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FURYLCYCLOHEXENONES.

2.* CONVERSION OF 6-ETHOXYCARBONYLCYCLOHEXENONES INTO 4,5-DIHYDROINDAZOLES. MOLECULAR AND CRYSTAL STRUCTURE OF 4-PHENYL-6-(5-METHYL-2-FURYL)-4,5-DIHYDROINDAZOL-3-ONE

E. B. Usova, L. I. Lysenko, G. D. Krapivin,
V. E. Zavodnik, and V. G. Kul'nevich

4,5-Dihydrodiazoles containing furyl substituents in positions 4 or 6 were obtained by condensation of hydrazine hydrate and 6-ethoxycarbonylcyclohexenones. XSA showed that in the crystalline state, the pyrazolone fragment of the dihydroindazole molecules has a betaine structure.

The previously described [1, 2] 3- and 5-furylcyclohexenones (I) are active 1,3-bielectrophiles, which suggests the possibility of using them in reactions with binucleophilic reagents to construct heterocycles condensed in the cyclohexene fragment — derivatives of pyrazole, isoxazole, etc. There is little information on such heterocyclic systems, but there are data on the different kinds of biological activity of similar compounds [3-5]. For this reason, it was interesting to obtain new bicyclic derivatives of pyrazole — dihydroindazoles containing a furan fragment as one of the substituents.

Cyclohexenones (Ia-e) were condensed with hydrazine hydrate by boiling the reagents in alcohol in the presence of catalytic quantities of acetic acid. The products of condensation were colorless crystalline substances (IIa-e) readily soluble in polar organic solvents but not in water (Table 1).

TABLE 1. Physicochemical Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	IR spectrum, ν, cm^{-1}	Yield, %
		C	H	N			
IIa	$C_{17}H_{14}N_2O_2$	$\frac{73,52}{73,35}$	$\frac{5,32}{5,07}$	$\frac{9,85}{10,07}$	141...143	1600	36
IIb	$C_{17}H_{14}N_2O_2$	$\frac{73,32}{73,35}$	$\frac{5,22}{5,07}$	$\frac{10,15}{10,07}$	181...183	3200 (NH); 1600	53
IIc	$C_{18}H_{16}N_2O_2$	$\frac{70,41}{70,10}$	$\frac{5,39}{5,23}$	$\frac{9,30}{9,09}$	124...126	3320 (NH); 1600	96
IId	$C_{18}H_{16}N_2O_2$	$\frac{71,18}{73,94}$	$\frac{5,24}{5,52}$	$\frac{9,35}{9,59}$	136...137	1600	80
IIe	$C_{18}H_{15}BrN_2O_2$*	$\frac{58,52}{58,37}$	$\frac{3,85}{4,09}$	$\frac{7,38}{7,57}$	164...165	3300 (NH); 1640, 1610	46

*Found, %: Br 21.05. Calculated, %: Br 21.33.

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*See [1] for Communication 1.

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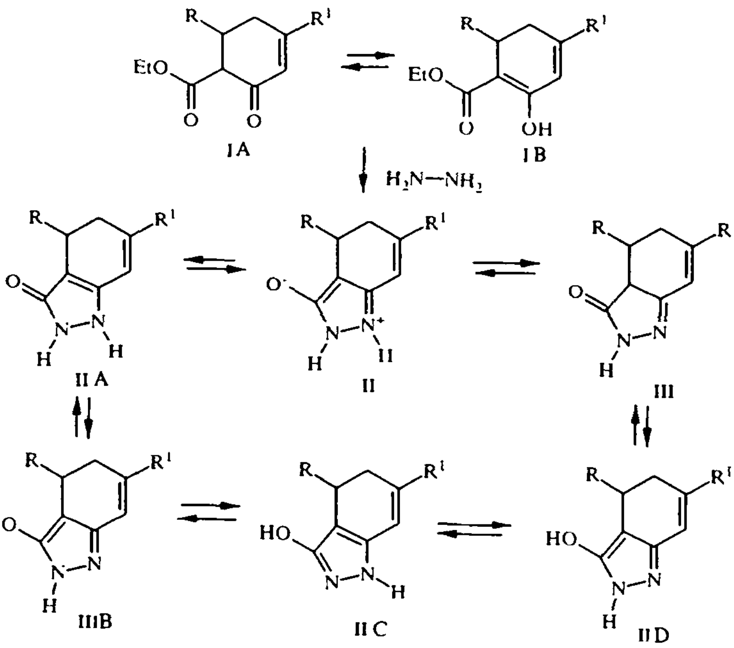

