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INTERACTION OF ESTERS OF β-AROYLACRYLIC ACIDS WITH *o*-PHENYLENEDIAMINES AND 1,2-DIAMINO-4-PHENYL-IMIDAZOLE

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3-Phenacylquinoxalin-2-ones were synthesized by the reaction of the ethyl esters of β-aroylacrylic acids with o-phenylenediamines, while interaction with 1,2-diamino-4-phenylimidazole gave ethyl 7-amino-2-aryl-5-phenyl-3,4-dihydroimidazolo[1,5-b]pyridazine-4-carboxylates. Their chemical properties have been investigated.

Keywords: dihydroimidazolo[1,5-*b*]pyridazine-4-carboxylates, *o*-phenylenediamines, 1,2-diamino-4-phenylimidazole, β-aroylacrylic acid ethyl esters, chemical properties, cyclocondensation.

β-Aroylacrylic acids are convenient polyelectrophilic reagents in the synthesis of heterocycles, for which the addition reaction of N-, S-, P-, or C-nucleophiles occurs exclusively at the α-carbonyl-electrophilic center of the molecule [1-3]. The products of C-nucleophilic addition were successfully isolated on interaction of the acids with 1,2-diamino-4-phenylimidazole, however cyclization of the intermediates is accompanied by decarboxylation and aromatization, which enabled the preparation only of heteroaromatic derivatives of imidazopyridazine [4]. This limitation was taken off when using N-arylamides of aroylacrylic acids in reaction with the amine indicated [5].

With the aim of broadening the synthetic potential of β-aroylacrylic acids, the behavior of their ethyl esters **1a-f** was studied in reaction with *o*-phenylenediamines **2a,b** and 1,2-diamino-4-phenylimidazole (**3**). Several electrophilic centers are present in the molecules of α,β-unsaturated γ-keto esters **1**, *viz.* atoms C(2) and C(4) and the carbon atom of the ester group, which is hopeful for many reaction routes with nucleophilic reagents.

The initial γ-keto esters **1a-f** were synthesized by known literature methods [6-8]. Their interaction (in the example of compounds **1a,b**) with diamine **2a** in methanol leads to 3-phenacylquinoxalin-2-ones **4a,b**, isolated in high yield. The latter were obtained previously by the reaction of the appropriate β-aroylacrylic acids with *o*-PDA (*o*-phenylenediamine) [9].

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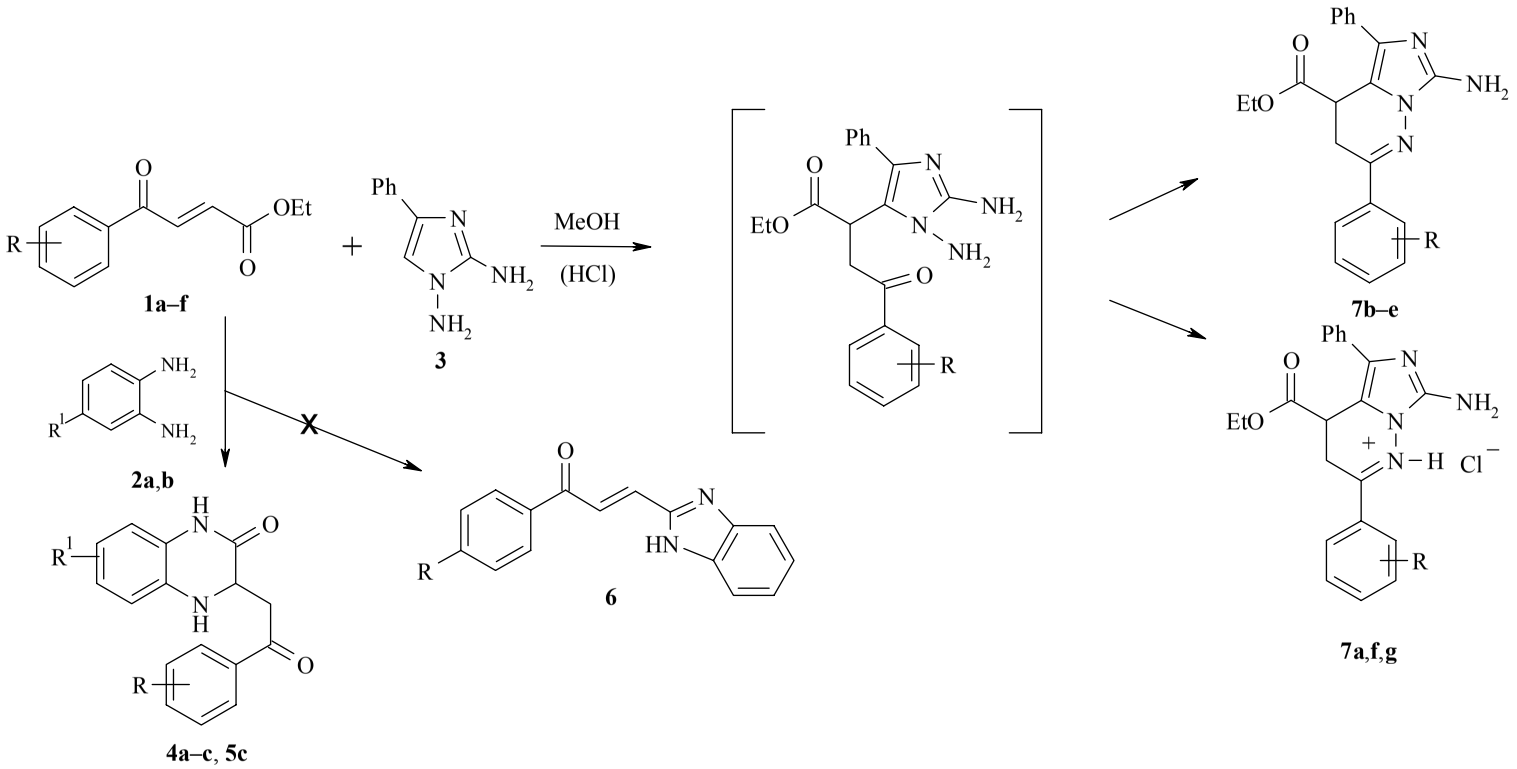


