CONDENSED IMIDAZO-1,2,4-AZINES.

7.* REACTION OF 2-HYDRAZINOBENZ(NAPHTH)IMIDAZOLES WITH ACETYLACETONE

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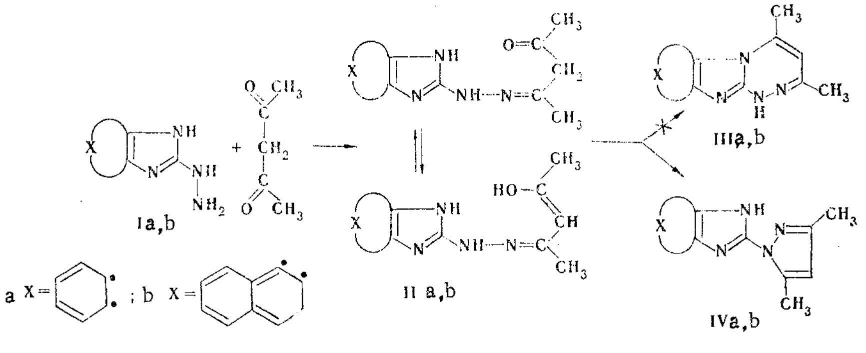
UDC 547.772'785.1.07:543.422'51:539.26

Hetaryl analogs of biphenyl, viz., 2-(3',5'-dimethyl-1'-pyrazolyl)benz(naphth)imidazoles, were obtained instead of the expected benz(naphth)imidazo-1,2,4-triazepines in the condensation of 2-hydrazinobenz(naphth)imidazoles with acetylacetone. The structure of the final products was established on the basis of the PMR and mass spectra and by the data from x-ray diffraction analysis.

We have previously shown [2] that a seven-membered ring is formed in the reaction of β-dicarbonyl compounds with 1,2-diaminoimidazoles, as a result of which the corresponding imidazo[1,2-b]-1,2,4-triazepines are produced. The formal similarity between 1,2-diaminoimidazoles and 2-hydrazinoimidazoles, inasmuch as they are substituted cyclic amidrazones [3], compelled us to study the reaction of acetylacetone with 2-hydrazinobenzimidazole (Ia) and 2-hydrazinonaphth[1,2-d]imidazole (Ib).

The condensation of acetylacetone with imidazoles Ia, b was realized in an organic solvent (ethanol or acetic acid) in the presence of catalytic amounts of mineral acids or without a catalyst. Considering the ease of formation of hydrazones in the 2-hydrazinobenz(naphth)imidazole series [4] and the lability of the proton of the NH group of the imidazole ring we assumed that ring formation would take place in the 1(3) position of the benz(naphth)imidazole ring to give substituted benz(naphth)imidazo-1,2,4-triazepines (IIa, b). Moreover, taking into account the data in [5] on the reaction of 8-hydrazinoxanthenes with acetoacetic ester it might be assumed that another possible pathway of the condensation reaction would be the formation of the corresponding pyrazole ring, which leads to heteroanalogs (IV) of biphenyl. Intermediate hydrazones II were not isolated.



An analysis of the PMR spectrum of the product (IIIa or IVa) shows the presence of two signals of protons of C-methyl groups in the form of singlets of identical intensity at 2.27 and 2.69 ppm, as well as signals of the proton of a methylidyne group at 6.20 ppm (s, 1H), and the proton of the NH group of benzimidazole at 12.75 ppm (broad s, 1H). Signals of the aromatic protons are recorded in the PMR spectrum in the form of a complex multiplet at 7.02-7.25 ppm (4H). The other synthesized compound (IIIb or IVb) has a similar spectrum. The NH group in the indicated compounds shows up distinctly in the IR spectra (νNH = 3200-3400 cm^{-1})

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*See [1] for communication 6.

Kherson Industrial Institute, Kherson 325008. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 88-92, January, 1983. Original article submitted March 10, 1982.

and is also readily acetylated. However, these data did not make it possible to make an unambiguous assignment in favor of structure III or IV.

A large amount of factual material regarding the dissociative ionization of heteroanalogs of biphenyl [6-8] and various derivatives of di- and triazepines [9, 10] has been accumulated. We were therefore justified in using mass spectrometry to solve this problem. It is known [6] that detachment of a substituent from the heteroatom at the N—C bond is possible for N-substituted pyrazoles, pyrroles, indoles, and other π-electron-donor hetaryls, whereas cations of the heterocycle and pseudomolecular ions of the hetaryl compounds that constitute the given system (due to migration of hydrogen from the departing neutral fragment to the charged fragment [11]) will be recorded in the mass spectra of synthesized compounds of the IVa, b type. In fact (Table 1), peaks of quasimolecular ions of benzimidazole (IVa, m/z 118) and naphthimidazole (IVb, m/z 168), as well as peaks of 3,5-dimethylpyrazoline cations (m/z 95), are recorded in the mass spectra of the synthesized compounds. The mass spectra of the metastable ions (obtained by the DADI technique) confirm the direct formation of the indicated ions from M^+. The formation of $[M - CH_3CN]^+$ (a), $[a - H]^+$, $[a - 2H]^+$, and $[a - HCN]^+$ ions characterizes the pyrazole part of the molecule (Table 1). The subsequent fragmentation of the pseudomolecular fragment ions of benzimidazole or naphthimidazole is in good agreement with the data in [12].

