DIHYDRO-1,2-DIAZAPHENAZINES

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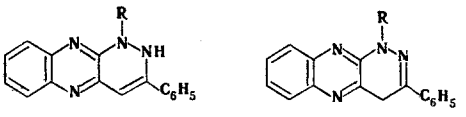
Derivatives of dihydro-1,2-diazaphenazines were obtained by cyclization of the phenylhydrazones and hydrazones of 2-acetonyl- and 2-phenacyl-3-quinoxalones by refluxing in glacial acetic acid. Data characterizing their structures are presented.

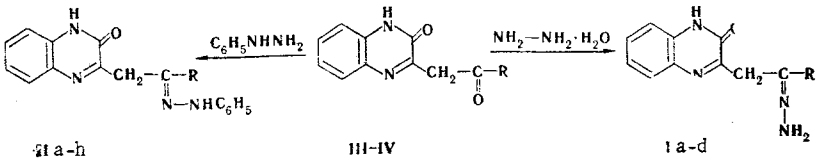
Very little study has been devoted to the reaction of unsubstituted phenacylquinoxalones with hydrazine and phenylhydrazine. Only two compounds [1] for which Bodforss [1] proposed the following structure without presenting evidence were obtained:



R = H, C_6H_5

The aim of the present research was a study of the cyclization of hydrazones (I) and phenylhydrazones (II) of 2-acetonyl- and 2-phenacyl-3-quinoxalones with different substituents in the side chain.

Starting compounds I and II were obtained by prolonged heating of 2-acetonyl- and 2-phenacyl-3-quinoxalones (III and IV) with hydrazine hydrate and phenylhydrazine in alcohol solution in accordance with the following scheme:



Ia-h III-IV Ia-d

III R = CH_3; IV R = C_6H_5

The IR spectra of I and II contain lines at 3350-3370 (stretching vibrations of the N–H group in the phenylhydrazine residue), 3265-3280 (stretching vibrations of the NH_2 group in the hydrazine residue), 3050-3070 (stretching vibrations of the N–H bond in the quinoxaline ring), 1675-1680 (stretching vibrations of an amide carbonyl group), 1612-1625 (stretching vibrations of the C–N bond in an amide), 1595-1600 (deformation vibrations of the N–H bond in the quinoxaline ring), and 1490-1518 cm^{-1} (vibrations due to a condensed benzene ring).

Compounds I and II are readily cyclized by refluxing in glacial acetic acid, and the cyclization is independent of the character of the grouping in the acetonyl or phenacyl residue. As one should have expected, the absorption bands at 3350-3370, 3265-3280, and 1675-1680 cm^{-1} vanish in the IR spectra of the cyclization products.

Judging from the literature data [2], in the cyclization of I one might expect the formation of dihydrodiazaphenazine derivatives. At the same time, it is known [3, 4] that phenylhydrazones of 1,3-diketones

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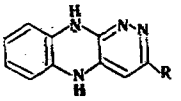
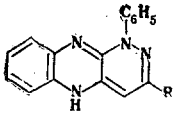
TABLE 1. 3-Alkyl(aryl)dihydro-1,2-diazaphenazine



R	mp, °C[a]	Empirical formula	Found, %			Calculated, %			Yield, %
			C	H	N	C	H	N	
$C(CH_3)_3$	243—244	$C_{14}H_{16}N_4$	70,2	6,5	23,4	70,0	6,6	23,3	99
C_6H_5	294—295	$C_{16}H_{12}N_4$	73,8	4,7	21,2	73,8	4,6	21,5	89
p-$CH_3OC_6H_4$	277—278	$C_{17}H_{14}N_4O$	70,5	4,9	19,0	70,3	4,8	19,3	97
p-ClC_6H_4	211—212	$C_{16}H_{11}ClN_4$	65,2	3,7	18,4	65,1	3,7	19,0	54

[a]From nitromethane.