1 a R = H, **b** R = 4-Me, **c** R = 4-Cl, **d** R = 4-Br, **e** R = 4-OMe, **f** R = 2,4-Me_2; **2 a** R^1 = Me, **b** R^1 = NO_2; **4 a** R = R^1 = H, **b** R = 4-Me, R^1 = H; **c** R = 6-NO_2, R^1 = 4-Cl; **5c** R = 7-NO_2, R^1 = 4-Cl; **7 a** R = H, **b** R = 4-Me, **c** R =4-Cl, **d** R = 4-Br, **e,f** R = 4-OMe, **g** R = 2,4-Me_2

TABLE 1. Characteristics of the Synthesized Compounds **7-9**

Compound	Empirical formula	Found, % / Calculated, % N	mp, °C	IR spectrum, ν, cm^{-1} (in KBr)	Yield, %
7a	$C_{21}H_{20}N_4O_2 \cdot HCl$	13.80 / 14.12	224-225	1682, 1720, 3200, 3300	58
7b	$C_{22}H_{22}N_4O_2$	14.90 / 14.96	213-214	1652, 1725, 3292, 3396	61
7c	$C_{21}H_{19}ClN_4O_2$	14.10 / 14.19	218-219	1646, 1720, 3295, 3390	70
7d	$C_{21}H_{19}BrN_4O_2$	12.65 / 12.75	228-229	1648, 1719, 3303, 3400	62
7e	$C_{22}H_{22}N_4O_3$	14.55 / 14.35	196-197	1650, 1720, 3303, 3400	66
7f	$C_{22}H_{22}N_4O_3 \cdot HCl$	13.50 / 13.12	222-223	1682, 1722, 3245, 3353	60
7g	$C_{23}H_{24}N_4O_2 \cdot HCl$	13.40 / 13.19	164-165	1682, 1722, 3210, 3303	63
7i	$C_{21}H_{19}ClN_4O_2 \cdot HBr$	12.00 / 11.78	236-237	1686, 1723, 3273, 3375	65
8a	$C_{23}H_{21}ClN_4O_5$	13.00 / 12.82	226-227	1645, 1665, 1722, 3390	60
8b	$C_{23}H_{21}BrN_4O_5$	11.82 / 11.64	231-232	1650, 1670, 1726, 3425	55
9a	$C_{21}H_{22}N_6O$	22.10 / 22.44	207-208	1660, 3396, 3260, 3198	88
9b	$C_{19}H_{17}BrN_6O$	19.90 / 19.76	255-256	1658, 3486, 3376, 3316	69

