NOVEL APPROACH TO THE SYNTHESIS OF A XANTHINE HOMOLOG

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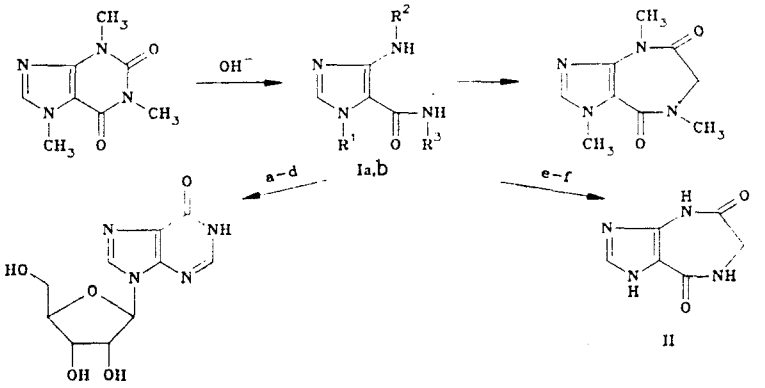
The method for preparation of 4,5,7,8-tetrahydro-6H-imidazo[4,5-e][1,4]diazepine-5,8-dione (II), a xanthine homolog, from inosine that was developed by the Americans Bridson and Weirich [1] illustrates well an additional route for synthesis of imidazo[4,5-e][1,4]diazepines from natural purines. The possibility of occurrence of the scheme "purine to its homolog" was shown previously for caffeine [2].

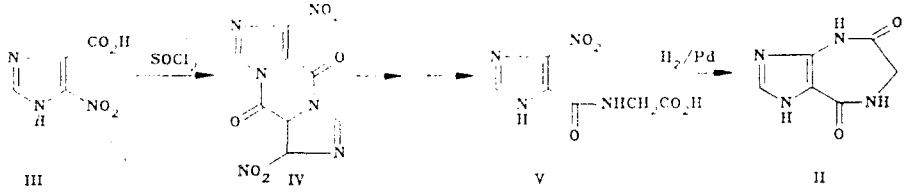


a $C_6H_5CH_2Br$; b HCl; c NaH, $BrCH_2CO_2C_2H_5$; d NaOH; e △; f Pd/C; I a $R^1=R^2=R^3=CH_3$; b $R^1=C_6H_5CH_2$; $R^2=H$; $R^3=CH_2COOH$

Essentially, this scheme consists in conversion of the starting purine to compounds of type I with their subsequent conversion to diazepine or in two steps with subsequent reaction with chloroacetyl chloride and a base [2, 3] or with intramolecular cyclization when $R^3 = CH_2COOH$ [1].

Despite the known examples of the successful occurrence of the scheme "purine to its homolog" [1-3], we should note that the wide use of such an approach is restrained by the relative scarcity and high cost of some natural purines, especially nucleosides.

For the development of an alternative approach to the synthesis of compound II from available starting materials, we propose the following scheme: during the boiling of 4-nitro-5-imidazolecarboxylic acid (III) [4] in thionyl chloride, diimidazodiketopiperazine IV is obtained, which is typical of imidazolemono- and dicarboxylic acids [5]. Acid V is synthesized by the reaction of compound IV with glycine ethyl ester hydrochloride and subsequent alkaline hydrolysis. Hydrogenation of the latter over palladium black occurs with simultaneous cyclization to diazepine II.



4,5,7,8-Tetrahydro-6H-imidazo[4,5-e][1,4]diazepine-5,8-dione (II). Its mp is >340°C (with decomposition) [1]. PMR spectrum (DMSO): 12.99 (1H, singlet, 1-H); 10.89 (1H, singlet, 4-H); 8.00 (1H, triplet, 7-H); 7.81 (1H, singlet, 2-H); 3.72 ppm (2H, doublet, CH_2). M^+ 166.

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LITERATURE CITED

1. P. K. Bridson and T. P. Weirich, *J. Heterocycl. Chem.*, **25**, 1179 (1988).
2. É. I. Ivanov, A. V. Bogatskii, and K. S. Zakharov, *Dokl. Akad. Nauk SSSR*, 591 (1980).
3. T. Ohsaki, T. Kuriki, T. Ueba I. Sakakibara, and M. Asano, *Chem. Pharm. Bull.*, **34**, 3573 (1986).
4. L. P. Kulev and R. N. Gireva, *Zh. Prikl. Khim.*, **30**, 811 (1957).
5. E. Godefroi, C. Eyeken, and C. Westering, *J. Org. Chem.*, **29**, 3707 (1964).

FORMATION OF DERIVATIVES OF 1,2,4-TRIAZOLOQUINAZOLINES IN THE REACTIONS OF 3-AMINO-1,2,4-TRIAZOLES WITH CYCLOHEXANONE

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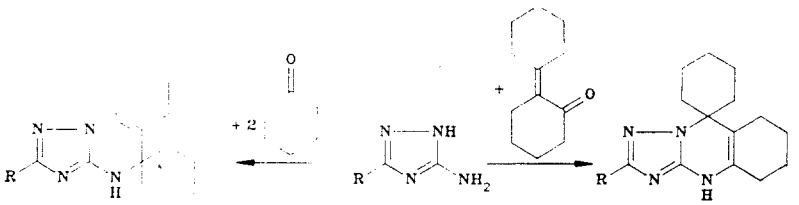
It is known [1, 2] that the reactions of binucleophiles with ketones containing the activated methyl or methylene group, or with the products of the self-condensation of these ketones, may lead to one and the same substance. We established that the boiling of the solutions of the 3-amino-1,2,4-triazoles (Ia, b) and cyclohexanone in DMF in the course of 4-6 h (reaction A) leads to the formation of the compounds (IIa, b), for which the mass spectra and the data of the elemental analysis indicate that the condensation of the ketone with the amine takes place with the 2:1 molar ratio, and with the cleavage of 2 moles of water.

Under the analogous conditions, the condensation of the amines (Ia, b) with 2-cyclohexylidenecyclohexane (reaction B) leads to the formation of the substances (IIIa, b) having the same composition and molecular mass as the compounds (II). However, according to the data of the TLC, the IR spectra (the region of the fingerprints), and the PMR spectra, the compounds (II) and (III) are different discrete substances; this permitted the proposition that the isomeric derivatives of 1,2,4-triazoloquinazolines are formed in the reactions A and B.



I–III a R=H, b R=NH.

The choice between the structures (II) and (III) for the substances obtained was made on the basis of the direction of the cyclocondensation of 3-amino-1,2,4-triazole with α,β-unsaturated ketones (corresponding to the reaction B), which we established previously [3], as well as by the comparison of the position of the signal of the imine proton in the PMR spectra of these compounds. In the case of the substances (IIIa, b), the values of δ_{NH} are typical of the derivatives of 4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine [3], whereas the signal of the imine proton is noticeably displaced to the region of higher field in the spectra of the compounds (IIa, b). These facts indicate the varying disposition of the imino group in relation to the C=C bond in the compounds under comparison: The enamine character of this group in the compounds (IIIa, b) determines its high acidity and, consequently, also the higher values of the δ_{NH}.

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