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Reactions of Isomeric Arylchloropyruvates and Glycidates with Hydrazines

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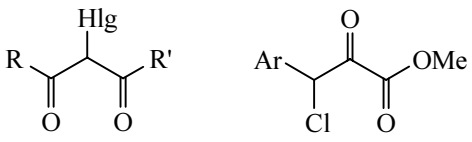
Abstract—Reactions of arylchloropyruvic acids esters with aryl- and hetarylhydrazines give rise to pyrazolinedione hydrazones as a result of a tandem condensation of the substituted hydrazines with arylchloropyruvates. In contrast to this process in reaction with hydrazine hydrate a ready reduction unexpectedly occurs by Kizhner–Wolff mechanism affording 3-hydroxydihydrocinnamic acid hydrazide as the principal product. The isomeric arylglycidate reacts along the same pattern.

The condensations of α-halocarbonyl compounds with hydrazines often occur in a complex way affording several products. The main reason of this is the instability of unsubstituted and monosubstituted hydrazones of carbonyl compounds [1] containing a halogen atom in the α-position [1, 2]. Therefore even in the course of the corresponding hydrazone preparation 1,4-elimination frequently takes place affording an azoolefin molecule [3, 4]. In many cases further reaction pathway is governed by the reactivity of the intermediately formed azoolefin that undergoes isomerization into hydrazones of α,β-unsaturated carbonyl compounds which in their turn get involved into versatile 1,4-cycloadditions. The addition of an arylhydrazine may furnish a diazoolefin, osazone, and their reaction product [5]. Besides in some cases the azoolefins suffer dimerization by Diels–Alder reaction [6]. When the intermediate azoolefin contains in its structure both a diene and dienophile fragments an intramolecular cyclization may also occur by the same mechanism [7]. The azoolefins unsubstituted at the nitrogen are prone to nitrogen elimination giving an olefin, similarly to Kizhner reduction [8]. The various concurrent reactions proceeding in the system chloropyruvate **Ia, Ib**–hydrazine or phenylhydrazine commonly prevent isolation of individual products and their identification at the use of equimolar reagents ratio since the hydrazine and many among its derivatives show abnormal high nucleophilic activity with respect to the sp^2-hybridized carbon atom linked to the corresponding leaving groups [1, 9]. On the other hand, condensation of hydrazine and its derivatives with carbonyl compounds affording hydrazones is well known and is widely used for aldehydes and ketones identification [10]. At the same time the hydrazines alkylation occurs usually at the more substituted nitrogen. With a bulky alkylating agent the attack may be directed also on the other nitrogen atom [11].

The above mentioned concise analysis of the published data reveals that the reactions of hydrazones even with the simplest representatives of the α-haloketones, like ω-haloacetophenones and α-chloroacetone, take multiple routes affording cyclic and non-cyclic compounds of various types. The number of probable and sometimes unpredictable reactions with nucleophilic reagents increases even more due to the possible processes involving additional functional groups introduced into the structure of the α-haloketones [8, 9, 12, 13]. In this connection we deemed it interesting to study the behavior in the condensation with various hydrazines of functionalized α-chloroketones: methyl phenyl- (**Ia**) and 3-nitrophenylchloropyruvates (**Ib**), and of one among the chloroepoxides isomeric to the above esters, methyl 3-(3-nitrophenyl)-2-chloroglycidate (**II**) (the precursor of the chloropyruvate). These compounds might act either like functionally-substituted α-chloroketones, or like unsubstituted ketones, or like esters of β-chlorocarboxylic acids.



Ia, Ib

Ar = Ph (**a**), 3-$O_2NC_6H_4$ (**b**).