With the aim of synthesizing 3-(2-benzimidazolyl)propenones **6** we investigated the interaction of ester **1a** and diamine **2a** on boiling in 2-propanol in the presence of catalytic amounts of HCl, on carrying out the reaction in toluene, and also on fusing the starting materials [10]. However exclusively quinoxalone **4a** was isolated in these experiments. The α-carbon atom of the molecule acts as the center for initial nucleophilic attack in all cases. This is indicated, particularly, by the formation of a mixture of 6/7-nitroquinoxalin-2-ones (**4c** + **5c**) in the reaction of ester **1c** with diamine **2b** (ratio of isomers was 4 : 1). The same ratio of isomers was also obtained in the reaction of diamine **2a** with *p*-chlorobenzoylacrylic acid, where nucleophilic addition by the more basic amino group occurs at the α-position [9].

Compounds **7b-e** and **7a,f,g** were obtained in satisfactory yield (see EXPERIMENTAL) on boiling diaminoazole **3** with esters **1a-f** briefly in methanol, without a catalyst, or in the presence of catalytic amounts of HCl respectively. Their structures were confirmed by IR and ^{1}H NMR spectra. In the IR spectra (KBr disks) of compounds **7b-e** bands were observed for the stretching vibrations of the ester carbonyl group at 1720-1725, and intense bands at 1645-1650 cm^{-1} attributed to the stretching vibrations of the hydrazone group. Two medium intensity bands were seen at 3200-3400 cm^{-1} which indicates preservation of the primary amino group. The same set of absorption bands was characteristic of the IR spectra of products **7a,f,g**, but the bands of the stretching vibrations of the C=N bond were displaced by 30 cm^{-1} towards higher frequency, which indicates the presence of a less conjugated system.

Signals were displayed in the ^{1}H NMR spectra of compounds **7a-g** for the protons of the ABX system of the dihydropyridazine ring, a doublet of doublets, and a doublet for the protons of the methylene group, a doublet for the methine proton, a triplet and a quartet for the ethoxycarbonyl group, a two-proton singlet for the amino group on the imidazole ring (signal disappears on deuterium exchange) at 6.1-6.2 (compounds **7b-e**) and 8.1-8.3 ppm (compounds **7a,f,g**), and multiplets for the protons of the two aromatic nuclei. The geminal