In the fragmentation of compounds of the III type the first act of fragmentation should also involve the elimination of a CH_3CN particle to give ion a, but dehydrogenation processes should not occur in this case either in the step involving the formation of ion a or in the M^+ ion itself [9]. The formation of ions with m/z 95, 118, and 168 directly from M^+ is also unlikely in the fragmentation of compounds of the III type. Thus the mass-spectral data demonstrate convincingly that the synthesized compounds have pyrazolylimidazole structures IVa, b.

To confirm this conclusion and to make a detailed study of the relative spatial orientation of the two hetaryl rings with respect to the C—N bond we investigated the molecular-crystal structure of IVa by x-ray diffraction analysis.

The structure of a molecule of this compound with an indication of the interatomic distances and bond angles averaged with respect to two independent conformations of the molecule (K_1 and K_2), which is a peculiarity of the structure of IVa, which includes these two independent conformations, is shown in Fig. 1. In the K_1 conformer the relative angle of rotation of the benzimidazole fragment and the plane of the pyrazole ring about the $C_{(6)}—N_{(1)}$ bond is 3.19°, as compared with 3.4° in the K_2 conformer, i.e., the molecule is virtually planar (Table 2). Specific signs of the fragmentation of a coplanar (M^+, $[M - H]^+$, $[M - CH_3]^+$, and M^{2+} ions [7, 8]) and a noncoplanar system ($[Het + H]^+$ and $[C_5H_7N_2]^+$ ions [11]) are observed in the mass spectra of IVa and IVb evidently for this reason (Table 1). The bond lengths and angles (Fig. 1) are in good agreement with the values found in other nitrogen-containing heterocyclic derivatives [13-15] and indicate the existence of substantial delocalization of the π electrons. Formally speaking, the C—N and N—N single bonds are shortened while the C═N and —N═N double bonds are lengthened as compared with the corresponding standard values (C—N 1.474 Å, N—N 1.451 Å, C—N 1.25 Å, and N—N 1.19 Å [16]); this has also been shown [7, 8, 17] for hetaryl analogs of biphenyl with C—C fusion between the rings.

The principal factor responsible for the difference in the K_1 and K_2 conformations is evidently participation of the hydrogen atom attached to the $N_{(4)}$ atom of the benzimidazole ring in the formation of an intermolecular hydrogen bond with the $N_{(2)}$ atom of the pyrazole ring [$N_{(4)}K_1 \ldots K_{(2)}K_2$ 2.91(2) Å and $N_{(2)}K_1 \ldots N_{(4)}K_2$ 3.03 Å], which leads to the formation of $K_1 \ldots K_2$ dimeric associates in a crystal of the IVa molecule. Unfortunately, the low accuracy in the determination of the bond lengths (δ = 0.02-0.03 Å) because of the limited character of the diffraction data (730 independent reflections for 32 atoms) does not make it possible to carry out a rigorous analysis of the distribution of the bond lengths in the K_1 and K_2 conformers. A similar phenomenon in a system of the biphenyl type that contains a benzimidazole ring was demonstrated in [18], in which the study was made in the liquid phase.

One should, of course, expect a certain difference in the bond lengths in the K_1 and K_2 conformers because of the high degree of conjugation between the rings in the planar Q molecule. For example, the length of the interannular $N_{(1)}—C_{(6)}$ bond in the K_2 structure [1.38(2) Å] is shorter than in the K_1 structure [1.43(2)Å].

TABLE 1. Principal Ion Peaks in the Mass Spectra of IVa, b

Ion	m/z values (relative intensities of the ion peaks in percent relative to the maximum peak)*	
	IVa	IVb
$M^+[W_M]$	212 (100,0) [21,3]	262 (100,0) [14,2]
$[M-H]^+$	211 (17,8)	261 (15,7)
$[M-CH_3]^+$	197 (6,9)	247 (6,1)
$[M-CH_3CN]^+$ (a)	171 (11,3)	221 (12,7)
$[a-H]^+$	170 (24,7)	220 (22,5)
$[a-2H]^+$	169 (5,0)	219 (3,0)
$[a-HCN]^+$	144 (6,3)	194 (7,1)
$[Het+H]^+$†	118 (22,5)	168 (14,6)
M^{2+}	106 (8,6)	131 (20,8)
	91 (7,7)	141 (4,3)
	90 (9,5)	140 (14,7)
	77 (5,4)	—
$[C_6H_7N_2]^+$	95 (4,1)	95 (7,3)

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*The peaks with intensities ⩾3% are presented.

†The pseudomolecular benzimidazole ion for IVa and pseudomolecular naphthimidazole ion for IVb are designated by Het.