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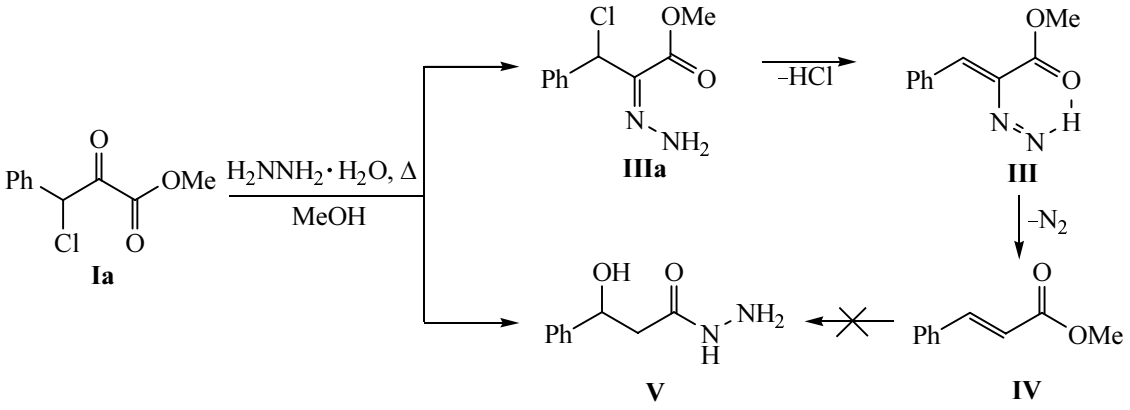
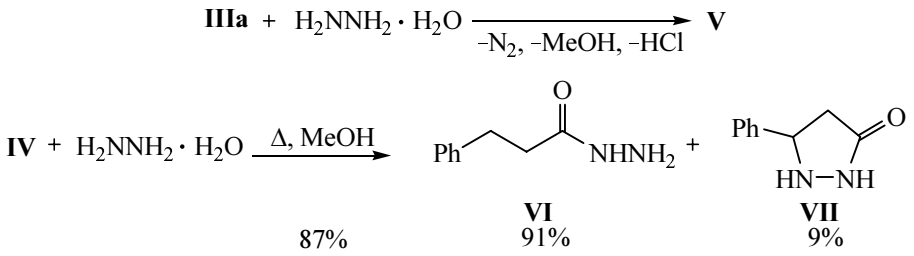
Scheme 1.



Scheme 2.



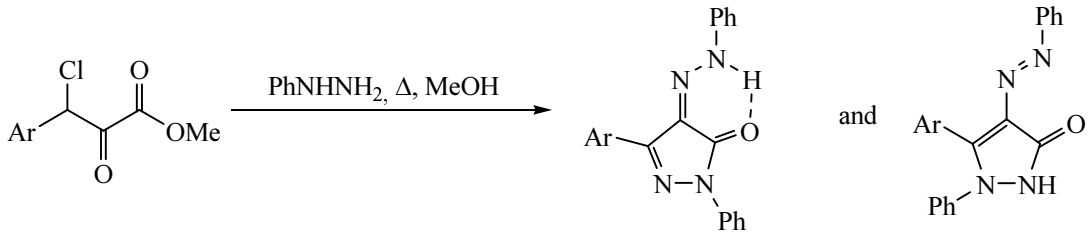
The study of reaction between arylchloropyruvates **Ia** and **Ib** and hydrazines revealed that the best results were obtained in the process carried out in a boiling methanol solution at the molar reagents ratio of 1:3. From the products of reaction between compound **Ia** and hydrazine hydrate we isolated a substance whose spectral characteristics did not fit to those of azoolefin **III** [2] and/or olefin **IV** [1, 2], the expected products of these reactions. The presence in the H^1 NMR spectrum signals from protons of the CH_2CH group in the form of an *ABX* system, and also the lack of the methoxy group signal and appearance of broadened singlets with the intensity ratio 2:1 in the region δ 4.17 and 9.28 ppm belonging to the protons of a hydrazide moiety suggest that the reaction of chloropyruvate **Ia** with hydrazine hydrate occurs involving all electrophilic sites, namely, with the reduction of the cabonyl group by Kizhner–Wolff reaction [1], the hydrazinolysis of the ester group, and the hydrolysis of the benzylhalide fragment resulting in 3-phenyl-3-hydroxypropionic acid hydrazide (**V**) (Scheme 1).