TABLE 2. The NMR Spectra of Compounds **7-9**

Compound	Chemical shifts, d, ppm. (SSCC, *J*, Hz)					
	$C_{(3)}H_2$ ($1H_A$, dd, $1H_B$, d, J_{AB} = 17.7, J_{BX} = 0)	$C_{(4)}H$ (1H, d, J_{AX} = 6.5)	$N_{(7)}H_2$ (2H, s)	CH_3 (3H, t), CH_2 (2H, q, *J* =7.6)	CH_3, OCH_3	H_{arom}
7a	3.10, 3.67	4.69	8.26	0.96, 4.00		8.11 (2H, d, *J* = 8.0, *o*-Ar); 7.73 (2H, d, *J* = 6.8, *o*-C_6H_5); 7.61-7.45 (6H, m)
7b	2.82, 3.39	4.55	6.08	0.97, 3.97	2.35 (3)	7.90 (2H, d, *J* = 7.8, *o*-Ar); 7.76 (2H, d, *J* = 7.8, *o*-C_6H_5); 7.39-7.20 (5H, m)
7c	2.84, 3.43	4.54	6.15	0.96, 3.95	—	8.00 (2H, d, *J* = 8.4, *o*-Ar); 7.75 (2H, d, *J* = 7.2, *o*-C_6H_5); 7.62 (2H, d, *J* = 8.6, *m*-Ar); 7.38-7.20 (3H, m, *m* + *p*-C_6H_5)
7d	2.84, 3.42	4.54	6.18	0.97, 3.97	—	7.97 (2H, d, *J* = 8.0, *o*-Ar); 7.76 (2H, d, *J* = 7.4, *o*-C_6H_5); 7.67 (2H, d, *J* = 8.0, *m*-Ar); 7.39-7.25 (3H, m, *m* + *p*-C_6H_5)
7e	2.80, 3.42	4.52	6.05	0.97, 4.00	3.80 (3)	7.96 (2H, d, *J* = 8.8, *o*-Ar); 7.76 (2H, d, *J* = 7.6, *o*-C_6H_5); 7.01 (2H, d, *J* = 8.8, *m*-Ar); 7.38-7.18 (3H, m, *m* + *p*-C_6H_5)
7f	2.82, 3.46	4.67	8.15	0.97, 3.99	3.84 (3)	8.10 (2H, d, *J* = 9.0, *o*-Ar); 7.71 (2H, d, *J* = 6.8, *o*-C_6H_5); 7.06 (2H, d, *J* = 9.0, *m*-Ar); 7.52-7.40 (3H, m, *m* + *p*-C_6H_5)
7g	2.87, 3.42	4.61	8.07	1.02, 4.05	2.31 (3), 2.42 (3)	7.71 (2H, d, *J* = 7.4, *o*-C_6H_5); 7.55-7.34 (4H, m, *m* + *p*-C_6H_5 + Ar); 7.15-7.12 (2H, m, Ar)
7i	2.97, 3.60	4.69	8.33	0.96, 3.95	—	8.19 (2H, d, *J* = 8.6, *o*-Ar); 7.71 (2H, d, *J* = 7.2, *o*-C_6H_5); 7.61 (2H, d, *J* = 8.6, *m*-Ar); 7.53-7.35 (3H, m, *m* + *p*-C_6H_5)
8a	2.99, 3.49	4.69	10.2*	0.96, 3.97	2.10 (3)	7.97 (2H, d, *J* = 8.6, *o*-Ar); 7.82 (2H, d, *J* = 7.6, *o*-C_6H_5); 7.58 (2H, d, *J* = 8.8, *m*-Ar); 7.44-7.27 (3H, m, *m*+ *p*-C_6H_5)
8b	2.98, 3.48	4.68	10.19*	0.96, 3.94	2.10 (3)	7.89 (2H, d, *J* = 8.4, *o*-Ar); 7.82 (2H, d, *J* = 7.6, *o*-C_6H_5); 7.72 (2H, d, *J* = 8.6, *m*-Ar); 7.45-7.27 (3H, m, *m* + *p*-C_6H_5)
9a	2.71, 3.08	4.18	5.82, 4.24*[2], 9.33*[3]	—	2.23 (3), 2.41 (3)	7.61 (2H, d, *J* = 7.9, *o*-C_6H_5); 7.34-7.18 (4H, m, *m* + *p*-C_6H_5, Ar); 7.12-7.08 (2H, m, Ar)
9b	2.92, 3.12	4.27	6.08, 4.20*[2], 9.34*[3]	—	—	7.92 (2H, d, *J* = 8.9, *o*-Ar); 7.64 (4H, d, *J* = 8.2, *m*-Ar + *o*-C_6H_5); 7.36-7.12 (3H, m, *m* + *p*-C_6H_5)

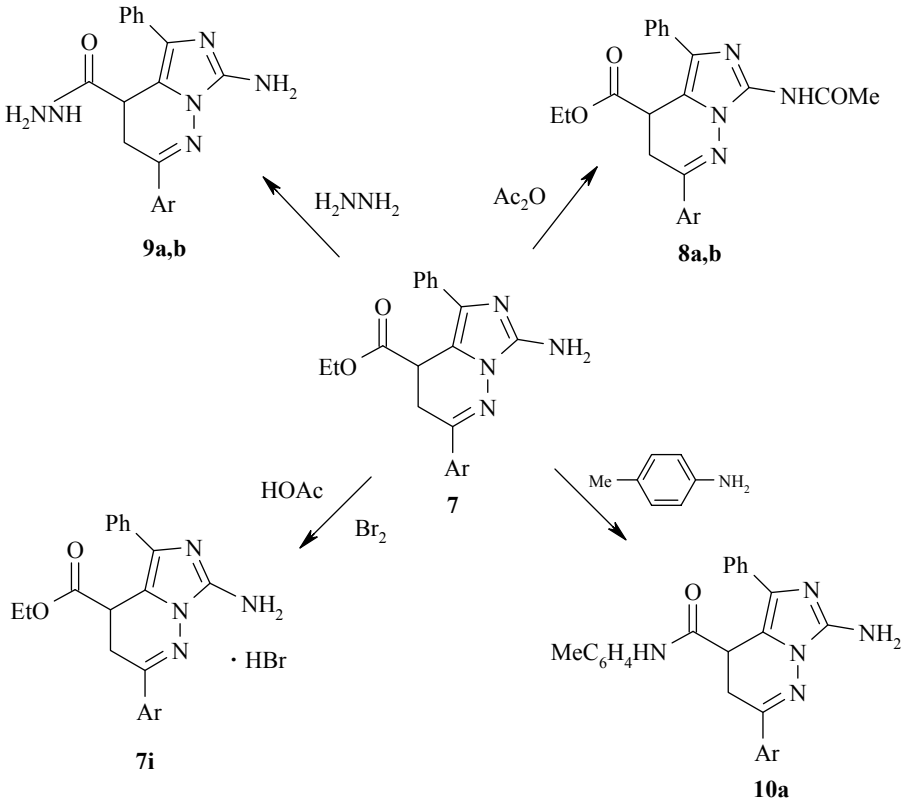
* δ NH.

