2-ARYLFURO[2,3-b]QUINOXALINES

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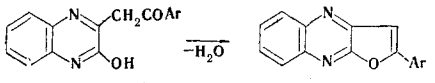
2-Arylfuro[2,3-b]quinoxalines were obtained by cyclization of 2-phenacyl-3-quinoxalones in the presence of polyphosphoric acid or a mixture of phosphorus oxychloride and phosphorus pentachloride.

Continuing our synthetic investigations of quinoxaline derivatives for the purpose of searching for new physiologically active substances and for the study of the keto–enol tautomerism of phenacylquinoxalines, we turned to an examination of the cyclization of 2-phenacyl-3-quinoxalones.

We found that the cyclization proceeds in the presence of polyphosphoric acid. The cyclization products are 2-arylfuro[2,3-b]quinoxalines (II) (Table 1).



I II

The reaction products are analogs of furanoquinoline alkaloids that raise the tonus of systoles, induce constriction of the blood vessels, and manifest themselves most actively in their effect on the smooth musculature [1-3].

We were unable in even one case to obtain halo derivatives of quinoxaline by the action of $POCl_3$ and PCl_5. Compound I cyclized in all cases. In connection with the fact that cyclization occurs under milder conditions, the reaction of I with a solution of PCl_5 and $POCl_3$ can be recommended as a preparative method for the synthesis of II.

The structures of II were confirmed by a study of their UV and IR spectra. The UV spectra of 2-phenyl-3-quinoxalones contain two absorption maxima at about 420 and 280 nm. Cyclization is accompanied by a sharp hypsochromic shift of the major absorption maximum by about 50 nm. The IR spectra of the synthesized compounds correspond completely to the 2-arylfuro[2,3-b]quinoxaline structure. The spectrum does not contain the bands due to the deformation vibrations of the N–H group (1580 cm^{-1}) and the stretching vibrations of an amide carbonyl (1680 cm^{-1}) and an enol hydroxyl group (3200 cm^{-1}) that are present in the spectra of quinoxalylacetophenones.

Signals of protons of a methylene group are absent in the PMR spectrum, but the spectrum does contain a large number of overlapped signals at 7.2-7.9 ppm, which are due to the absorption of aromatic protons that are impossible to assign to definite groups of atoms.

EXPERIMENTAL

The UV spectra of 10^{-3}–10^{-4} M solutions of the compounds in ethanol were recorded with an SF-4 spectrometer. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrophotometer. The PMR spectra (10% solutions in $CDCl_3$ at 20° with hexamethyldisiloxane as the standard) were recorded with a JNM-C-60HL spectrometer.

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TABLE 1. 2-Arylfuro[2,3-b]quinoxalines (II)

Ar	Synthet. method	mp, °C	Empirical formula	N, % found	N, % calc.	Yield, %
C_6H_5	A	189—190	$C_{16}H_{10}N_2O$	11,4	11,4	54
p-$CH_3C_6H_4$	A	215—216	$C_{17}H_{12}N_2O$	10,7	10,8	96
p-$C_2H_5C_6H_4$	A	170—171	$C_{18}H_{14}N_2O$	10,3	10,2	59
p-$CH_3OC_6H_4$	A	162—163	$C_{17}H_{12}N_2O_2$	9,8	10,1	99
2,5-$(CH_3)_2C_6H_3$	A	116—117	$C_{18}H_{14}N_2O$	10,0	10,2	92
p-BrC_6H_4	B	204—205	$C_{16}H_9BrN_2O$	8,7	8,6	83
p-ClC_6H_4	B	257—258	$C_{16}H_9ClN_2O$	9,7	10,0	93
$C_6H_5CH=CH$	B	133—135	$C_{18}H_{12}N_2O$	10,2	10,3	73
C_4H_3S*	B	208—209	$C_{14}H_8N_2OS$	11,0	11,1	99
C_4H_3O †	B	187—188	$C_{14}H_8N_2O_2$	12,0	11,9	99

*2-Thienyl.

† 2-Furyl.

TABLE 2. 2-Phenacyl-3-quinoxalones (I)

Ar	mp, °C	Empirical formula	N, % found	N, % calc.	Yield, %
p-$CH_3C_6H_4$	229—230	$C_{17}H_{14}N_2O_2$	10,1	10,1	85
p-$C_2H_5C_6H_4$	242—243	$C_{18}H_{16}N_2O_2$	9,3	9,6	89
2,5-$(CH_3)_2C_6H_3$	231—232	$C_{18}H_{16}N_2O_2$	9,5	9,6	97
p-BrC_6H_4	273—274	$C_{16}H_{11}BrN_2O_2$	7,8	7,9	99
p-ClC_6H_4	270—271	$C_{16}H_{11}ClN_2O_2$	9,1	9,4	77
C_4H_3S*	287—288	$C_{14}H_{10}N_2O_2S$	10,2	10,4	86

*2-Thienyl.

2-Phenacyl-3-quinoxalones (I). A solution of an equimolecular amount of o-phenylenediamine in diethyl ether was added to a solution of methyl aroylpyruvate [4] in the same solvent, and the mixture was allowed to stand for 30 min, after which the copious yellow crystalline precipitate was removed by filtration and recrystallized from glacial acetic acid. The newly synthesized I are presented in Table 2.

2-Arylfuro[2,3-b]quinoxalines (Table 1). A. A mixture of 0.01 mole of 2-phenacyl-3-quinoxalone and 10 ml of polyphosphoric acid was heated at 125-130° for 2.5 h. The cooled reaction mixture was poured into water, and the resulting precipitate was removed by filtration, washed successively with 10% NaOH solution until the filtrate was no longer yellow and then with water until the medium was neutral, and recrystallized from ethanol.

B. A mixture of 0.01 mole of 2-phenacyl-3-quinoxalone, 10 ml of phosphorus oxychloride and 4 g of phosphorus pentachloride was heated at 106-107° for 2 h and then worked up as in method A.

Compounds II were soluble in organic solvents and insoluble in water. Stable, deeply colored, halochromic salts were formed by the action of concentrated H_2SO_4 in solutions of II.

LITERATURE CITED

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