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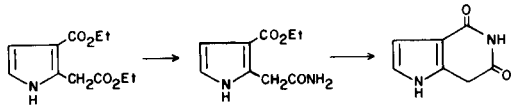
A facile chemical synthesis of 1*H*-pyrrolo[3,2-*c*]pyridin-4,6(5*H*,7*H*)dione (3,7-dideazaxanthine) has been accomplished from ethyl 3-ethoxycarbonylpyrrole-2-acetate.

J. Heterocyclic Chem., 14, 1291 (1977)

Sir:

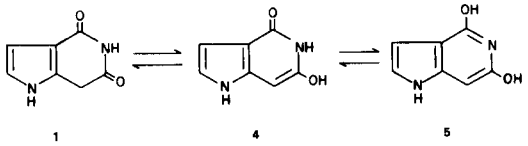
In the search for understanding the biological significance of the various nitrogen atoms of purines and purine nucleosides and in the development of chemotherapeutic agents derived therefrom, a variety of beneficial results (1) have evolved from studying deazapurines and deazapurine nucleosides. In this direction 3-deazaadenosine (2), 1-deazaguanosine (3), 3-deazaguanine (4), 3-deazaguanosine (4), 3-deazaguanylic acid (4), 7-deazaadenine (5), 7-deazaadenosine (tubercidin) (6), and 3-deazaxanthine (7) have been scrutinized. In contrast, however, little attention (8) has been devoted to preparing the dideazapurine systems in which one nitrogen has been removed from the pyrimidine ring and the other from the imidazole moiety to result in the 1*H*-pyrrolo[3,2-*c*]- and 1*H*-pyrrolo[2,3-*b*]pyridine (or 3,7- and 1,7-dideazapurine, respectively) ring systems. This communicaiton describes the synthesis of 1*H*-pyrrolo[3,2-*c*]pyridin-4,6(5*H*,7*H*)dione (3,7-dideazaxanthine) (**1**) as a new representative of this latter class of purine analogs.

The preparation of **1** commenced by converting ethyl 3-ethoxycarbonylpyrrole-2-acetate (**2**) (9) into 3-ethoxycarbonylpyrrole-2-acetamide (10) (**3**; m.p. 143-144°;



as silky white needles, from benzene-petroleum ether, in 62% yield) with refluxing 28% ammonium hydroxide for 10 minutes. Subsequent treatment of **3** in 95% ethanol with 10% aqueous sodium hydroxide for 10 minutes at 80° yielded the desired **1**, m.p. >300°, in 84% yield as buff colored needles (11) following recrystallization from acetic acid. The attainment of **1** in this manner is supported by its spectral analyses: ^{1}H nmr (DMSO-d_6): δ 4.1 (s, 2 H, CH_2), 6.75 (t, J = 3.0 and 2.7 Hz, 1 H, H-7 or H-8) (12), 7.25 (t, J = 3.0 and 2.7 Hz, 1 H, H-7 or H-8) (12), 11.2 (broad, 1 H, pyrrole N-H), 12.3 (broad, 1 H, imide N-H); ir (KBr): 3300-3170 (broad N-H), 1715-1690 (two C=O) cm^{-1}; uv λ max (*p*H 7, ethanol): 241 nm (ε, 8,300), 279 (ε, 6,540); λ max (*p*H 1): 245 (ε, 5,000), 290 (ε, 4,000); λ max (*p*H 11): 267 (ε, 10,940), 315 (ε, 9,120); ms (70 eV) m/e (peak assignment, relative intensity): 150 (M^+, 100%), 107 (M^+-CONH, 54), 79 (M^+-$(CO)_2$NH, 73).

Inspection of **1** suggests that it could exist as shown in the diketo form (**1**) or the monoketo (**4**) or dihydroxy (**5**) tautomers. This situation was considered through examination of the pmr spectrum of the product (see above) which displayed a two proton singlet at δ 4.1 assignable to the two protons at C-3 (12) of **1**. This structural assignment is further corroborated by the previously presented infrared spectral data in which two carbonyl bands were discernible and the mass spectral analyses which demonstrated a pattern characteristic of cyclic imides (13).



Acknowledgement.

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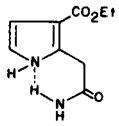
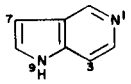
(10) Microanalyses and spectral data are consistent with the assigned structure. It is interesting to note, however, that the two amide N-H protons of **2** indicated pmr non-equivalency in hexadeuteriodimethylsulfoxide with two distinct absorptions at δ 6.8 and 7.2. One rationalization of this would be to assume that **2** exists predominantly in the hydrogen bonded form **i** when in the solvent employed.



i



ii

(11) Satisfactory microanalytical data was obtained for **1**.

(12) A purine numbering scheme (**ii**) has been employed to achieve a more direct correlation with purine and its derivatives.

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