*[2] δ NH_2 hydrazide fragment.

*[3] δ NH hydrazide fragment.

constant of the ABX system of protons of the dihydropyridazine ring was equal to 17.7 Hz. One of the vicinal constants reached 6.5 Hz, while the second constant approached zero, i.e. the vicinal protons of the dihydropyridazine ring are disposed at an angle close to 90°.

The spectral data and also the results of elemental analysis indicate the formation of ethyl 7-amino-2-aryl-5-phenyl-3,4-dihydroimidazo[1,5-*b*]pyridazine-4-carboxylates **7b-e** or their hydrochlorides **7a,f,g**. The hydrazone group of the pyridazine fragment acts as the center of protonation, as indicated by the increase of its frequency in IR spectra to 1680 cm^{-1}. Protonation of the C=N bond of the pyridazine, and not the imidazole, ring is also confirmed by the ^1H NMR spectra. It follows from Table 2 that the *o*-protons of the 2-aryl substituent in salts **7a,f,g** undergo a low field displacement, while the positions of the *o*-protons of the phenyl group in position 5 are unchanged on going from base to salt.



7i, **8a** Ar = 4-ClC_6H_4; **8b**, **9b** Ar = 4-BrC_6H_4; **9a** Ar = 2,4-$Me_2C_6H_3$; **10a** Ar = Ph

The structures of dihydropyridazines **7** were also confirmed by X-ray structural analysis using compound **7c** as example (Fig. 1). The dihydropyridazine ring is in a *distorted sofa* conformation (folding parameters [11]: S = 0.51°, θ = 44.4°, Ψ = 17.2°). The deviations of the C(1) and C(6) atoms from the mean square plane of the remaining atoms were 0.14 and 0.58 Å respectively. Bond lengths and the conformation of the heterocycle in the **7c** molecule were analogous to those of the 7-amino-2-(*p*-methoxyphenyl)-5-(*p*-methylphenyl)-4-phenyl-3,4-dihydroimidazo[1,5-*b*]pyridazine studied previously [12].

The chlorophenyl substituent is folded relative to the endocyclic N(3)-C(4) double bond of the bicyclic fragment ([torsion angle N(3)–C(4)–C(10)–C(11) 23.4(3)°), probably as a result of repulsion between the atoms of the aromatic and the dihydropyridazine rings [intramolecular shortened contacts H(15A)···H(5B) 2.07 Å (sum of van der Waals radii [13] 2.34 Å), H(15A)···C(5) 2.70 (2.87), H(5B)···C(15) 2.63 Å (2.87 Å)]. The ester substituent is in a pseudoaxial position (torsion angle C(4)–C(5)–C(6)–C(7) 78.7(2)°).

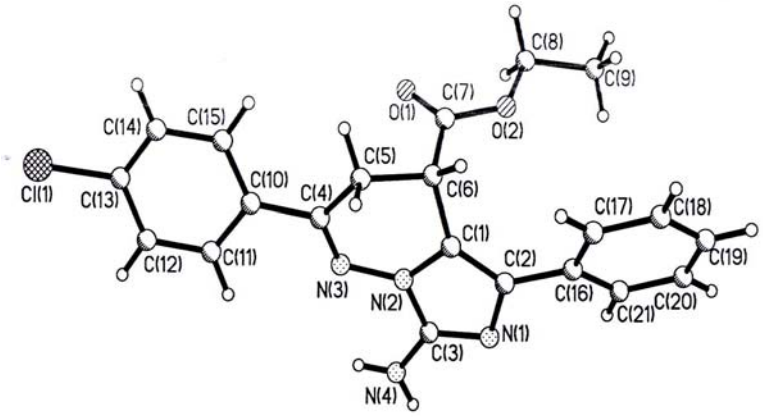


Fig. 1. Molecular structure of compound **7c**.