The standard reaction products of α-chloroketones and hydrazines are commonly azoolefins that further are converted into olefins [12]. In the event described here the expected products were azocompound **III** and methyl cinnamate **IV**. But inasmuch as the reaction of the latter with the hydrazine hydrate does not afford compound **V** (resulting from the hydration of the olefin bond and the hydrazinolyzis) but a dihydrocynnamic acid hydrazide (**VI**) (a product of the olefin bond reduction followed by hydrazinolyzis) and 3-pyrazolidone (**VII**) (Scheme 2), it is presumable that the keto function in the phenylchloropyruvate **I** is reduced into a methylene group before the 1,4-elimination of HCl from the intermediate hydrazone **IIIa** to give azoolefin **III** which should have provided methyl ester **IV** and further the dihydrocynnamic acid hydrazide; most likely, the hydrazone intermediate **IIIa** undergoes the Kizhner–Wolff reduction and then hydrazinolyzis and hydrolyzis of the α-chlorobenzyl function leading finally to hydrazide **V**.

The Kizhner–Wolff reduction under these mild conditions is a remarkable fact for this reaction usually requires high temperature (200–230°C) and a presence of strong bases [1, 14].

The reaction of methyl arylchloropyruvates **Ia** and **Ib** with phenylhydrazine, weaker base than hydrazine (pK_a 5.27 and 7.95 respectively [15]), in the boiling methanol gave rise to crystalline substances of light-orange (**VIIIa**) and bright-red (**VIIIb**) color depending on the initial chloropyruvates **Ia** and **Ib**. Based on the analytical and spectral data we assigned these reaction products isomeric structures **VIII** and **IX**.

Scheme 3.



Ia, Ib **VIIIa, VIIIb** **IX**

Ar = Ph (**a**), 3-$O_2NC_6H_4$ (**b**).

The presence in the IR spectra of solutions (0.01 mol l^{-1}) of products obtained from pyruvates **Ia** and **Ib** in reaction with phenylhydrazine of an absorption band belonging to chelated lactam C=O (1680 and 1675 cm^{-1}) and NH groups (3200–3240 cm^{-1}) evidences according to published data [16] the formation of an intramolecular hydrogen bond that is probable in the isomers of hydrazone type **VIIIa** and **VIIIb** and impossible in the aza form **IX** although the light-orange and bright-red colors of the final products suggest the aza structure of compounds. The unambiguous choice between the structures **VIII** and **IX** in favor of **VIII** was based on the X-ray diffraction study.

Compound **VIII** crystallized in a rhombic space group with one independent molecule in the asymmetrical part of the unit cell. The conformation of the molecule is approximately planar (Fig. 1) with the following dihedral angles between the flat five-membered ring and the planes of the benzene rings of the substituents C^6C^{11} 9.7(2), $C^{14}C^{19}$ 2.1(2), $C^{20}C^{25}$ 3.5(2) deg. The nitro group also proved to be in the plane of the molecule: the torsional angle $O^{28}N^{26}C^{22}C^{23}$ equaled to 7.8(4) deg. This reciprocal position of the fragments in the molecule was favorable for formation of several intramolecular contacts of the types C–H···O and C–H···N and of a hydrogen bond N–H···O (dotted line on Fig. 1). The parameters of the hydrogen bond N^{13}–H^{13}···O^3 are as follows: $d(H^{13}\cdots O^3)$ 1.92(3) Å, angle $N^{13}H^{13}O^3$ 139(2) deg.

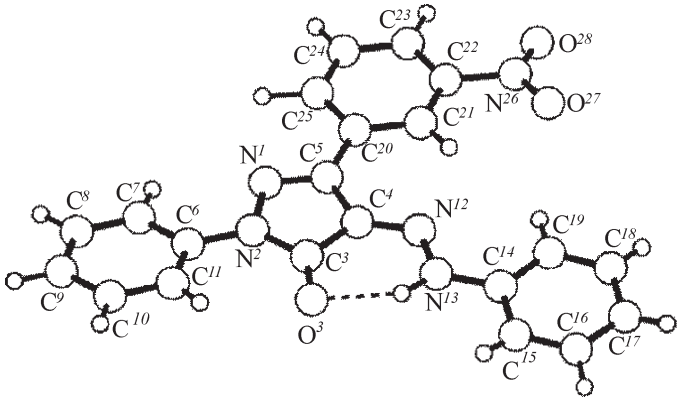


Fig. 1. Geometry of 4-(phenylhydrazono)-3-oxo-2-phenyl-5-(3-nitrophenyl)pyrazoline (**VIIIb**) molecule in a crystal (the hydrogen bond is shown by a dotted line).