I, IIa R = 2-furyl, R^1 = C_6H_5; b R = C_6H_5, R^1 = 2-furyl; c R = 4-$CH_3OC_6H_4$, R^1 = 2-furyl; d R = C_6H_5, R^1 = 5-methyl-2-furyl; e R = 4-BrC_6H_4, R^1 = 5-methyl-2-furyl

Several bicyclic structures (II-III) in equilibrium, with the possible predominance of some tautomeric forms, can be hypothesized for products of the reaction of compounds I with hydrazine hydrate. However, structure III cannot correspond to the actual products, since their PMR spectra (see Table 2) contain the signals of only four protons of an alicyclic compound. Three of them resonate as an ABX spin system and can be assigned to protons in positions 4 and 5, while the signal of the fourth has the form of a singlet and satisfactorily corresponds to the signal of a 7-H proton with respect to the magnitude of the chemical shift. There is thus no signal of an aliphatic proton in position 3a of tautomeric form II in the spectra, and it can thus be excluded from further examination, but it is nevertheless still unclear whether the pyrazole fragment of molecule II exists in one of the possible tautomeric forms (A-D) or whether there is some equilibrium mixture of tautomers IIa, IIb, and IIc in the solution.

It was not possible to obtain information on the structure of compounds II from the PMR spectra because the spectra were recorded in an acetone–trifluoroacetic acid mixture of solvents due to the poor solubility of the substances, and this naturally prevented observation of the signals of possible OH and NH groups. The absence of the absorption band of an amide carbonyl group characteristic of pyrazolones (1650-1710 cm^{-1} [6, 7]) and the presence of a broad absorption band in the 3200-3300 cm^{-1} region corresponding to NH and OH group stretching vibrations in the IR spectra of compounds II probably suggests predominance of structures IIb-IId in the solid state (the spectra were recorded in the form of a suspension in liquid petrolatum). This was also confirmed by the ^{13}C NMR spectrum of compound IIb: the signal of the $C_{(3)}$ atom is observed in a stronger field (156.79 ppm) in comparison to the standard signal of the carbon atom of the amide carbonyl group [8].

For definitively answering the question of the structure of the pyrazolone fragment in molecule II, an x-ray structural analysis of the solvate of compound IId, obtained by slow crystallization from alcohol solution, was conducted. The projection of a three-dimensional model of molecule IId and numeration of the atoms (numeration of the atoms differs from the IUPAC numeration) is shown in Fig. 1. The coordinates of the atoms, basic interatomic distances, and valence angles are reported in Tables 3, 4, and 5 (the coordinates of atoms of the alcohol molecule associated in the crystal are also reported in Table 3).

As Fig. 1 shows, the pyrazole fragment of the molecule most probably has betaine structure IIb with charge separation: negative in the $O_{(1)}$ oxygen atom and positive in the protonated $N_{(1)}$ nitrogen atom of the pyridine type. The $C_{(2)}-C_{(7)}$ and $C_{(1)}-N_{(1)}$ bonds, which are significantly shorter than the $C_{(1)}-C_{(2)}$ and $C_{(7)}-N_{(2)}$ bonds, are formally double bonds. The $O_{(1)}-C_{(7)}$ bond length (1.399 Å) is intermediate between the CO single and double bond lengths [9, 10]. The heterocycle itself is planar (plane 1), and the root-mean-square deviation does not exceed 0.0085 Å. The $O_{(1)}$, $Hn_{(1)}$, and $Hn_{(2)}$ atoms are rigorously positioned in the plane of the heterocycle.