The phenyl substituent is unfolded relative to the plane of the imidazole fragment (torsion angle C(1)–C(2)–C(16)–C(21) 25.9(3)°), which is probably the result of two opposing factors: on the one hand, repulsion between the H(21) and H(6) atoms (intramolecular shortened contact H(21)···H(6) 2.20 (2.34)), and on the other hand, the attractive interaction of H(17)···N(1) 2.61 Å (2.67 Å).

Dimers are formed in the crystal of the **7c** molecule as a result of an intermolecular hydrogen bond N(4)–H(4NB)···N(1)′ (*-x* + ½, *-y* - ½, *-z* + 2) H···N 2.15 Å, N–H···N 160°.

The C(2) atom of the molecule therefore acts as the center of nucleophilic attack in reactions of esters of β-aroylacrylic acids with both 1,4- and 1,3-azabinucleophiles. The further course of the reaction is determined by the formation of the thermodynamically more stable six-membered rings, quinoxaline or pyridazine respectively. In the latter case the α-effect of the hydrazine amino group of diaminoazole **3** favors its formation.

We have also studied some chemical properties of imidazopyridazines **7**. On boiling imidazopyridazines **7c,d** in acetic anhydride, the acetyl derivatives **8a,b** are formed in satisfactory yield. Bromination of imidazopyridazine **7c** with bromine in acetic acid did not lead to the expected 3-bromo derivative, only the hydrobromide of imidazopyridazine **7i** was isolated from the reaction mixture. Base **7c** and also the salt forms of imidazopyridazines **7a,i** were not successfully reduced by $NaBH_4$ in acetic acid.

TABLE 3. Bond Lengths (*l*) in the Structure of Compound **7c**

Bond	*l*, Å	Bond	*l*, Å
N(1)–C(3)	1.322(2)	N(1)–C(2)	1.405(3)
O(1)–C(7)	1.195(2)	C(1)–C(2)	1.362(2)
Cl(1)–C(13)	1.743(2)	C(1)–N(2)	1.387(2)
C(1)–C(6)	1.497(3)	N(2)–C(3)	1.371(2)
N(2)–N(3)	1.387(2)	O(2)–C(7)	1.320(2)
O(2)–C(8)	1.450(3)	C(2)–C(16)	1.471(3)
N(3)–C(4)	1.281(2)	C(3)–N(4)	1.346(3)
C(4)–C(10)	1.478(3)	C(4)–C(5)	1.495(3)
C(5)–C(6)	1.527(2)	C(6)–C(7)	1.512(3)
C(8)–C(9)	1.514(3)	C(10)–C(11)	1.323(3)
C(10)–C(15)	1.338(3)	C(11)–C(12)	1.387(3)
C(12)–C(13)	1.321(3)	C(13)–C(14)	1.290(3)
C(14)–C(15)	1.385(3)	C(16)–C(21)	1.377(3)
C(16)–C(17)	1.393(3)	C(17)–C(18)	1.384(3)
C(18)–C(19)	1.362(4)	C(19)–C(20)	1.371(3)
C(20)–C(21)	1.383(3)		