The involvement of O^{27} and O^{28} atoms of the nitro group in the molecule **VIII** into the intermolecular contacts of the type C–H···O with benzene ring protons of the neighbor symmetrically bonded molecules [$H^{25'}$ (–1/2 + x, 1/2 – y, 1 – z) and $H^{9''}$(–1 + x, y, –2 + z) with parameters: $d(O^{28}\cdots H^{25'})$ 2.37(3) Å, angle $C^{25'}H^{25'}O^{28}$ 148.4(7) deg, and $d(O^{27}\cdots H^{9''})$ 2.50(3) Å, angle $C^{9''}H^{9''}O^{27}$ 153.8(5) deg] results in a supramolecular associate in the shape of a *V*-like infinite band of molecules linked by the hydrogen bonds (Fig. 2). The packing of these structural motifs is governed by a large number of π-π contacts between the aromatic fragments of the molecules with the shortest distance between the ring centers of 3.65(2) Å and with dihedral angles in the range 2–9 deg.

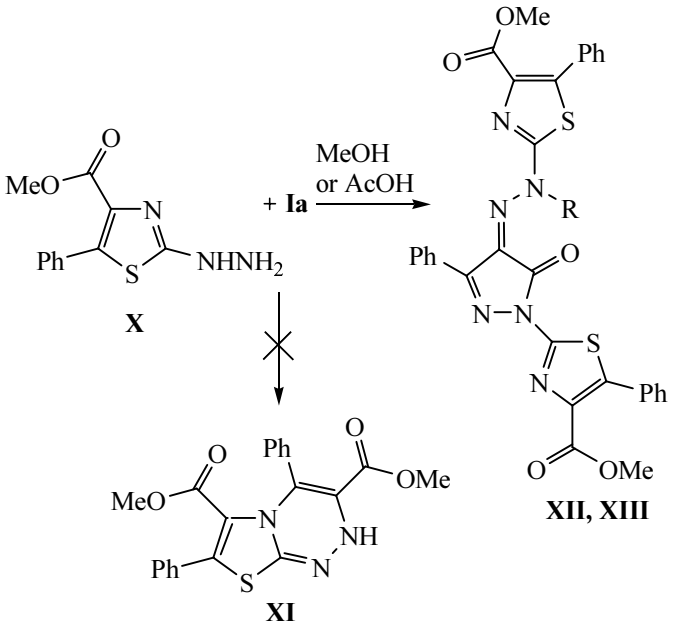
Thus in the crystal **VIIIb** a two-dimensional layer structure arises with different types of intermolecular interactions existing in the layer in two directions: in the crystallographic direction (101), namely, along the diagonal of the plane *XOZ*, the bonding of molecules occurs through C–H···O contacts whereas in the perpendicular direction only π-π contacts are formed. The accounting for only one of the revealed interaction types, e.g., for contacts between the aromatic systems of the molecules would result in a different (isomorphic) supramolecular structure.

The overall packing in the crystal occurs as a stacking of the above described layers along the crystallographic axis *OY* (Fig. 3); therewith the adjacent layers are mutually perpendicular.

Inasmuch as in going from the hydrazine hydrate to the phenylhydrazine the direction of the reaction with chloropyruvates **Ia** and **Ib** was as described above altered

we studied interaction of chloropyruvate **Ia** with a hetarylhydrazine by an example of 2-hydrazino-4-methoxycarbonyl-5-phenylthiazole (**X**) [17–19] whose structure contained an imine moiety in the α-positions to the hydrazine group suggesting that in the process fused products might form [20–22], for instance, compound **XI**. The reaction of chloropyruvate **Ia** with 2-hydrazinothiazole in methanol gave rise to a crystalline substance of bright-red color. Based on the elemental analysis, IR and ^{1}H NMR, and also mass spectra (with precision evaluation of the ion masses) that revealed the formation of a molecular ion with *m/z* 622 corresponding to an empirical formula $C_{31}H_{22}N_6O_5S_2$ the compound was assigned structure **XII** analogous to 5-phenylpyrazolidones **VIIIa** prepared by reaction of phenylhydrazine with chloropyruvates **Ia** and **Ib**. The annelation product, thiazolo[2,3-*C*]triazine (**XI**), did not form under the given conditions.