TABLE 2. PMR Spectra of 5,6-Dihydroindazol-7-ones IIa-e

Compound	Chemical shifts, δ, ppm, SSCC (*J*), Hz			
	alicyclic compound	R	R^1	OH, NH
IIa	2,50 (1H, d.d, 5-Hα); 3,12 (1H, d.d.d, 5-Hβ); 4,25 (1H, d.d, 4-H); 6,80 (1H, d, 7-H); $J_{5\alpha5\beta} = 16$; $J_{5\alpha4} = 8{,}5$; $J_{5\beta4} = 4{,}2$; $J_{5\beta7} = 2{,}5$	5,80 (1H, d, 3-H); 6,25 (1H, d. d, 4-H); 7,28 (1H, d, 5-H); $J_{34} = 3{,}6$; $J_{45} = 1{,}8$	7,30...7,60 (5H, m)	10,3...10,7 br.
IIb	2,92 (1H, d.d, 5-Hα); 3,08 (1H, d.d.d, 5-Hβ); 4,23 (1H, d.d, 4-H); 6,84 (1H, d, 7-H); $J_{5\alpha5\beta} = 16$; $J_{5\alpha4} = 8{,}3$; $J_{5\beta4} = 4{,}9$; $J_{5\beta7} = 2{,}4$	7,20...7,22 (5H, m)	6,45 (1H, d. d, 4-H); 6,52 (1H, d, 3-H); 7,54 1H, d, 5-H); $J_{34} = 3{,}4$; $J_{45} = 1{,}8$	10,3...10,7 br.
IIc	2,92 (2H, m, 2 × 5-H); 4,81 (1H, m, 4-H); 6,70 (1H, d, 7-H); $J_{75} = 2{,}0$	6,8 (2H, d, 2-H, 6-H); 7,2 (2H, d, 3-H, 5-H); 3,1 (3H, s, OCH_3); $J_{35} = J_{28} = 9{,}0$	6,45 (1H, d. d, 4-H); 6,60 (1H, d, 3-H); 7,47 (1H, d, 5-H); $J_{34} = 4{,}0$; $J_{45} = 1{,}8$	10,3...10,7 br.
IId	2,85 (1H, d.d, 5-Hα); 3,00 (1H, d.d.d, 5-Hβ); 4,20 (1H, d.d, 4-H); 6,70 (1H, d, 7-H); $J_{5\alpha5\beta} = 13{,}8$; $J_{5\alpha4} = 6{,}0$; $J_{5\beta4} = 3{,}5$; $J_{5\beta7} = 2{,}0$	7,10...7,25 (5H, m)	2,30 (3H, s, CH_3); 6,00 (1H, d, 4-H); 6,45 (1H, d, 3-H); $J_{34} = 3{,}4$	10,3...10,7 br.
IIe	2,90 (1H, d.d, 5-Hα); 3,10 (1H, d.d.d, 5-Hβ); 4,32 (1H, d.d, 4-H); 6,75 (1H, d, 7-H); $J_{5\alpha5\beta} = 17$; $J_{5\alpha4} = 9{,}5$; $J_{5\beta4} = 2{,}0$; $J_{5\beta7} = 2{,}0$	7,10...7,25 (4H, m)	2,15 (3H, s, CH_3); 6,00 (1H, d, 4-H); 6,50 (1H, d, 3-H); $J_{34} = 3{,}6$	10,3...10,7 br.

