NEW REARRANGEMENT IN THE 3-INDOLINONE SERIES

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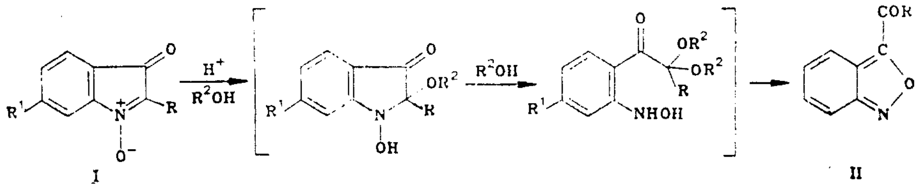
UDC 547.756'572'543.422.8

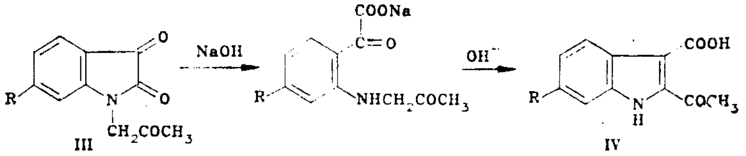
In an aqueous alcohol solution of hydrogen chloride 1-(2-propionylphenyl)amino-2-alkoxy-2-methyl-3-indolinone undergoes rearrangement to 2-(2-acetylcarbonyl)phenyl-3-ethylindazole. The structure of the rearrangement product was investigated by x-ray diffraction analysis.

It is known that isatogens [1-5] and N-acetylisatins [6, 7], the structures of which can be regarded as 3-indolinone derivatives, are capable of undergoing rearrangement — the former by the action of catalytic amounts of acid in alcohol are converted to benzo[c]isoxazoles,* while the latter by the action of bases are converted to indole derivatives (see Schemes 1 and 2).

Scheme 1



Scheme 2



It is apparent from these schemes that in both cases the rearrangement of the heterocyclic part of starting substrates I and III takes place with the participation of the carbonyl function directly bonded to the aromatic carbocycle.

In studying the acid-catalyzed transformation of 1-arylamino-2,2-disubstituted 3-indolinones Va, b to ascertain whether rearrangement of the indicated compounds in the same way as the transformation of isatogens I (pathway 1) is possible we observed a new type of recyclization. It was found that 3-indolinones Va, b undergo rearrangement to indazoles X in high yields rather than to compounds of the same class VIII, which should have been formed if the process were realized via the scheme of the transformation of isatogens I (see Scheme 3).

The structures of the product of recyclization of 3-indolinones Va, b was established by x-ray diffraction analysis, since, as one can see from alternative structures VIII and X, their identification by other physicochemical methods is extremely difficult.

In the X molecule (see Fig. 1 and Table 1) the heterocyclic fragment is planar, while the appreciable shortening of the $N_{(1)}$—$C_{(2)}$ [1.352(3) Å], $C_{(3)}$—$C_{(4)}$ [1.363(5) Å], $C_{(5)}$—$C_{(6)}$ [1.356(4) Å], and $C_{(1)}$—$C_{(7)}$ [1.391(3) Å] bonds indicates the absence of pronounced delocalization of these double bonds in the bicyclic system, i.e., the significant contribution of the o-quinoid structure. The plane of the phenyl ring is turned 42.7° with respect to the plane of the

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*It is interesting that the final benzo[c]isoxazole structure of the product of rearrangement of the isatogens was not established until 1965 [5], although the first studies devoted to this reaction were published in 1919 [8].

