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FORMATION OF DERIVATIVES OF N-HYDROXYINDOLES, ANNELATED WITH FURAZAN AND FUROXAN RINGS

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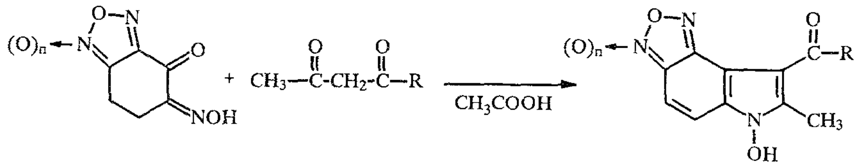
Upon reaction of 4-oxo-5-hydroxyimino-4,5,6,7-tetrahydrobenzofurazan and tetrahydrobenzofuroxan with acetylacetone, 8-acetyl-6-hydroxy-7-methylpyrrolo[2,3-e]benzofurazan and -benzofurazan-3-oxide are formed; and upon reaction with acetoacetate, 8-ethoxycarbonyl-6-hydroxy-7-methylpyrrolo[2,3-e]benzofurazan and -benzofurazan-3-oxide are formed.

In a study of the chemical properties of the 4-oxo-5-hydroxyimino-4,5,6,7-tetrahydrobenzofurazan (I) and 4-oxo-5-hydroxyimino-4,5,6,7-tetrahydrobenzofuroxan (II) which we described earlier, we unexpectedly found that upon their reaction with acetylacetone, 8-acetyl-6-hydroxy-7-methylpyrollo[2,3-e]benzofurazan (III) and 8-acetyl-6-hydroxy-7-methylpyrrolo[2,3-e]benzofurazan-3-oxide (IV) are formed respectively. The reaction of the isonitroso ketones I and II with acetoacetate leads to 8-ethoxycarbonyl-6-hydroxy-7-methylpyrrolo[2,3-e]benzofurazan (V) and 8-ethoxycarbonyl-6-hydroxy-7-methylpyrrolo[2,3-e]benzofurazan-3-oxide (VI) respectively (see Scheme 1). The structure of compounds III-IV is consistent with the spectral data (see Tables 1 and 2) and the elemental analysis results.

Scheme 1



I, II

III-VI

I n = 0; II n = 1; III n = 0, R = CH_3; IV n = 1, R = CH_3; V n = 0, R = OC_2H_5;
VI n = 1, R = OC_2H_5

The sequence of formation of the derivatives of 1-hydroxyindoles has not been studied so far. As a working hypothesis, we can assume that the reaction begins with condensation of the keto group of the isonitroso ketones I, II (whose acceptor

TABLE 1. Characteristics of Synthesized Compounds

Com-pouns	Empirical formula	$T_{пл}$,°C*	UV spectrum λ_{max}, nm (log ε)	IR spectrum cm^{-1}(C=O)	Yield, %
III	$C_{11}H_9N_3O_3$	301...303	205 (4,13); 238 (4,35); 271 (4,14); 374 (3,75)	1620	69
IV	$C_{11}H_9N_3O_4$	218...220	207 (4,05); 229 (4,05); 279 (3,98); 407 (3,15)	1610	63
V	$C_{12}H_{11}N_3O_4$	229...231	206 (4,19); 233 (4,35); 249 (4,35); 366 (3,73)	1680	46
VI	$C_{12}H_{11}N_3O_5$	237...239	204 (4,42); 261 (3,35); 268 (4,37); 400 (3,96)	1700	68

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*Compounds III-VI were recrystallized from alcohol.

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TABLE 2. PMR Spectra and Mass Spectra of Synthesized Compounds

Compound	PMR spectrum in $(CD_3)_2SO$, δ, ppm, spin–spin coupling constant (J), Hz	Mass spectrum*, %)
III	2,59 (3H, s, CH_3); 2,78 (3H, s, CH_3); 7,61 (1H, d, =CH, J_{AB} = 12); 7,74 (1H, d, =CH, J_{AB} = 12); 11,98 (1H, s, OH)	231 (100) M^+, 216 (23), 215 (13), 214 (87), 197 (20), 196 (18), 185 (18), 171 (18), 43 (76)
IV	2,59 (3H, s, CH_3); 2,78 (3H, s, CH_3); 7,14 (1H, dd =CH, J_{AB} = 12); 7,54 (1H, d, =CH, J_{AB} = 12); 11,83 (1H, s, OH)	247 (100) M^+, 231 (32), 230 (70), 214 (21), 187 (59), 172 (23), 171 (17), 170 (23), 44 (22), 43 (74)
V	1,38 (3H, t, CH_3); 2,62 (3H, s, CH_3); 4,32 (2H, q, CH_2); 7,51 (1H, d, =CH, J_{AB} = 9); 7,73 (1H, d, =CH, J_{AB} = 9); 12,01 (1H, s, OH)	261 (40) M^+, 216 (28), 215 (95), 199 (21), 198 (100), 44 (20)
VI	1,55 (3H, t, CH_3); 2,57 (3H, s, CH_3); 4,24 (2H, q, CH_2); 7,01 (1H, d, =CH, J_{AB} = 9); 7,40 (1H, d, =CH, J_{AB} = 9); 12,15 (1H, s, OH)	277 (38) M^+, 232 (13), 173 (20), 97 (13), 85 (17), 83 (20), 71 (37), 69 (27), 57 (25), 50 (40), 44 (100)