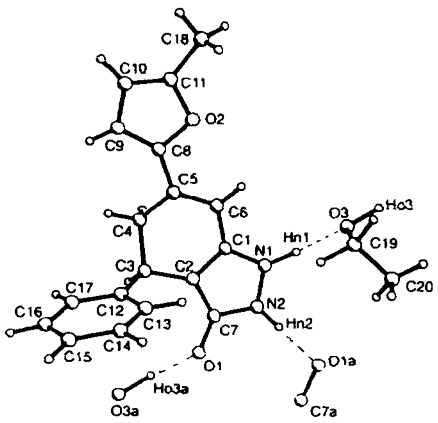

Fig. 1. Projection of a three-dimensional model of the solvate of compound IId and numeration of atoms.

The alicyclic fragment of the molecule is nonplanar and has a distorted twist-boat conformation. The folding parameters [11] are $S = 0.47$, $\theta = 49.3°$, and $\varphi = 112.6°$. The almost planar part of the alicyclic compound (plane 2) is formed by $C_{(6)}$, $C_{(1)}$, $C_{(2)}$, and $C_{(3)}$ atoms (corresponding to a torsion angle equal to 1.5°). The angle between planes 1 and 2 is 3.7°. The $C_{(4)}$ and $C_{(5)}$ atoms protrude out of plane 2 on the same side by 0.6580 and 0.2626 Å, respectively. The spatial position of the atoms in the bicyclic system is shown in Fig. 2.

The phenyl substituent at the $C_{(3)}$ atom occupies a pseudoaxial position which is not traditional for heavy substituents (the $C_{(2)}-C_{(3)}-C_{(12)}-C_{(13)}$ torsion angle is 23.2°). The furan ring is positioned so that the $C_{(8)}-C_{(9)}$ double bond formally shields the ordinary $C_{(4)}-C_{(5)}$ bond in the alicyclic compound. A nonvalence interaction is possible between the $O_{(2)}$ and $H_{(6)}$ atoms, since the $O_{(2)}...H_{(6)}$ distance is equal to 2.545 Å, which is less than the sum of the van der Waals radii of the O and H atoms (respectively equal to 1.40 and 1.16 Å [12]).

TABLE 3. Coordinates of Atoms* (Å × 10^4) and Temperature Factors (Å^2 × 10^3) in the Molecule of Compound IId

Atom	*x*	*y*	*z*	*U*†
$O_{(1)}$	6179(2)	3816(2)	4059(2)	51(1)
$O_{(2)}$	-830(2)	-2508(2)	152(2)	56(1)
$N_{(1)}$	1980(3)	2728(3)	3413(2)	51(1)
$N_{(2)}$	3415(3)	3720(3)	4026(3)	48(1)
$C_{(1)}$	2345(3)	1555(4)	2591(2)	43(1)
$C_{(2)}$	3997(3)	1783(3)	2673(2)	40(1)
$C_{(3)}$	4765(3)	595(3)	1914(2)	40(1)
$C_{(4)}$	3507(4)	-239(4)	824(2)	48(1)
$C_{(5)}$	1779(4)	-711(4)	943(3)	44(1)
$C_{(6)}$	1203(3)	214(4)	1777(3)	48(1)
$C_{(7)}$	4683(4)	3144(3)	3606(3)	40(1)
$C_{(8)}$	774(4)	-2113(4)	84(3)	49(2)
$C_{(9)}$	1059(4)	-3205(5)	-822(3)	67(2)
$C_{(10)}$	-418(5)	-4319(4)	-1337(3)	75(2)
$C_{(11)}$	-1529(4)	-3885(4)	-736(3)	63(2)
$C_{(12)}$	5379(3)	-643(3)	2388(2)	42(1)
$C_{(13)}$	4780(4)	-1045(4)	3216(3)	57(2)
$C_{(14)}$	5359(5)	-2214(5)	3599(3)	73(2)
$C_{(15)}$	6551(5)	-2976(4)	3180(3)	73(2)
$C_{(16)}$	7155(4)	-2581(4)	2349(3)	67(2)
$C_{(17)}$	6581(4)	-1416(4)	1964(3)	51(1)
$C_{(18)}$	-3270(5)	-4520(5)	-823(3)	87(2)
$O_{(3)}$	-1023(3)	2653(3)	3910(2)	82(1)
$C_{(19)}$	-1018(5)	1653(6)	4611(4)	99(2)
$C_{(20)}$	-944(6)	2651(7)	5732(4)	135(3)

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*The coordinates of hydrogen atoms are not reported and can be obtained from the authors.