The reaction between chloropyruvate **Ia** and 2-hydrazinothiazole **X** occurred analogously in the boiling acetic acid, but the product **XIII** suffered acetylation. This is supported in particular by the precision mass evaluation of the molecular ion at *m/z* 664 in agreement with the empirical formula $C_{33}H_{24}N_6O_6S_2$ for compound **XIII**. The ^{1}H NMR spectrum is also consistent with the assumed structure. However it should be mentioned that in the ^{1}H NMR spectrum of compound **XIII** registered in DMSO-d_6 the singlet of the acetyl group is considerably broadened compared to the resonances of the



R = H (**XII**), MeC(O) (**XIII**).

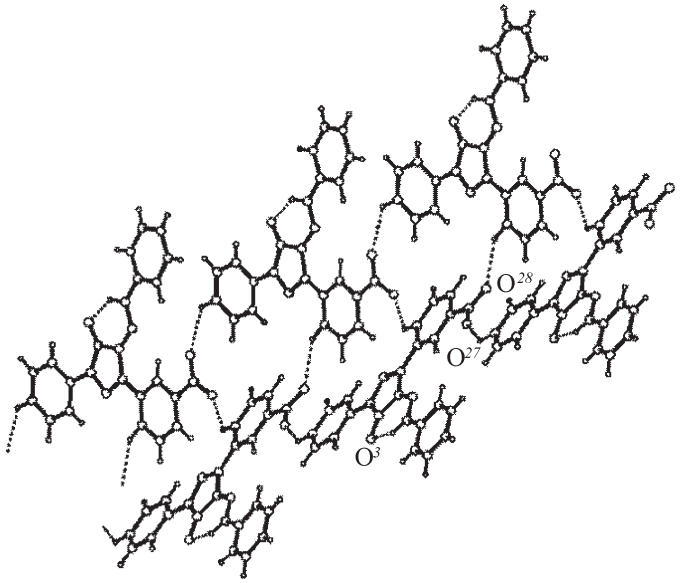


Fig. 2. *V*-Shaped motifs of molecules in the crystal of pyrazoline **VIIIb** connected by hydrogen bonds (the hydrogen bonds are shown by dotted lines).

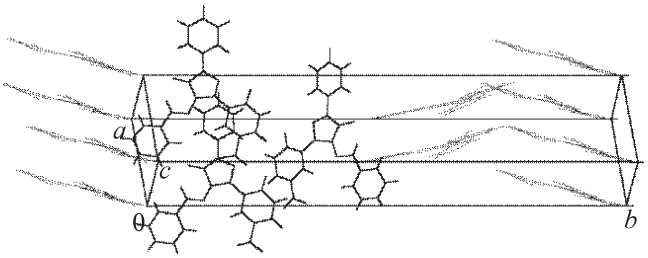


Fig. 3. Packing of molecules in pyrazoline **VIIIb** crystal.

methoxycarbonyl groups apparently testifying to the occurrence of exchange process involving acylotropy [23]. In contrast to previously reported data [20–22, 24] the formation from such systems both in methanol and acetic acid of excusively pyrazolinone structures **XII** and **XIII** and not a thiazolo[2,3-*C*]triazine compound **XI** demonstarated once more that the direction of reaction between 2-hydrazinothiazoles with carbonyl compounds is not always dependent on the reaction conditions, in particular, on the solvent.

Compound **XII** also crystallized without solvate molecules, and the asymmetrical part of the unit cell contained a single molecule. All three five-membered rings of the molecule are located virtually in the same plane: the rings $S^6C^7N^8C^9C^{10}$ and $S^{13}C^{14}N^{15}C^{16}C^{17}$ form dihedral angles with the plane of the ring $N^1N^2C^3C^4C^5$ equal to 4.2(5) and 5.8(5) deg respectively, and the angle between them is 2.5(5) deg. Therewith the phenyl substituents attached to the five-membered rings are turned from the molecule plane, the torsion angles for