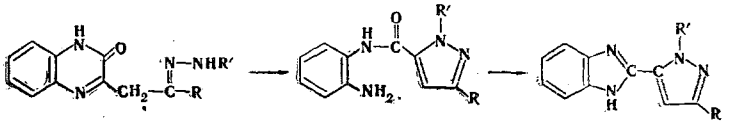
TABLE 2. 1-Phenyl-3-alkyl(aryl)dihydro-1,2-diazaphenazines



R	mp, °C	Empirical formula	Found, %			Calculated, %			Yield, %
			C	H	N	C	H	N	
CH_3	210—211[a]	$C_{17}H_{14}N_4$	74,3	5,2	20,5	74,4	5,1	20,4	76
$C(CH_3)_3$	285—286[a]	$C_{20}H_{20}N_4$	75,9	6,3	17,7	75,9	6,3	17,8	96
C_6H_5	237—238[b]	$C_{22}H_{16}N_4$	78,8	4,5	16,4	78,5	4,7	16,7	92
p-$CH_3C_6H_4$	238—239[a]	$C_{23}H_{18}N_4$	78,8	5,0	16,0	78,8	5,1	16,0	99
p-$C_2H_5C_6H_4$	217—218[c]	$C_{24}H_{20}N_4$	79,4	5,3	15,5	79,1	5,5	15,5	96
p-$CH_3OC_6H_4$	269—270[a]	$C_{23}H_{18}N_4O$	75,4	5,0	15,3	75,4	4,9	15,3	90
p-BrC_6H_4	251—252[a]	$C_{22}H_{15}BrN_4$	63,4	3,7	13,2	63,6	3,6	12,9	93
p-ClC_6H_4	253—254[d]	$C_{22}H_{15}ClN_4$	71,0	4,1	15,0	71,2	4,0	15,0	95

[a]From toluene. [b]From methanol. [c]From ethanol. [d]From nitromethane.

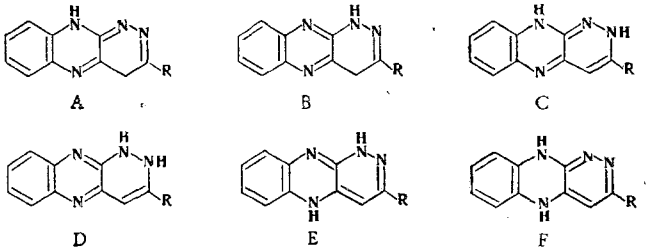
and their imines readily form a pyrazole ring. Consequently, the cyclization may proceed through thermodynamically stable V to give pyrazolobenzimidazole VI:



V VI

In order to ascertain the structure of the cyclization product, we synthesized 2-(1,3-diphenyl-5-pyrazolyl)benzimidazole (VI) from 1,5-diphenylpyrazole-3-carboxylic acid VII and o-phenylenediamine by the Isagulyants–Anufrieva method [5]. We found that the compound obtained in this reaction was not identical to the product of cyclization of 2-phenacyl-3-quinoxalone phenylhydrazone. At the same time, the reaction product had the absorption characteristic for 2-substituted benzimidazoles in the IR region [6].

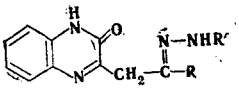
Thus the product of cyclization of I has one of the following six structures, the foundation of which is a dihydrodiazaphenazine ring:



A B C D E F

Structures A and B can be excluded, inasmuch as the signal of a methylene group is absent in the PMR spectra of the cyclized compound. The chief absorption maximum in the UV spectra of dihydro-1,2-diazaphenazines lies at 308 nm, while quinoxalones have this maximum at ~420 nm. This makes it possible

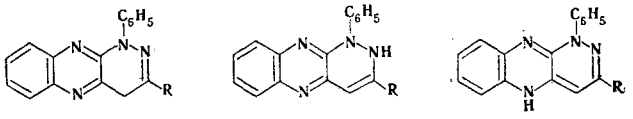
TABLE 3. Hydrazones and Phenylhydrazones of 2-Acetonyl- and 2-Phenacyl-3-quinoxalones