†The equivalent isotropic factors were determined as one-third of the projection of the orthogonalized *U*(*i*, *j*) tensor.

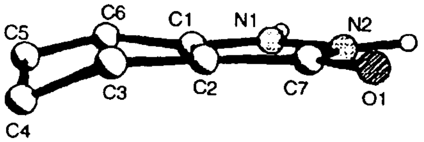

Fig. 2. Spatial arrangement of atoms in the bicyclic fragment of compound IId.

The lengths of the $C_{(1)}-C_{(2)}$, $C_{(1)}-C_{(6)}$, and $C_{(5)}-C_{(6)}$ formally single bonds, shortened in comparison to the standard lengths, indicate the presence of π-bonding between the heterocycles via the $C_{(5)}-C_{(6)}$ double bond.

In the crystal, the molecules of IId are directly bound together by a system of hydrogen bonds and via an ethanol molecule (Fig. 3). In the unit cell, two molecules of IId are positioned toward each other by pyrazole fragments which are associated with each other by a complementary pair of $O_{(1)}\ldots Hn_{(2a)}$ and $O_{(1a)}\ldots Hn_{(2)}$ hydrogen bonds with identical parameters: the $N_{(2)}-Hn_{(2)}$ and $Hn_{(2)}\ldots O_{(1a)}$ interatomic distances are respectively equal to 0.963 and 1.739 Å, and the $N_{(2)}-Hn_{(2)}\ldots O_{(1a)}$ valence angle is 177.1°.

In turn, each pair of molecules of IId is bound by a system of hydrogen bonds with the participation of the hydroxyl groups of the alcohol molecules, $Hn_{(1)}\ldots O_{(3)}-Ho_{(3)}\ldots O_{(15)}$ and $Hn_{(1c)}\ldots O_{(3a)}-Ho_{(3a)}\ldots O_{(1)}$ with neighboring pairs of molecules (Fig. 3), i.e., $O_{(1)}$ oxygen atoms participate in two hydrogen bonds: direct intermolecular binding of two molecules of II due to the contact described above and indirect binding of molecular dimers with each other via the hydroxyl groups of the alcohol molecules. The parameters of the $O_{(1)}\ldots Ho_{(3a)}$ hydrogen bond are: the $O_{(3a)}-Ho_{(3a)}$ and $Ho_{(3a)}\ldots O_{(1)}$ interatomic distances are equal to 1.152 and 1.672 Å, respectively, and the $C_{(7)}-O_{(1)}\ldots Ho_{(3a)}$ and $O_{(1)}\ldots Ho_{(3a)}-O_{(3a)}$ valence angles are