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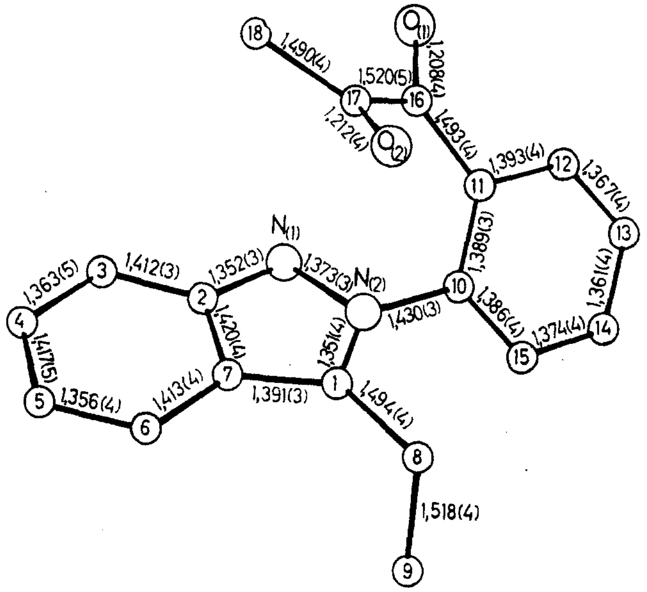
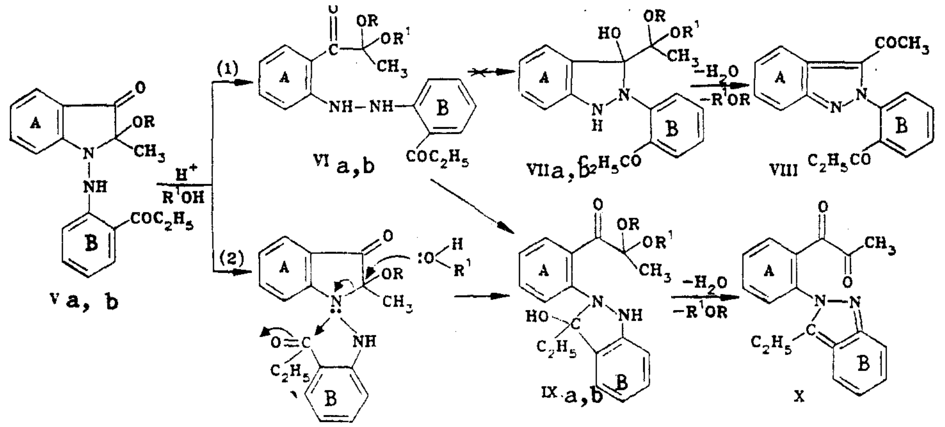


Fig. 1. Structure of the X molecule and bond lengths (in angstroms).

Scheme 3



heteroring, while the twisting of the molecule along the $C_{(11)}$—$C_{(16)}$ bond reaches 25.5°. The acetylcarbonyl group, the carbonyl $O_{(1)}$ and $O_{(2)}$ atoms of which exist in an s-trans-configuration, is also substantially planar — torsion angle $O_{(1)}C_{(16)}C_{(17)}O_{(2)}$ reaches −140.6(4)°. It is evident that this conformation is due to the short intramolecular contacts between the ortho substituents in the phenyl ring, the shortest of which are as follows: $N_{(1)}\cdots C_{(17)}$ 2.718(3) Å, $N_{(1)}\cdots C_{(16)}$ 2.781(3) Å, and $N_{(2)}\cdots C_{(17)}$ 2.908(3) Å (the sum of the van der Waals radii of the N and C atoms is 3.2 Å) [9]. The indazole X molecule contains yet another short $C_{(8)}\cdots C_{(15)}$ contact [3.260(3) Å]. In addition to the nonplanar configuration of the substituent, these short contacts also lead to substantial nonequivalence of the exocyclic bond angles at the $N_{(2)}$ and $C_{(1)}$ atoms. Shortened intermolecular contacts are absent in the molecule.

The results of the recyclization of 3-indolinones Va, b show that if the formation of intermediates VI, from which both possible indazoles VIII and X can be competitively obtained, occurs during the reaction, the intramolecular interaction of the nitrogen atom of the A ring with the carbonyl group of the B ring in these intermediates is realized more preferably than vice versa. However, one cannot exclude the possibility that VIa, b are not formed at all during the transformation and that the process takes place with synchronous cleavage of the C—N bond in the heterorings of substrates Va, b with the formation of a bond between the nitrogen atom of the A ring and the carbon atom of the carbonyl group of the B ring (pathway 2, Scheme 3).

