ADDITION OF INDOLE TO FERVENULIN-3-ONE AND ITS 4-N-OXIDE

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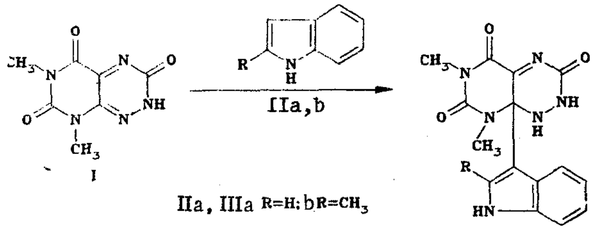
On heating 2,3,5,6,7,8-hexahydro-6,8-dimethylpyrimido[5,4-e][1,2,4]triazine-3,5,7-trione (fervenulin-3-one) (I) in ethanol in the presence of hydrochloric acid, it reacts with o-p-enylenediamine with the formation of 8a-(3,4-diaminophenyl)fervenulin-3-one [1].

We also found that fervenulin-3-one reacts with the indoles IIa,b in boiling butanol in the absence of acid catalysis with the formation of the 8a-indolyl derivatives of 1,2,3,5,6,7,8,8a-octahydro-6,8-dimethylpyrimido[5,4-e][1,2,4]triazine-3,5,7-trione (IIIa,b).



I

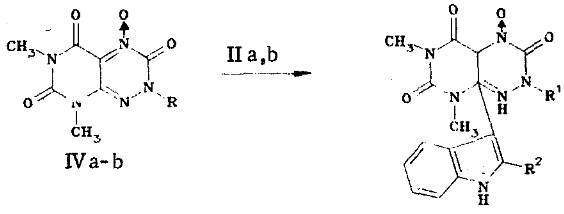
IIa,b

IIa, IIIa R=H; b R=CH_3

IIIa,b

To begin with, the magnitudes of the chemical shifts and the SSCCs of the protons of the 1- and 2-NH groups of the compounds IIIa (8.09 and 9.95 ppm, J = 1.7 Hz) and IIIb) (8.18 and 10.08 ppm, J = 1.9 Hz), which are close to those of 8a-(3,4-diaminophenyl)fervenulin-3-one (7.80 and 9.84 ppm, J = 1.9 Hz) [1], indicate the addition of indoles at the 8a position of fervenulin-3-one.

The reaction of the fervenulin-3-one-4-oxides IVa,b with the indoles IIa,b leads to the 8a-indolyl derivatives of 1,2,3,5,6,7,8,8a-octahydro-4-oxido-6,8-dimetbylpyrimido[5,4-e][1,2,4]triazine-3,5,7-trione (Va-c) in boiling butanol in the course of 2-4 h.



IVa-b

II a,b

Va-d

II, IV a R=H, b R=CH_3; V a $R^1=R^2=H$; b $R^1=H$, $R^2=CH_3$; c $R^1=R^2=CH_3$

All the signals of the protons corresponding to the proposed structure are in the PMR spectra of compounds Va-c. Thus, compound (Vc) has the following PMR spectrum (in DMSO-D_6): 2.25 (singlet, CH_3), 3.12 (singlet, N-CH_3), 3.14 (singlet, N-CH_3), 3.40 (singlet, N-CH_3), 6.80-7.45 (multiplet, CH arom.), 9.65 (singlet, 1-NH), and 11.41 ppm (broad singlet, NH). The value of the CS of the $C_{(8a)}$ atom of compound (Va) in the ^{13}C NMR spectrum comprises 65.0 ppm; this is characteristic of sp^3-hybridized junctional carbon atoms in compounds with the annular 1,2,4-triazine ring [1]. The mass of compounds (Vb,c), determined by mass spectrometry, corresponds to the calculated value. In addition, compound IIIa is formed with a yield of 55-60% on heating the product Va in ethanol in the presence of hydrochloric acid.

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The compounds are presented as follows [mp (°C), yield (%), IR spectrum in mineral oil (cm^{-1})]: IIIa, 269-270, 70, 1668, 1678, 1694, 1738 (CO), 3120, 3236, 3310, 3356, 3425, and 3445 (NH); IIIb, 214-215, 70, 1672, 1680, 1698, 1730 (CO), 3078, 3215, 3317, and 3346 (NH); Va, 262-263, 80, 1670, 1683, 1697, 1710, 1740 (CO), 3122, 3245, 3330, and 3447 (NH); Vb, 221-222, 85, 1684, 1694, 1705, 1733, (CO), 3110, 3205, 3390, 3475 (NH); Vc, 220-221, 75, 1670, 1680, 1690, 1708, 1741 (CO), 3180, 3325, 3375, and 3425 (NH).

The conversions described for fervenulin-3-one and its 4-N-oxide with indoles reveal new routes for the modification of the pyrimidotriazine antibiotics and are of interest in the consideration of the possible routes of transformation of these compounds in the living organism.

LITERATURE CITED

1. Yu. A. Azev, E. O. Sidorov, and I. I. Mudretsova, Khim. Geterotsikl. Soedin., No. 12, 1692 (1985).

NEW SYNTHESIS OF PYRROLO[1,2-a]PYRROLE DERIVATIVES

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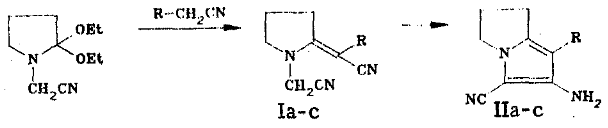
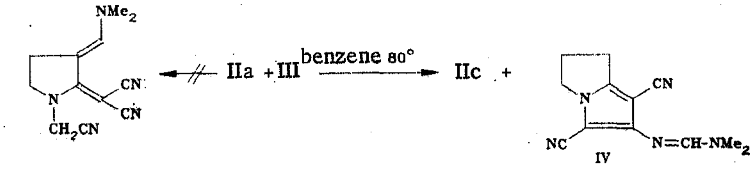
It is known that the reactivity of electron acceptor substituents in the β-position of enamines is significantly lowered on account of the electron donor effect of the enamine amino group [1].

Nonetheless, the enaminonitriles Ia-c (obtained by treating the diethylacetal of N-cyanomethyl-2-pyrrolidone [2] with compounds possessing an active methylene unit) readily take part in intramolecular Thorpe-Ziegler cyclization [3] to form pyrrolo[1,2-a]pyrroles (IIa-c) under mild conditions (Bu^{t}OH, Bu^{t}ONa, 82°C).



I, IIa R=COOC$_2$H$_5$; b R=CONH$_2$; c R=CN

Moreover, cyclization of this type takes place even when only weakly basic agents like DMF diethylacetal (III) are used. Further, the velocity for the closing of the pyrrole ring is higher than the expected condensation at position 3 of the pyrrolidine ring. The result of the reaction of Ic with III is thus the bicycle IIc and the product of further condensation of the latter with the acetal III (compound IV).



Recorded compound, mp in °C (crystallization solvent), yield, %: Ia, 196-198 (alcohol), 92; Ib, 97-98 (2-propanol), 68; Ic, 59-61 (2-propanol), 72; IIa, >300 (DMFA), 94; IIb, 246-247 (DMFA), 92; IIc, >300 (DMFA), 44; IV, 178-180 (alcohol), 25.

Elemental analytical data were in agreement with those calculated and the structures of the synthesized compounds were shown by IR, PMR and mass spectroscopy.

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