Compound	R	R′	mp, °C	Empirical formula	N, % found	N, % calc.	Yield, %
Ia	$C(CH_3)_3$	H	166—167	$C_{14}H_{18}N_4O$	21,6	21,7	80
Ib	C_6H_5	H	199—200	$C_{16}H_{14}N_4O$	20,2	20,2	98
Ic	p-$CH_3OC_6H_4$	H	234—235	$C_{17}H_{16}N_4O_2$	19,6	19,9	75
Id	p-ClC_6H_4	H	211—212	$C_{16}H_{13}ClN_4O$	17,6	17,9	43
IIa	CH_3	C_6H_5	240—242	$C_{17}H_{16}N_4O$	19,1	19,2	87
IIb	$C(CH_3)_3$	C_6H_5	206—207	$C_{20}H_{22}N_4O$	17,0	16,8	90
IIc	C_6H_5	C_6H_5	203—204	$C_{22}H_{18}N_4O$	15,7	15,8	95
IId	p-$CH_3C_6H_4$	C_6H_5	217—218	$C_{23}H_{20}N_4O$	15,2	15,2	74
IIe	p-$C_2H_5C_6H_4$	C_6H_5	164—165	$C_{24}H_{22}N_4O$	14,4	14,7	92
IIf	p-$CH_3OC_6H_4$	C_6H_5	215—216	$C_{23}H_{20}N_4O_2$	14,4	14,6	92
IIg	p-BrC_6H_4	C_6H_5	222—223	$C_{22}H_{17}BrN_4O$	13,2	12,9	87
IIh	p-ClC_6H_4	C_6H_5	218—219	$C_{22}H_{17}ClN_4O$	14,2	14,4	95

to reject structures C and D, the absorption of which should not differ substantially from the absorption of the starting quinoxalone. Of the remaining structures (E and F), structure F is the most plausible one, inasmuch as the trend of the absorption curve in the UV region is almost identical to the trend of the curve obtained for 10-methyl-3-phenyldihydro-1,2-diazaphenazine, the structure of which was proved by chemical methods [2].

The formation of a compound having one of the following three structures is possible in the cyclization of II:

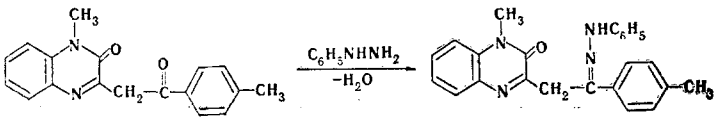


A B C

For the same reasons, structure C is the most probable one.

Information on the synthesized diazaphenazines is presented in Tables 1 and 2.

As one should have expected, the phenylhydrazone obtained under the usual conditions from N-methyl-2-(4-methylphenacyl)-3-quinoxalone is not cyclized by heating in glacial acetic acid in view of the impossibility of enolization of the amide carbonyl group.



EXPERIMENTAL

The UV spectra of 10^{-3}-10^{-4} M solutions of the compounds in ethanol were recorded with an SF-4 spectrophotometer. The IR spectra of mineral-oil suspensions of the compounds were recorded with a UR-10 spectrometer (with NaCl and LiCl prisms). The PMR spectra of trifluoroacetic acid solutions were recorded with a JNM-C-60 HL spectrometer.

2-Acetonyl- and 2-Phenacyl-3-quinoxalone Hydrazones (I). A 30-ml sample of hydrazine hydrate was added to 0.019 mole of III or IV, and the mixture was heated for 1 h on a water bath. Absolute ethanol (30 ml) was then added, and the mixture was heated at the boiling point of the solvent for 12 h. It was then poured into 100 ml of 20% acetic acid, and the precipitated I was removed by filtration.

2-Acetonyl- and 2-Phenacyl-3-quinoxalone Phenylhydrazones (II). A 25-ml sample of phenylhydrazine was added to 0.011 mole of III or IV, and the mixture was heated on a water bath for 1 h. Absolute ethanol (20 ml) was then added, and the mixture was heated at the boiling point of the solvent for 14 h. It was then poured into 200 ml of 20% acetic acid, and the resulting precipitate of hydrazone II was removed by filtration.