TABLE 2. Coefficients of the Equation of the P and Q Planes Ax + By + C = D of the K_1 and K_2 Conformers and Deviations (A) of the Atoms from Them

Molecules	Plane*	Atoms	A	B	C	D
	P	$N_{(1)}$ $N_{(2)}$ $C_{(1)}$ $C_{(2)}$ $C_{(3)}$				
K_1		0,00 0,00 0,00 0,00 0,00	0,003	0,872	−0,490	−0,293
K_2		0,00 0,00 0,00 0,00 0,00	0,054	−0,861	−0,508	−1,578
	Q	$N_{(3)}$ $N_{(4)}$ $C_{(6)}$ $C_{(7)}$ $C_{(8)}$ $C_{(9)}$ $C_{(10)}$ $C_{(11)}$ $C_{(12)}$				
K_1		0,02 −0,01 0,00 0,00 −0,02 0,03 0,02 −0,02 −0,01	−0,526	0,735	−0,428	−0,631
K_2		0,01 0,00 −0,02 0,03 −0,01 −0,01 0,06 −0,04 −0,02	−0,027	−0,885	−0,465	−1,759

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*The dihedral angles between the P and Q planes are 31.9° (K_1) and 3.4° (K_2).

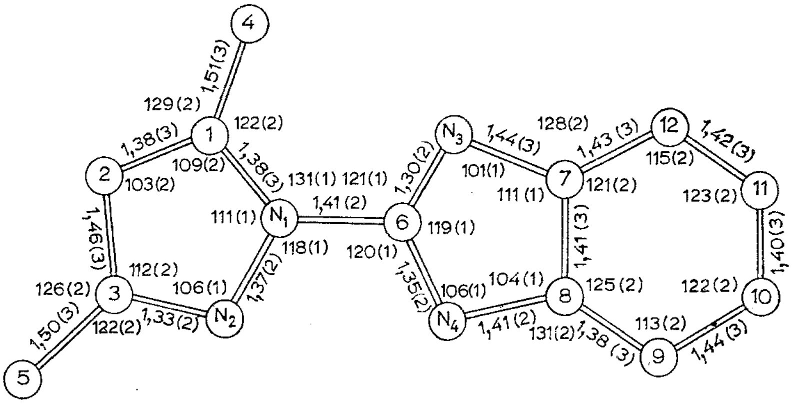

Fig. 1. Bond lengths and angles in the IVa molecule.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were obtained with a UR-10 spectrometer. The PMR spectra of solutions in d_6-DMSO were recorded with a Brucker WH-90 MHz spectrometer with tetramethylsilane as the internal standard. The mass spectra were obtained with a Varian MAT-311A spectrometer with direct introduction of the samples into the ion source under standard recording conditions [7, 8]. The x-ray diffraction study was made with a Syntex-R1 diffractometer with λCu K_α, an Ni filter, $\theta/2\theta$ scan, $2 \leqslant 2\theta \leqslant 116°$, and 729 reflections $CF^2 \geqslant 26$; the structure was decoded by direct methods and was refined by the method of least squares within the fully matrix isotropic approximation up to R = 0.080. The crystals of IVa were rhombic: a = 12.927(3), b = 8.162(2), c = 20.623(4) Å, V = 2175.9(9) $Å^3$, ρ_{calc} = 1.30 $g\text{-}cm^{-3}$, z = 8, and space group Pbc^21.

Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates with development with iodine vapors or UV irradiation. The R_f values were found in the methanol–carbon tetrachloride system (2:1).

2-Hydrazinobenzimidazole (Ia) and 2-hydrazinonaphth[1,2-d]imidazole (Ib) were obtained by the methods in [18] and [19], respectively.

General Method for the Preparation of 2-(3',5'-Dimethyl-1'-pyrazolyl) benz(naphth)imidazoles (IVa, b). A solution of 0.005 mole of 2-hydrazinobenz(naphth)imidazole (Ia, b) in 5-7 ml of acetylacetone was refluxed for 45-60 min, after which it was cooled and treated with 40-50 ml of aqueous methanol (1:1), and the mixture was heated to the boiling point and allowed to stand at room temperature for 10-12 h. The precipitated crystals of 2-(3',5'-dimethyl-1'-pyrazolyl)benzimidazole (IVa) and 2-(3',5'-dimethyl-1'-pyrazolyl)naphth[1,2-d]imidazole (IVb) were removed by filtration and recrystallized from aqueous methanol (1:1). This procedure gave 1.1 g (84.0%) of IVa with mp 134-136°C. Found, %: C 68.1; H 5.9; N 26.2. $C_{12}H_{12}N$. Calculated, %: C 67.9; H 5.7; N 26.4. Compound IVa had R_f 0.8. This procedure also gave 0.7 g (66.0%) of IVb with mp 139-140°C. Found, %: C 73.5; H 5.6; N 21.1. $C_{16}H_{14}N_4$. Calculated, %: C 73.3; H 5.4; N 21.4. R_f 0.75.

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