TABLE 1. Bond Angles in the X Molecule

Angle	ω°	Angle	ω°
$N_{(2)}N_{(1)}C_{(2)}$	103,1(2)	$C_{(1)}C_{(8)}C_{(9)}$	112,7(2)
$N_{(1)}N_{(2)}C_{(1)}$	114,1(2)	$N_{(2)}C_{(10)}C_{(11)}$	118,9(2)
$N_{(1)}N_{(2)}C_{(10)}$	116,1(2)	$N_{(2)}C_{(10)}C_{(15)}$	120,0(2)
$C_{(1)}N_{(2)}C_{(10)}$	129,5(2)	$C_{(11)}C_{(10)}C_{(15)}$	120,9(2)
$N_{(2)}C_{(1)}C_{(7)}$	105,8(2)	$C_{(10)}C_{(11)}C_{(12)}$	117,9(3)
$N_{(2)}C_{(1)}C_{(8)}$	125,5(2)	$C_{(10)}C_{(11)}C_{(16)}$	124,1(2)
$C_{(7)}C_{(1)}C_{(8)}$	128,7(2)	$C_{(12)}C_{(11)}C_{(16)}$	119,1(3)
$N_{(1)}C_{(2)}C_{(3)}$	127,8(2)	$C_{(11)}C_{(12)}C_{(13)}$	121,0(3)
$N_{(1)}C_{(2)}C_{(7)}$	111,6(2)	$C_{(12)}C_{(13)}C_{(14)}$	120,1(3)
$C_{(3)}C_{(2)}C_{(7)}$	120,6(2)	$C_{(13)}C_{(14)}C_{(15)}$	121,0(3)
$C_{(2)}C_{(3)}C_{(4)}$	117,5(3)	$C_{(10)}C_{(15)}C_{(14)}$	119,1(3)
$C_{(3)}C_{(4)}C_{(5)}$	122,1(3)	$O_{(1)}C_{(16)}C_{(11)}$	121,0(3)
$C_{(4)}C_{(5)}C_{(6)}$	121.4(3)	$O_{(1)}C_{(16)}C_{(17)}$	118,0(3)
$C_{(5)}C_{(6)}C_{(7)}$	118,3(3)	$C_{(11)}C_{(16)}C_{(17)}$	120,6(2)
$C_{(1)}C_{(7)}C_{(2)}$	105,3(2)	$O_{(2)}C_{(17)}C_{(16)}$	119,1(2)
$C_{(1)}C_{(7)}C_{(6)}$	134,6(2)	$O_{(2)}C_{(17)}C_{(18)}$	123,9(3)
$C_{(2)}C_{(7)}C_{(6)}$	120,1(2)	$C_{(16)}C_{(17)}C_{(18)}$	116,7(2)

TABLE 2. Coordinates ($\cdot 10^4$) and Equivalent Isotropic Temperature Factors (B) of the Atoms in the Structure of X

Atom	x	y	z	B, Å^2
$O_{(1)}$	3829(1)	704(2)	7730(1)	7,4(1)
$O_{(2)}$	2603(1)	1943(2)	8261(1)	5,46(8)
$N_{(1)}$	4368(1)	2100(2)	9668(1)	3,33(8)
$N_{(2)}$	4010(1)	3458(2)	9404(1)	3,20(7)
$C_{(1)}$	3618(1)	3931(2)	9743(1)	3,26(9)
$C_{(2)}$	4197(1)	1733(3)	10214(1)	3,31(9)
$C_{(3)}$	4436(2)	454(3)	10694(1)	4,2(1)
$C_{(4)}$	4211(2)	340(3)	11225(2)	4,9(1)
$C_{(5)}$	3737(2)	1432(3)	11288(1)	4,8(1)
$C_{(6)}$	3491(1)	2657(3)	10826(1)	4,1(1)
$C_{(7)}$	3728(1)	2836(2)	10281(1)	3,24(9)
$C_{(8)}$	3175(2)	5359(3)	9566(2)	4,4(1)
$C_{(9)}$	3606(2)	6513(3)	10205(2)	6,5(2)
$C_{(10)}$	4040(1)	4088(3)	8767(1)	3,46(9)
$C_{(11)}$	3905(1)	3175(3)	8150(1)	3,84(9)
$C_{(12)}$	4005(2)	3783(3)	7571(1)	5,2(1)
$C_{(13)}$	4196(2)	5247(4)	7590(2)	5,9(1)
$C_{(14)}$	4314(2)	6127(3)	8194(2)	5,6(1)
$C_{(15)}$	4256(2)	5561(3)	8796(2)	4,5(1)
$C_{(16)}$	3658(2)	1587(3)	8070(1)	4,4(1)
$C_{(17)}$	3098(1)	1084(3)	8320(1)	4,4(1)
$C_{(18)}$	3143(2)	−506(3)	8546(2)	6,3(1)