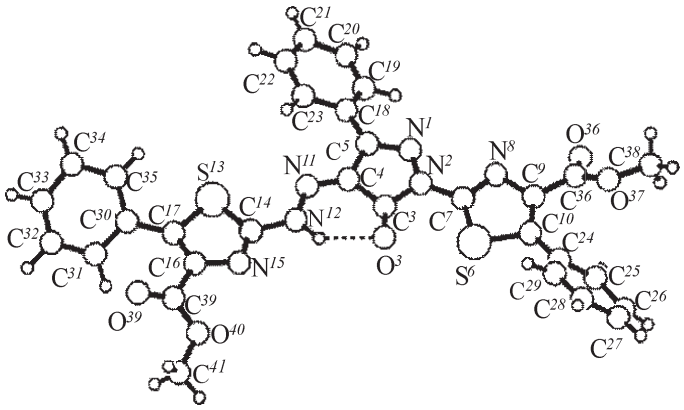


Fig. 4. Geometry of 2-(4'-methoxycarbonyl-5'-phenyl)-thiazolyl-3-oxo-4-(4'-methoxycarbonyl-5'-phenyl)thiazolyl-hydrazono-5-phenylpyrazoline (**XII**) molecule in a crystal (the hydrogen bond is shown by a dotted line).

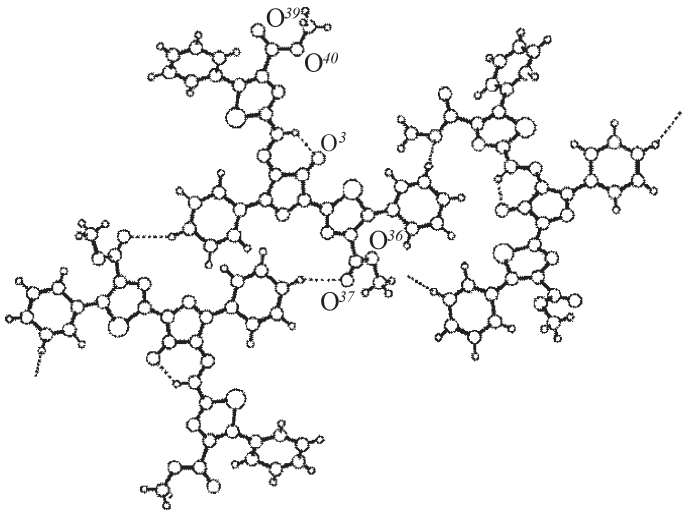


Fig. 5. Dimers formation in the pyrazoline **XII** crystall (the hydrogen bonds are shown by dotted lines, only the oxygens involved into hydrogen bonds are numbered).

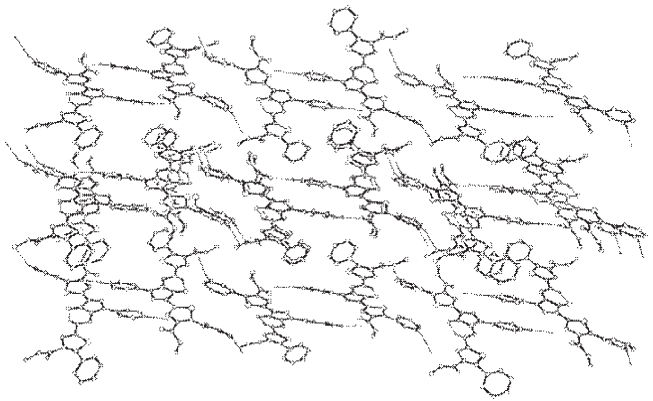


Fig. 6. Packing of pyrazoline **XII** in the crystal viewed along the *OY* axis.

the benzene rings lay in the range of 22.4(6)–46.8(5) deg. However this turn of the rings does not hamper the formation of the numerous intramolecular contacts of the type C–H···O, C–H···S, and C–H···N involving the protons of the phenyl rings. To the observed classic hydrogen bonds belongs only the intramolecular bond N^{12}–H^{12}···O^{3} [d(H^{12}···O^{3}) 2.00 Å, angle $N^{12}H^{12}O^{3}$ 131.6 deg] analogous to that observed in the crystal of compound **VIIIb** but with somewhat longer H···O distance (Fig. 4).