TABLE 4. Bond Lengths (*d*, Å) in the Molecule of Compound IId

Bond	*d*	Bond	*d*
$O_{(1)}-C_{(7)}$	1,339(3)	$O_{(2)}-C_{(8)}$	1,437(4)
$O_{(2)}-C_{(11)}$	1,386(3)	$N_{(1)}-N_{(2)}$	1,409(3)
$N_{(1)}-C_{(1)}$	1,355(4)	$N_{(2)}-C_{(7)}$	1,407(4)
$C_{(1)}-C_{(2)}$	1,431(4)	$C_{(1)}-C_{(6)}$	1,462(3)
$C_{(2)}-C_{(3)}$	1,515(4)	$C_{(2)}-C_{(7)}$	1,407(3)
$C_{(3)}-C_{(4)}$	1,570(4)	$C_{(3)}-C_{(12)}$	1,530(5)
$C_{(4)}-C_{(5)}$	1,573(5)	$C_{(5)}-C_{(6)}$	1,375(4)
$C_{(5)}-C_{(8)}$	1,461(4)	$C_{(8)}-C_{(9)}$	1,358(5)
$C_{(9)}-C_{(10)}$	1,453(5)	$C_{(10)}-C_{(11)}$	1,369(6)
$C_{(11)}-C_{(18)}$	1,542(5)	$C_{(12)}-C_{(13)}$	1,389(5)
$C_{(12)}-C_{(17)}$	1,427(5)	$C_{(13)}-C_{(14)}$	1,397(6)
$C_{(14)}-C_{(15)}$	1,413(6)	$C_{(15)}-C_{(16)}$	1,393(7)
$C_{(16)}-C_{(17)}$	1,393(6)	$O_{(3)}-C_{(19)}$	1,453(7)
$C_{(19)}-C_{(20)}$	1,443(7)		

TABLE 5. Valence (φ, deg) and Torsion (θ, deg) Angles in the Molecule of Compound IId

Angle	φ	Angle	φ
$O_{(1)}-C_{(7)}-C_{(2)}$	131,1(3)	$C_{(1)}-C_{(2)}-C_{(3)}$	122,4(2)
$C_{(7)}-N_{(2)}-N_{(1)}$	111,8(2)	$C_{(6)}-C_{(5)}-C_{(8)}$	120,6(3)
$N_{(2)}-N_{(1)}-C_{(1)}$	105,5(2)	$C_{(5)}-C_{(8)}-C_{(9)}$	131,9(3)
$N_{(1)}-C_{(1)}-C_{(2)}$	110,2(2)	$C_{(8)}-C_{(9)}-C_{(10)}$	105,1(3)
$C_{(10)}-C_{(2)}-C_{(7)}$	107,9(3)	$C_{(9)}-C_{(10)}-C_{(11)}$	110,3(3)
$C_{(2)}-C_{(7)}-N_{(2)}$	104,6(2)	$C_{(10)}-C_{(11)}-O_{(2)}$	107,2(3)
$C_{(2)}-C_{(1)}-C_{(6)}$	125,6(3)	$C_{(11)}-O_{(2)}-C_{(8)}$	107,8(2)
$C_{(1)}-C_{(6)}-C_{(5)}$	114,8(3)	$O_{(2)}-C_{(8)}-C_{(9)}$	109,5(2)
$C_{(6)}-C_{(5)}-C_{(4)}$	121,1(2)	$O_{(2)}-C_{(11)}-C_{(18)}$	116,4(3)
$C_{(5)}-C_{(4)}-C_{(3)}$	117,1(2)	$C_{(2)}-C_{(3)}-C_{(12)}$	114,4(3)
$C_{(4)}-C_{(3)}-C_{(2)}$	105,5(2)		
Angle	**θ**	**Angle**	**θ**
$C_{(1)}-C_{(2)}-C_{(3)}-C_{(4)}$	26,8	$C_{(4)}-C_{(5)}-C_{(6)}-C_{(1)}$	-5,7
$C_{(2)}-C_{(3)}-C_{(4)}-C_{(5)}$	-41,1	$C_{(5)}-C_{(6)}-C_{(1)}-C_{(2)}$	-11,2
$C_{(3)}-C_{(4)}-C_{(5)}-C_{(6)}$	34,2	$C_{(6)}-C_{(1)}-C_{(2)}-C_{(3)}$	-1,5

respectively 133.7 and 168.3°. Parameters of the $Hn_{(1)}...O_{(3)}$ hydrogen bond: the $N_{(1)}-Hn_{(1)}$ and $Hn_{(1)}...O_{(3)}$ interatomic distances are equal to 1.045 and 1.799 Å, and the $N_{(1)}-Hn_{(1)}...O_{(3)}$ and $Hn_{(1)}...O_{(3)}-C_{(19)}$ valence angles are 164.5 and 107.3°, respectively. As a result of such binding, the pairs of molecules of IId in the crystal are joined in wavy ribbons curved along plane *ac*.

