MECHANISM OF TRANSFORMATION OF PYRIMIDO[5,4-e]-1,2,4-TRIAZINE-5,7-DIONES INTO IMIDAZO[4,5-e]-1,2,4-TRIAZIN-6-ONES IN ALKALINE MEDIA

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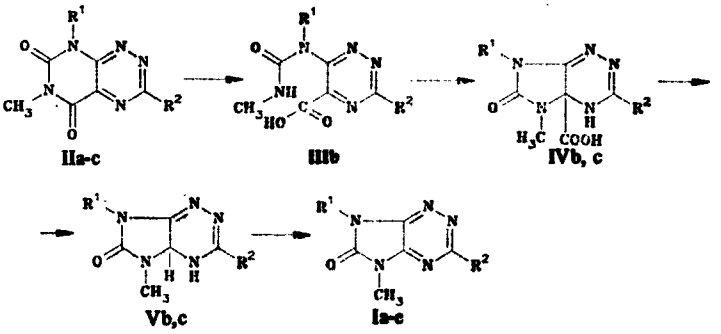
UDC 547.859'873'781.04

To explain the formation of imidazo[4,5-e]-1,2,4-triazin-6-ones (Ia) from pyrimido[5,4-e]-1,2,4-triazine-5,7-diones (IIa) in alkaline media, a mechanism has been proposed for transforming compounds IIa into 6-oxoimidazo[4,5-e]-1,2,4-triazine-4a-carboxylic acids IVa, similar to benzilic rearrangement, followed by decarboxylation of acid IVa and oxidation into Ia, but without confirmation of the experimental data [1, 2].



I, II a R^1=H, CH_3, C_2H_5; R^2=C_6H_5, 4-ClC_6H_4, 4-$CH_3OC_6H_4$; I—V b R^1=R^2=H; I, II, IV, V c R^1=CH_3; R^2=H

In the study of the reactivity of antitumorigenic antibiotics rheumycin (IIb), fervenulin (IIc), and xanthothricin (VI) in aqueous-alkaline media, we found by PMR spectroscopy and with control of pH values that the formation of imidazotriazinones I from compounds II proceeds through a stage of hydrolysis of the amidic $C(_5)$—$N(_6)$ bond of uracil ring, followed by a nucleophilic attack by the $N(_6)$ atom on the $C(_{4a})$ atom, and closure into an imidazole ring. The intermediate compounds IIIb and IVb,c were isolated in an individual state, and were characterized by physicochemical methods. In an aqueous medium at pH ~12, compound IIb hydrolyzes to form 5-carboxy-6-(3-methylureido)-1,2,4-triazine (IIIb) in a yield of 45%, mp 219-221°C (dec., from ethanol). On alkalization to pH > 13, compound IIIb cyclizes into 6-oxoimidazo[4,5-e]-1,2,4-triazine-4a-carboxylic acid IVb in a yield of 75%, mp 184-187°C (dec., from water). In solutions in DMSO and DMFA, acid IVb quantitatively decarboxylates to form the unstable 5-methylimidazo[4,5-e]-1,2,4-triazin-6-one (Vb), which oxidized by a 1% aqueous solution of potassium permanganate to compound Ib in a yield of 95% (based on IVb), mp 230-233°C (from ethanol). The transformation of pyrimidotriazinones IIc and VI in alkaline media proceeds in a similar way [3]. Because of the instability of products of the hydrolysis of compounds IIc and VI at the $C(_5)$—$N(_6)$ bond, the methylated analogs of IIIb could not be isolated. The stability of compound IIIb in alkaline media, in contrast to that of hydrolysis products of compounds IIc and VI, can be explained by delocalization of the negative charge on the $N(_8)$ atom of the triazine ring, which leads to deactivation of the $C(_{4a})$ atom in the nucleophilic attack by the $N(_6)$ atom on it.

