ACYLATION OF 1-OXO-4-HYDROXYPYRIDAZINO[4,5-b]QUINOXALINE

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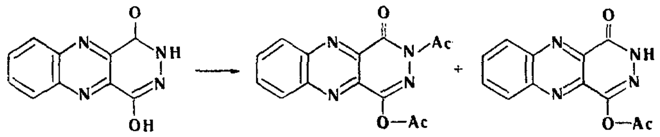
Monoacyl and diacyl derivatives were obtained, depending on the reaction conditions, by reaction of 1-oxo-4-hydroxypyridazino[4,5-b]quinoxaline with acylating agents. Reductive acetylation leads to compounds with three acetyl groups. The structures of all of the compounds obtained were confirmed by their IR and UV spectra.

In developing our research on the reactivity of pyridazino[4,5-b]quinoxaline [1,2], we carried out the acylation and reductive acetylation of 1-oxo-4-hydroxypyridazino[4,5-b]quinoxaline (I).

When I is treated with a mixture of acetic anhydride and glacial acetic acid for 4 h, the chief product is diacetyl derivative II. In addition, we were able to isolate a small amount of monoacetyl derivative III. When the reaction time was shortened to 3 h, III became the chief product.



I II III

The action of p-toluenesulfonyl chloride on I also leads to monotosyl compound IV.

The IR spectra of all three of the synthesized compounds (Table 1) contain absorption bands associated with the C=O vibrations of an amide grouping and heteroring double bonds; this makes it possible to reject a dihydroxy structure for these compounds. The bands at 1760-1780 cm^{-1} in the spectra of II and III should be assigned to the stretching vibrations of carbonyls of acetyl groups, as evidenced also by the absence of this band in the spectrum of tosyl derivative IV. The high-frequency region of the spectra of III and IV contains absorption bands related to the stretching vibrations of associated NH groups.

Thus, on the basis of the IR spectroscopic data, II has the 1-oxo-2-acetyl-4-acetoxypyridazino[4,5-b]quinoxaline structure, while III and IV are O-substituted derivatives of I.

The UV spectra of II-IV (Fig. 1) displayed similar spectral curves, and this makes it possible to assume an identical oxo-hydroxy structure [1] for the substances in solution.

The reductive acetylation of I was carried out with zinc in acetic anhydride—acetic acid. The results of elementary analysis showed that product V contains three acetyl groups; an absorption band of associated NH groups at 3200 cm^{-1} is present in its IR spectrum (in the crystalline state) (Table 1). Since two acetyl groups are incorporated in the pyridazine ring of the molecule when I is acylated under the same conditions but in the absence of zinc, it can be assumed that in this case two acetyl groups are attached to the pyridazine ring, and the third group is attached to the nitrogen atom of the pyrazine ring. Since the acetyl groups of the pyridazine ring could be attached to the oxygen atom or the ring nitrogen atoms, we undertook the synthesis of model compounds with fixed tautomeric dioxo (VIII) and oxo-hydroxy (IX) forms and studied the IR and UV spectra of all of the compounds obtained in order to solve this problem.

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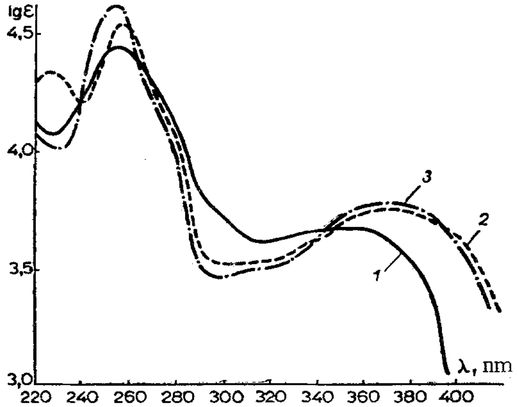
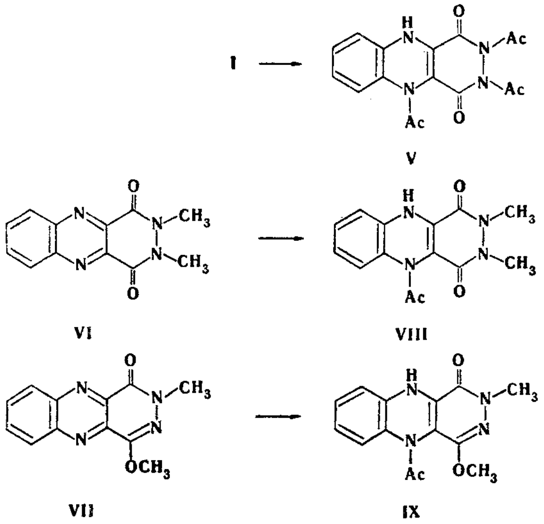