TABLE 3. Coordinates ($\cdot 10^3$) of the Hydrogen Atoms in the X Structure

Atom	x	y	z
$H_{(3)}$	477(1)	−26(3)	1064(1)
$H_{(4)}$	438(1)	−46(2)	1157(1)
$H_{(5)}$	361(1)	129(2)	1168(1)
$H_{(6)}$	314(1)	341(3)	1085(1)
$H_{(8.1)}$	307(1)	572(3)	908(1)
$H_{(8.2)}$	269(1)	511(2)	953(1)
$H_{(9.1)}$	330(1)	723(2)	1015(1)
$H_{(9.2)}$	369(1)	617(2)	1073(1)
$H_{(9.3)}$	406(1)	678(2)	1024(1)
$H_{(12)}$	394(1)	315(2)	718(1)
$H_{(13)}$	426(1)	557(2)	717(1)
$H_{(14)}$	445(1)	699(2)	824(1)
$H_{(15)}$	436(1)	610(3)	923(1)
$H_{(18.1)}$	368(1)	−78(3)	897(1)
$H_{(18.2)}$	286(1)	−74(3)	875(1)
$H_{(18.3)}$	302(1)	−112(2)	810(1)

EXPERIMENTAL

The PMR spectra of solutions of the compounds in CCl_4 were obtained with Varian T-60 and XL-100 spectrometers with tetramethylsilane (TMS) as the standard. The IR spectra were recorded with a UR-20 spectrometer. The mass spectra were obtained with an MKh-1303 spectrometer at an ionizing voltage of 80 eV

The results of elementary analysis for C, H, and N were in agreement with the calculated values.

2-(2-Acetylcarbonyl)phenyl-3-ethylindazole (X, $C_{18}H_{16}N_2O_2$). A. A mixture of 3.2 g (0.01 mole) of 1-(2-propionyl)phenylamino-2-methoxy-2-methyl-3-indolinone (Va) in 200 ml of ethanol and 150 ml of 2 N HCl was heated to 50°C and stirred at this temperature for 2.5 h. The alcohol was then removed by distillation, the residue was cooled to 10°C, and the solid material was removed by filtration and recrystallized from ethanol to give 2.2 g (73%) of X with mp 110-111°C. IR spectrum: 1680, 1710 cm^{-1} (C=N, C=O). PMR spectrum: 1.24 (3H, t, CH_2CH_3), 1.76 (3H, s, CH_3), 3.04 (2H, q, CH_2CH_3), 6.77-7.89 ppm (8H, m, Ar). Mass spectrum, m/z (I, %): M^+ 292 (12), 250 (25), 249 (100), 235 (23), 222 (24), 206 (24), 191 (7), 177 (22), 165 (14), 151 (10), 139 (8), 130 (11), 115 (12), 103 (8).

B. Similarly, 2.0 g (69%) of X was obtained from 3.4 g (0.01 mole) of 1-(2-propionyl)phenylamino-2-ethoxy-2-methyl-3-indolinone (Vb). All of the physicochemical characteristics of the sample obtained in experiment B were identical to those presented for X obtained in experiment A.

The X crystals were monoclinic and had the following parameters at 20°C: $a = 20.016(2)$, $b = 8.999(1)$, $c = 20.090(2)$ Å, $\beta = 121.78(1)°$, $Z = 8$, and space group C2/c. The cell parameters and intensities of 1897 reflections with $I \geq 2\sigma(I)$ were measured with a Hilger—Watts four-circle diffractometer [λ Mo K_α, graphite monochromator, $\theta/2\theta$ scanning ($\theta \leq 28°$)]. The structure of X was decoded by the direct method and was refined by the total-matrix method of least squares within the anisotropic approximation for all of the nonhydrogen atoms (see Table 2). All of the hydrogen atoms were revealed from Fourier differential syntheses and were refined isotropically with fixed $B_{iso} = 5$ Å^2 (see Table 3). The final divergence factors for structure X were $R = 0.050$ and $R_W = 0.052$. All of the calculations were made with an Eclipse S/200 computer by means of INEXTL programs [10].

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