The ^1H and ^{13}C NMR, mass spectrometry, and UV spectroscopy data for compounds Ib,c, IIIb, IVb,c and Vb,c completely agree with their structure.

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IDENTIFICATION OF AN INTERMEDIATE COMPOUND IN THE KOST REACTION

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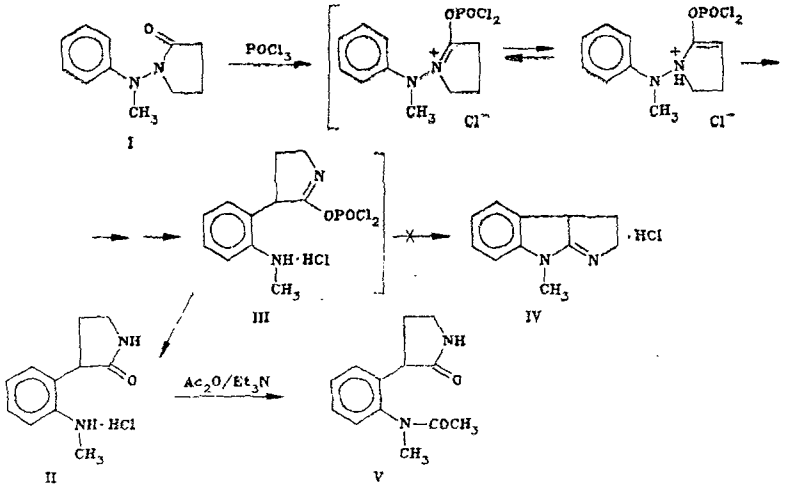
UDC 547.745'75.04

To explain experimental data obtained in the reaction of carboxylic acid hydrazides with phosphorus oxychloride, leading to the corresponding 2-aminoindoles, a scheme [1] has been proposed, which, however, was not confirmed by the isolation and identification of intermediate compounds.

After the reaction of N-methylphenylaminopyrrolid-2-one (I) with an excess of phosphorus oxychloride has been carried out in dry dioxane, and subsequent treatment, we isolated 3-[2-(methylamino)phenyl]pyrrolid-2-one, which could only be formed from the intermediate product in the Kost reaction of type III, but probably because of steric factors, this is not converted further into the derivatives of ezerine IV.



The yield of compound II was about 30%, mp 195-196°C (from acetone). IR spectrum: 3200-2600 ($\overset{+}{N}H$), 1710 (C=O), 1620 cm^{-1} (C=C). PMR spectrum (DMSO-D_6), δ: 1.8-4.3 (4H, m, CH_2), 3.50 (3H, s, N-CH_3), 4.5-5.1 (1H, m, CH), 6.7-7.7 ppm (4H, m, C_6H_4).

To confirm the structure of compound II, we prepared its N-acetyl derivative V, mp 123-124°C (from benzene). IR spectrum: 3290 (NH), 3080-3060 (CH), 1700 (C=O of pyrrolidone), 1640 ($COCH_3$), 1615 cm^{-1} (C=C). PMR spectrum (DMSO-D_6), δ: 1.77 (3H, s, $COCH_3$), 1.8-2.1 (2H, m, CH_2), 3.0-3.2 (2H, m, CH_2), 3.10 (3H, s, N-CH_3), 3.47 (1H, t, CH), 6.9-7.3 (4H, m, C_6H_4), 7.87 ppm (NH, br). Mass spectrum: M^+ 232. The course of fragmentation does not contradict the proposed structure. The data of elemental analysis of compounds I, II, and V agree with the calculated values.

The results obtained confirm the mechanism of the Kost reaction, including the formation of an intermediate of type III at one of its stages.

Branch of the S. Orzhonikidze All-Union Scientific-Research Institute of Pharmaceutical Chemistry, Staraya Kupavna, 142450. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, p. 279, February, 1985. Original article submitted August 28, 1984.

0009-3122/85/2102-0237$09.50