Fig. 1. UV absorption spectra (in alcohol): 1) 1-oxo-2-acetyl-4-acetoxypyridazino[4,5-b]-quinoxaline (II); 2) 1-oxo-4-acetoxypyridazino-[4,5-b]quinoxaline (III); 3) 1-oxo-4-tosyloxy-pyridazino[4,5-b]quinoxaline (IV).

TABLE 1. Absorption Bands (cm^{-1}) in the IR spectra of the Synthesized Compounds

Compound	Amide C=O	Acetyl C=O	C=C and C=N	NH
V	1675	1770 ($N_{2,3}$) 1703 (N_{10})	1490, 1587, 1620	3200
VIII	1685	1705	1493, 1585	3270
IX	1650	1690	1490, 1518, 1595, 1620	3325
II	1715	1782	1498, 1538, 1565, 1630	—
III	1690	1760	1488, 1540, 1555, 1623	3200
IV	1700	—	1490, 1560, 1603, 1623	3205



The IR spectrum of V contains three intense bands of carbonyl absorption (Table 1). Considering that only two bands are present in this region in the spectra of model compounds VIII and IX and that the position of the absorption band of the C=O group of the cyclic amide grouping was established for starting V and VII by previous studies [3], was assigned the bands of the carbonyl absorption to the amide and acetyl C=O groups in the spectra of V, VIII, and IX. The presence of amide carbonyl absorption in the spectrum of V excludes attachment of of the acetyl groups to the two oxygen atoms of the pyridazine ring.

The vibrations of the C=O groups in the spectra of V and VIII are very close. However, the frequency of the C=O group is shifted to the long-wave side in the spectrum of IX, which has a fixed oxo-hydroxy form. In addition, there is a band at 1518 cm^{-1}, which is absent in the spectra of V and VIII, in its spectrum in the region of the in-plane stretching vibrations of C=C and C=N bonds.

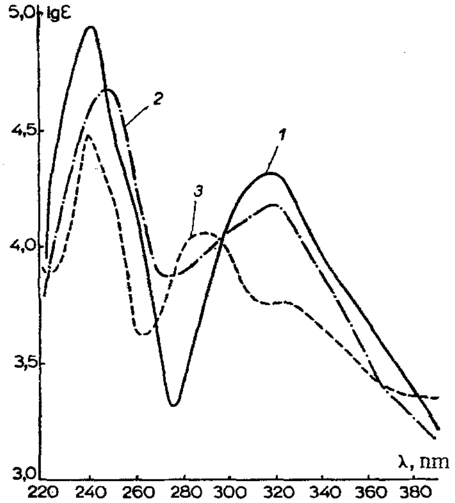


Fig. 2. UV Absorption spectra (in alcohol): 1) 1,4-dioxo-2,3,10-triacetyl-9,10-dihydropyridazino[4,5-b]quinoxaline (V); 2) 1,4-dioxo-2,3-dimethyl-10-acetyl-9,10-dihydropyridazino[4,5-b]quinoxaline (VIII); 3) 1-oxo-2-methyl-4-methoxy-10-acetyl-9,10-dihydropyridazino[4,5-b]-quinoxaline (IX).

All of the above information makes it possible to conclude that V has the 1,4-dioxo-2,3,10-triacetyl-9,10-dihydropyridazino[4,5-b]quinoxaline structure.

In the high-frequency region the bands of the NH groups in the spectra of V, VIII, and IX are shifted to the long-wave region as compared with the bands of free NH groups; this constitutes evidence for the presence of strong hydrogen bonds.