TABLE 4. Valence Angles (ω) in the Structure of Compound **7c**

Angle	ω, deg.	Angle	ω, deg
C(3)–N(1)–C(2)	105.77(17)	C(3)–N(1)–C(2)	105.77(17)
C(2)–C(1)–N(2)	104.87(19)	C(2)–C(1)–C(6)	138.5(2)
N(2)–C(1)–C(6)	115.51(17)	N(2)–C(1)–C(6)	115.51(17)
C(3)–N(2)–N(3)	122.43(19)	C(1)–N(2)–N(3)	128.89(17)
C(7)–O(2)–C(8)	118.93(18)	C(1)–C(2)–N(1)	110.46(18)
C(1)–C(2)–C(16)	129.3(2)	N(1)–C(2)–C(16)	120.15(19)
C(4)–N(3)–N(2)	115.03(18)	N(1)–C(3)–N(4)	127.3(2)
N(1)–C(3)–N(2)	110.2(2)	N(4)–C(3)–N(2)	122.42(19)
N(3)–C(4)–C(10)	115.9(2)	N(3)–C(4)–C(5)	124.29(18)
C(10)–C(4)–C(5)	119.7(2)	C(4)–C(5)–C(6)	114.84(18)
C(1)–C(6)–C(7)	106.83(17)	C(1)–C(6)–C(5)	109.07(18)
C(7)–C(6)–C(5)	112.27(17)	O(1)–C(7)–O(2)	123.6(2)
O(1)–C(7)–C(6)	125.7(2)	O(2)–C(7)–C(6)	110.64(19)
O(2)–C(8)–C(9)	105.2(2)	C(11)–C(10)–C(15)	115.5(2)
C(11)–C(10)–C(4)	121.3(2)	C(15)–C(10)–C(4)	123.2(2)
C(10)–C(11)–C(12)	122.4(2)	C(13)–C(12)–C(11)	120.5(3)
C(14)–C(13)–C(12)	118.0(2)	C(14)–C(13)–Cl(1)	121.8(2)
C(12)–C(13)–Cl(1)	120.0(3)	C(13)–C(14)–C(15)	121.9(3)
C(10)–C(15)–C(14)	121.6(3)	C(21)–C(16)–C(17)	117.7(2)
C(21)–C(16)–C(2)	122.1(2)	C(17)–C(16)–C(2)	120.2(2)
C(18)–C(17)–C(16)	121.0(3)	C(19)–C(18)–C(17)	120.3(3)
C(18)–C(19)–C(20)	119.6(3)	C(19)–C(20)–C(21)	120.4(3)
C(16)–C(21)–C(20)	121.0(2)		

Hydrazides **9a,b** were obtained by reacting esters **7d,g** with hydrazine hydrate. Amide **10a** was synthesized by fusing ester **7a** with *p*-toluidine.

Convenient routes for th functionalization of 7-amino-4-ethoxycarbonyl-3,4-dihydroimidazo-[1,5-*b*]pyridazine derivatives are proposed, which do not lead to aromatization of the dihydropyridazine fragment of the molecule.

EXPERIMENTAL

The ^{1}H NMR spectra were measured on a Varian Mercury VX-200 instrument (200 MHz) in solution in DMSO-d_6, internal standard was TMS. The IR spectra were recorded on an IR-75 instrument in KBr disks. A check on the course of reactions, and also on the homogeneity of the compounds obtained, was effected by TLC on Silufol UV-254 plates in the system toluene–ethyl acetate.

X-ray Structural Investigation. Crystals of **7c** were monoclinic, grown in ethanol, $C_{21}H_{19}ClN_4O_2$, at 20°C: a = 28.806(8), b = 8.835(3), c = 17.105(9) Å, β = 102.06(3)°, V = 3928(2) Å^3, M_r = 394.85, Z = 8, space group $C2/c$, d_{calc} = 1.335 g/cm^3, μ(MoKα) = 0.219 mm^{-1}, F(000) = 1648. The parameters of the unit cell and the intensities of 10301 reflections (3418 independent, R_{int} = 0.038) were measured on a Xcalibur-3 diffractometer (MoKα radiation, CCD detector, graphite monochromator, ω-scanning, $2\theta_{max}$ = 50).

The structure was solved by the direct method with the SHELXTL set of programs [14]. The positions of the hydrogen atoms were made apparent from an electron density difference synthesis and were refined by the "rider" model with $U_{iso} = nU_{eq}$ for the non-hydrogen atom linked to the given hydrogen (n = 1.5 for a methyl group and n = 1.2 for the remaining hydrogen atoms). The structure was refined on F^2 with the full matrix least squares method in an anisotropic approximation for non-hydrogen atoms to wR_2 = 0.074 for 3374 reflections

(R_1 = 0.035 for 1320 reflections with $F > 4\sigma(F)$, S = 0.709). The coordinates of atoms and the complete table of bond lengths and valence angles have been deposited in the Cambridge structural data bank (CCDC 664799).

Quinoxalones 4a,b, and also the mixture of quinoxalones **4c** + **5c** were obtained by the procedure reported in [9]. Yields were 62, 80, and 75% respectively.