The synthesized hydrazones (I and II) are presented in Table 3.

2-(1,3-Diphenyl-5-pyrazolyl)benzimidazole (VI). A mixture of 5 mmole of VII, 2.5 mmole of o-phenylenediamine, 0.48 g of KU-2 cation-exchange resin, and 15 ml of mesitylene was refluxed for 4 h. A 10-ml sample of 30% sodium hydroxide was added, and the resulting precipitate was removed by filtration along with the cation-exchange resin and dissolved in hot aqueous alcohol. The alcohol solution was cooled to precipitate 0.4 g (24%) of a product with mp 263-264° (from toluene). IR spectrum, cm^{-1}: 2400-3200 (strong N–H ... N hydrogen bond characterizing association of the benzimidazole molecules), 1540, 1600, and 1620 (stretching vibrations of C=C and C=N bonds). Found C 78.3; H 4.8; N 16.8%. $C_{22}H_{16}N_4$. Calculated: C 78.5; H 4.7; N 16.7%.

3-Alkyl(aryl)dihydro-1,2-diazaphenazines (Table 1). A 3.9-mmole sample of hydrazone I was refluxed with 10 ml of glacial acetic acid for 2 h. The mixture was then poured into 100 ml of cold water, and the resulting precipitate was removed by filtration.

1-Phenyl-3-alkyl(aryl)dihydro-1,2-diazaphenazines (Table 2). These compounds were similarly obtained from 1.8 mmole of phenylhydrazone II by refluxing with 5 ml of glacial acetic acid.

N-Methyl-2-(4-methylphenacyl)-3-quinoxalone Phenylhydrazone. This compound was obtained in the same way as phenylhydrazone II from 8 mmole of N-methyl-2-(4-methylphenacyl)-3-quinoxalone, 25 ml of phenylhydrazine, and 15 ml of absolute ethanol. Workup gave 3.1 g (95%) of a crystalline substance with mp 151-152° (from ethanol). Found: N 14.4%. $C_{24}H_{22}N_4O$. Calculated: N 14.6%.

1,3-Diphenyldihydro-1,2-diazaphenazine. A 0.64-g (1.8 mmole) sample of 2-phenacyl-3-quinoxalone phenylhydrazone gave 0.56 g (92%) of a product with mp 237-238° (from methanol). IR spectrum, cm^{-1}: 3060 (stretching vibrations of the N–H bond in the quinoxaline ring), 1623 (C–N stretching vibrations), 1598 (deformation vibration of the N–H bond in the quinoxaline ring), and 1503 (vibrations due to the condensed benzene ring). Found: C 78.8; H 4.5; N 16.4%. $C_{22}H_{16}N_4$. Calculated: C 78.5; H 4.7; H 16.7%.

1-Phenyl-4-methylphenyldihydro-1,2-diazaphenazine. A 0.66-g (1.8 mmole) sample of 2-(4-methylphenacyl)-3-quinoxalone gave 0.62 g (99%) of diazaphenazine with mp 238-239° (from toluene). IR spectrum, cm^{-1}: 3045, 1620, 1595, and 1504. UV spectrum, λ_{max} (ε): 240 (4.35), 258 (4.40), 290 (4.27), and 308 nm (4.10). Found: C 78.8; H 5.0; N 16.0%. $C_{23}H_{18}N_4$. Calculated: C 78.8; H 5.1; N 16.0%.

1-Phenyl-4-methoxyphenyldihydro-1,2-diazaphenazine. A 0.69-g (1.8 mmole) sample of 2-(4-methoxyphenacyl)-3-quinoxalone phenylhydrazone gave 0.59 g (90%) of diazaphenazine with mp 269-270° (from toluene). Found: C 75.4; H 5.0; N 15.3%. $C_{23}H_{18}N_4O$. Calculated: C 75.4; H 4.9; N 15.3%.

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