EXPERIMENTAL

The IR spectra were recorded on an IR-71 instrument for suspensions in liquid petrolatum. The PMR spectra were made on Tesla BS-467 A (60 MHz) and Bruker AC-200 P (200 MHz) spectrometers. The ^{13}C NMR spectrum was recorded on a Bruker AC-200 P.

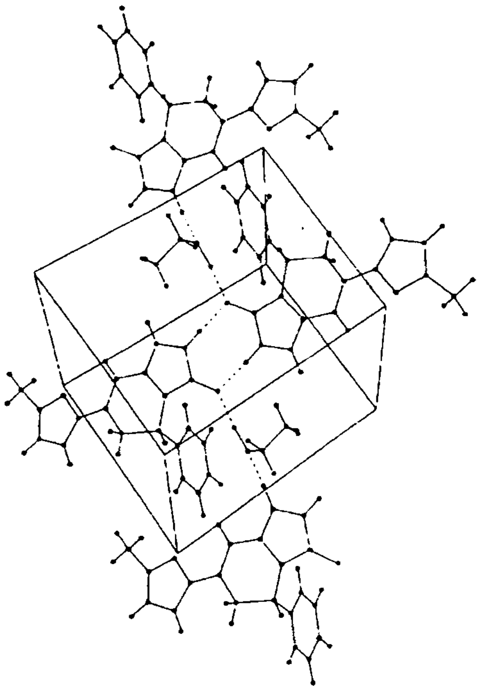

Fig. 3. Spatial position of the molecules in the unit cell of the crystal of compound IId solvate.

The x-ray structural analysis of compound IId was performed on an Enraf-Nonius CAD 4 automatic diffractometer in monochromatized MoKα radiation using the $\theta/2\theta$ scanning technique. Triclinic crystals of compound IId were grown from ethanol solution, unit cell parameters: a = 8.840(1), b = 8.818(1), c = 13.049(1) Å, α = 107.87 (1), β = 98.69(1), γ = 97.57(1)°, V = 9349.7(0.4) Å, P-1 space group, Z = 2. A total of 1242 reflections with $I > 3\sigma(I)$ was obtained. The structure was interpreted by a direct method with the SHELXTL software package [13] and refined in the anisotropic (isotropic for hydrogen atoms) approximation to divergence factors of R = 0.030 and R_w = 0.031.

4-Phenyl-6-(2-furyl)-4,5-dihydroindazol-3-on (IIb). Here 0.20 ml (0.002 mole) of hydrazine hydrate (52% aqueous solution) and 0.02 ml of glacial acetic acid were added to a solution of 0.62 g (0.002 mole) of 5-phenyl-3-(furyl-2)-6-ethoxycarbonylcyclohexen-2-one Ib in 5 ml of ethanol. The mixture was held in a water bath for 1.5 h. The crystals precipitated after evaporation of the solvent were filtered off and washed with cold ethanol. ^{13}C NMR spectrum ($CDCl_3$): 33.45 ($C_{(5)}$); 33.93 ($C_{(4)}$); 98.58 ($C_{(3a)}$); 107.27, 109.82, 111.61, and 125.79 (phenyl); 126.15, 126.84, 142.70, and 153.58 (2-furyl); 127.89 ($C_{(7)}$); 140.53 ($C_{(7a)}$); 145.12 ($C_{(6)}$); 156.79 ppm ($C_{(3)}$).

Dihydroindazoles IIa, c-e were prepared similarly from the corresponding furylcyclohexenones.

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