Compound 4a was isolated in 68% yield on carrying out the reaction in 2-propanol in the presence of catalytic amounts of HCl. On carrying out the reaction in toluene the yield was 72%, and on fusing the reactants 65%.

6-Nitroquinoxalone 4c. ^{1}H NMR spectrum, δ, ppm (J, Hz): 3.42 (1H, dd, J_{AB} = 17.2, J_{AX} = 6.4, H_A CH_2); 3.58 (1H, dd, J_{AX} = 6.4, H_B CH_2); 4.49 (1H, t, J_{BX} = 4.0, H_X CH); 6.65 (1H, br. s, NH); 6.94-7.89 (7H, m, Ar); 10.95 (1H, s, NH).

7-Nitroquinoxalone 5c. ^{1}H NMR spectrum, δ, ppm (J, Hz): 3.42 (1H, dd, J_{AB} = 17.2, J_{AX} = 6.4, H_A CH_2); 3.58 (1H, dd, J_{AX} = 6.4, H_B CH_2); 4.54 (1H, t, J_{BX} = 4.0, H_X CH), 6.65 (1H, br. s, NH); 6.94-7.89 (7H, m, Ar), 10.71 (1H, s, NH).

Ethyl 7-Amino-2-(4-methylphenyl)-5-phenyl-3,4-dihydroimidazo[1,5-*b*]pyridazine-4-carboxylate (7b). A mixture of diamine **3** (0.174 g, 1 mmol) and ester **1b** (0.218 g, 1 mmol) in EtOH (10 ml) was boiled under reflux for 1 h. The mixture was cooled, the solid was crystallized from ethanol, and compound **7b** (0.23 g) was obtained.

Bases 7c-e were obtained analogously. Base **7c** was also obtained in 56% yield on boiling salt **7i** in methanol in the presence of an excess of Et_3N.

Ethyl 7-Amino-2,5-diphenyl-3,4-dihydroimidazo[1,5-*b*]pyridazine-4-carboxylate Hydrochloride (7a). Conc. HCl (5 drops) was added to a mixture of diamine **3** (0.174 g, 1 mmol) and ester **1a** (0.204 g, 1 mmol) in EtOH (10 ml), and the mixture boiled under reflux for 1 h. The solid, which precipitated on cooling, was washed with ethanol.

Salts 7f,g were obtained analogously.

Ethyl 7-Amino-2-(4-chlorophenyl)-5-phenyl-3,4-dihydroimidazo[1,5-*b*]pyridazine-4-carboxylate Hydrobromide (7i). Bromine (0.1 ml, 1 mmol) in AcOH (5 ml) was added dropwise with stirring to a solution of compound **7c** (0.394 g, 1 mmol) in AcOH (10 ml). After the end of bromination the solution was stirred for 0.5 h, and poured onto ice. The solid was filtered off, and crystallized from ethanol.

Ethyl 7-(N-Acetylamino)-2-(4-chlorophenyl)-5-phenyl-3,4-dihydroimidazo[1,5-*b*]pyridazine-4-carboxylate (8a). A mixture of imidazopyridazine **7c** (0.394 g, 1 mmol) and Ac_2O (1 ml) was boiled under reflux for 10 min. The reaction mixture was poured into ice-water, the solid was filtered off, and crystallized from ethanol.

Compound 8b was obtained analogously.

7-Amino-2-(4-bromophenyl)-5-phenyl-3,4-dihydroimidazo[1.5-*b*]pyridazine-4-carbohydrazide (9b). A solution of pyridazine **7d** (0.475 g, 1 mmol) in 95% hydrazine hydrate (2.5 ml, 50 mmol) was heated on a water bath for 5 h. The yellow solid precipitated on cooling was washed with water, and crystallized from ethanol. Yield was 0.32 g.

Hydrazide 9a was obtained analogously.

4-[N-(4-Methylphenyl)carboxamido-7-amino-2,5-diphenyl-3,4-dihydroimidazo[1,5-*b*]pyridazine (10a). A mixture of salt **7a** (0.397 g, 1 mmol) and *p*-toluidine (0.160 g, 1.5 mmol) was maintained at 170°C for 1 h, then at 200°C for 0.5 h. The mixture was cooled, and benzene (10 ml) was added. The precipitated solid was recrystallized from ethanol. Yield was 0.25 g (65%) of mp 219-220°C (lit. 219°C [5]).

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