (s); NH_2, δ 2.33; CH, δ 5.2 (d), (J, 6 c.p.s.); NH (ar), δ 11.57 and NH (aliph.), δ 7.12]. The splitting of the methine proton signal by the amide proton is eliminated by deuterium exchange.

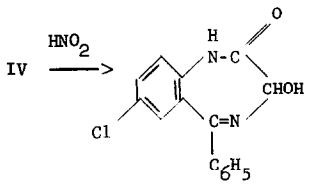
Confirmation of the structure of II is given by its cyclization to 3-acetamido-7-chloro-1,3-dihydro-5-phenyl-2H-1,4-benzodiazepin-2-one (III) [m.p. 271-272°; λ_{max}^{KBr} 3.13 (NH); 5.85 (lactam CO); 6.04 μ (amide CO)] which was brought about by gentle heat.



III IV

The methine proton of III appears as a doublet (δ 5.47) in the n.m.r. spectrum (d_6DMSO) by virtue of coupling (J, 8 c.p.s.) with the amide proton. Methanolysis of the acetyl group was accomplished at room temperature with hydrogen chloride catalysis to afford the

corresponding 3-amino derivative (IV) [m.p. 205-206°; λ_{max}^{KBr} 2.99, 3.06 (NH_2), 5.88 μ (CO)]



V

Treatment of IV with nitrous acid gave the known 7-chloro-5-phenyl-3-hydroxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (V) (1).

We are continuing to investigate the scope of the elimination-addition reaction.

REFERENCE

1. S. C. Bell and S. J. Childress, J. Org. Chem., 27, 1691 (1962).