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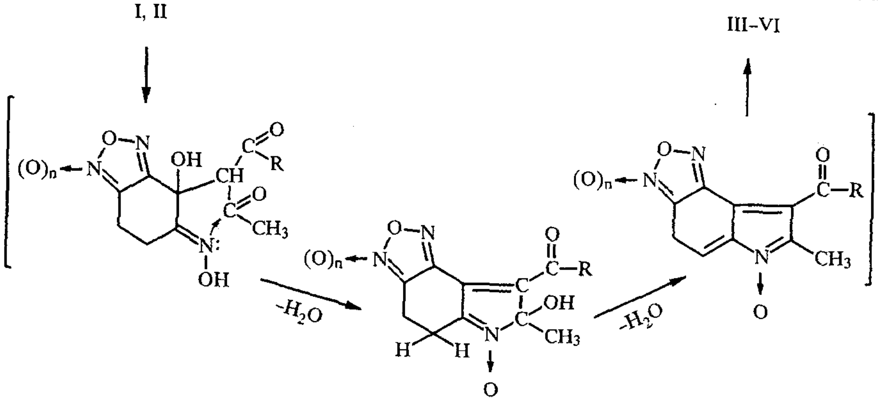
*Peaks with intensity higher than 10% are presented.

TABLE 3. Chemical Shifts in ^{13}C NMR Spectra of Synthesized Compounds, ppm

Compound	CH_3	CH_2	C=C, C=N	C=O
III	10,7 31,2		109,1 120,1 102,6 113,1 129,6 139,1 144,5 148,8	193,6
IV	10,7 31,3		106,1 117,6 103,7 112,7 113,7 130,8 138,6 148,4	193,6
V	10,0 14,2	59,6	109,1 119,5 103,8 103,9 129,7 136,4 144,3 148,8	163,3
VI	10,0 14,1	59,6	105,9 116,8 103,0 104,7 113,6 130,6 138,8 147,6	163,0

properties are enhanced as a result of the furazan or furoxan rings) with the methylene group of the β-dicarbonyl compound. Then nucleophilic attack by the oxime nitrogen occurs at the carbonyl carbon atom with closure of the pyrrole ring, after which the water molecule is cleaved and the intermediate compound A is formed, which then isomerizes to 1-hydroxyindole (see Scheme 2).

Scheme 2



Derivatives of 1-hydroxyindoles have attracted attention of researchers [2, 3], since some alkaloids isolated from plants belong to this class [4]. Furthermore, we have a basis for assuming [5] that synthesis of many alkaloids (occurring in plants) proceeds through a stage of formation of the intermediate derivatives of 1-hydroxyindoles. The synthesis methods for these compounds known so far are complicated, and the compounds themselves are practically unavailable. The route we observed to derivatives of 1-hydroxyindoles, starting from isonitroso ketones, probably is a general one and demands further study.

EXPERIMENTAL

The IR spectra were recorded on the UR-20 in KBr (concentration 0.25%). The UV spectra were recorded on the Specord UV-VIS. The PMR spectra were recorded on the Varian A-56-60. The ^{13}C NMR spectra were taken on the Bruker WP-200 in DMSO-d_6. The mass spectra were taken on the Finnigan MAT MS-8200 with ionizing potential 70 eV. The melting points were determined on a Kofler microheating stage. Elemental analysis of the compounds was done in the microanalysis laboratory of the Institute of Organic Chemistry, Siberian Branch, Russian Academy of Sciences. The yields, melting points, and spectra data for the synthesized compounds are presented in Tables 1-3.

The elemental analysis data for the synthesized compounds correspond to the calculated values.

8-Acetyl-6-hydroxy-7-methylpyrrolo[2,3-e]benzofurazan (III). 1.2 g (0.012 moles) acetylacetone was added to a solution of 1.67 g (0.01 moles) isonitroso ketone I in 40 ml acetic acid and the mixture was stirred at room temperature for three days. The residue was filtered and dried. 4.8 g compound III was obtained.

Compounds IV-VI were obtained by an analogous technique from the corresponding isonitroso ketone and β-dicarbonyl compound.

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