We also investigated the UV spectra of V, VIII, and IX (Fig. 2). A comparison of the spectra confirmed the above conclusion regarding the structure of the product of reduction of V, since a similarity in the spectral curves is observed in the case of V and VIII. However, the spectrum of IX differs substantially.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrophotometer. The UV spectra of alcohol solutions were recorded with a VSU-1 spectrophotometer.

Compounds VI and VII were synthesized by the method in [3].

Acetylation of 1-Oxo-4-hydroxypyridazino[4,5-b]quinoxaline. A) A 0.2-g (1 mmole) sample of I was refluxed in a mixture of 20 ml of acetic anhydride and 4 ml of glacial acetic acid for 4 h, after which the solution was concentrated in vacuo, and the precipitate was removed by filtration and extracted with heptane. The insoluble portion, which was III, was crystallized from alcohol to give 0.055 g (23%) of a light-yellow substance with mp >300°. Found: C 56.1; H 3.2; N 21.7%. $C_{12}H_8N_4O_3$. Calculated: C 56.2; H 3.1; N 21.9%.

Light-yellow crystals of diacetyl derivative II [0.18 g (65%)], with mp 219°, precipitated from the heptane solution. Found: C 56.2; H 3.2; N 18.3%. $C_{14}H_{12}N_4O_4$. Calculated: C 56.4; H 3.4; N 18.8%.

B) A 0.3-g (1.4 mmole) sample of I was refluxed in 15 ml of acetic anhydride for 3 h, after which the acetic anhydride was removed by distillation to dryness in vacuo. The solid material was extracted with heptane, and the insoluble portion was crystallized from alcohol to give 0.22 g (60%) of monoacetyl derivative III, which, according to its melting point and the results of elementary analysis, was identical to the compound obtained by method A. Workup of the heptane solution gave 0.13 g (32%) of II.

1-Oxo-4-tosyloxypyridazino[4,5-b]quinoxaline (IV). A 0.38-g (2 mmole) sample of p-toluenesulfonyl chloride was added to 0.2 g (1 mmole) of I in 75 ml of dry pyridine, and the mixture was stirred at room temperature for 24 h, after which it was poured over ice, during which a precipitate formed. The precipitate was removed by filtration to give 0.26 g (72%) of a light-yellow solid with mp >300° (from methanol). Found: C 55.2; H 3.2; N 14.8%. $C_{17}H_{12}N_4O_4S$. Calculated: C 55.4; H 3.3; N 15.2%.

1,4-Dioxo-2,3,10-triacetyl-9,10-dihydropyridazino[4,5-b]quinoxaline (V). A 0.4-g sample of zinc dust was added in portions to a refluxing solution of 0.3 g (1.4 mmole) of I in a mixture of 30 ml of acetic anhydride and 6 ml of glacial acetic acid, and the mixture was refluxed for 4 h. It was then filtered, and the filtrate was concentrated in vacuo. The resinous residue was triturated with water, and the solid material was removed by filtration and crystallized from alcohol to give 0.32 g (66.6%) of colorless crystals with mp 210°. Found: C 55.9; H 3.9; N 16.2%. $C_{16}H_{14}N_4O_5$. Calculated: C 56.1; H 4.1; N 16.4%. Compounds VIII and IX were obtained under similar conditions.

1,4-Dioxo-2,3-dimethyl-10-acetyl-9,10-dihydropyridazino[4,5-b]quinoxaline (VIII). This compound, with mp 119°, was obtained in 82.3% yield. Found: C 59.0; H 4.7; N 19.3%. $C_{14}H_{14}N_4O_3$. Calculated: C 58.7; H 4.9; N 19.6%.

1-Oxo-2-methyl-4-methoxy-10-acetyl-9,10-dihydropyridazino[4,5-b]quinoxaline (IX). This compound, with mp 203-204°, was obtained in 67.1% yield. Found: C 58.6; H 4.6; N 19.8%. $C_{14}H_{14}N_4O_3$. Calculated: C 58.7; H 4.9; N 19.6%.

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