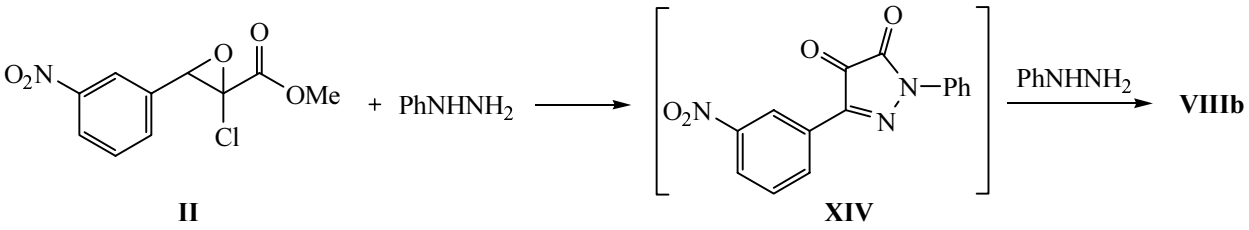
The analysis of intermolecular interactions in the crystal of compound **XII** shows the diversity of their types. The interactions involved are both of π···H and π-π type. However we believe that the main type of interactions governing the character of the arising supramolecular structures is the interaction of C–H···O type. Thus due to a couple of interactions C^{21}–H^{21}···$O^{36'}$(–x, 2 – y, –z) with parameters d($O^{36'}$···H^{21}) 2.48 Å and an angle $C^{21}H^{21}O^{36'}$ 154.8 deg a dimer is formed (Fig. 5). At the same time the interaction of the O^{40} atom of the methoxy group with the proton of the phenyl group $H^{28''}$[–x, 1 + y, 1/2 – z, d(O^{40}···$H^{28''}$) 2.58 Å and angle $C^{28''}H^{28''}O^{40}$ 156.1 deg] leads finally to binding the dimers in two mutually perpendicular directions and to formation of a three-dimensional net of molecules connected by the hydrogen bonds.

Noteworthy is the fact that in the crystals of this compound a localization of hydrophilic and hydrophobic regions is also observed but the supramolecular structure thus formed (consisting of bilayers with alternating hydrophilic and hydrophobic fragments) does not coincide with the supramolecular structure built up by hydrogen bonds (Fig. 6).

The reaction in a methanol solution of equimolar amounts of phenylhydrazine and chloroglycidate **II** unlike that with its isomer 3-nitrochloropyruvate **Ib** afforded pyrazolinedione **XIV** that by treatment with phenylhydrazine was converted into 4-phenylhydrazono-3-oxo-2-phenyl-5-(3-nitrophenyl)pyrazoline (**VIIIb**) (Scheme 4).

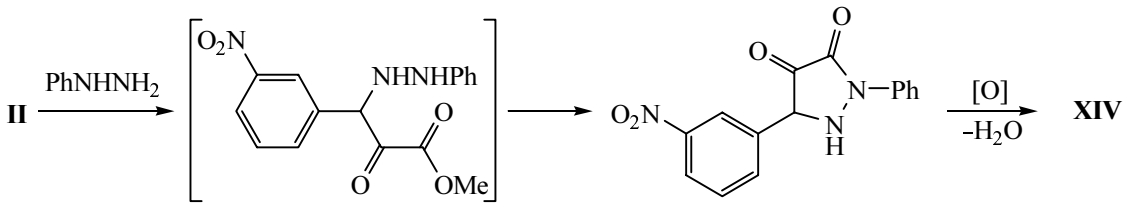
The following data confirm the formation of compound **XIV**: elemental analysis proving the presence of three nitrogens in its composition, the presence in the IR spectrum of two distinct absorption bands from two different carbonyl groups ($\nu^{ket}_{C=O}$ 1705, $\nu^{amide}_{C=O}$ 1675 cm^{-1}), the appearance in the ^1H NMR spectra exclusively signals from aromatic ring protons, and finally, the result of its reaction with phenylhydrazine furnishing hydrazino-pyrazoline **VIIIb** whose structure was unambiguously

Scheme 4.



II **XIV**

Scheme 5.



proved by the X-ray diffraction study. The formation of pyrazolinedione **XIV** under mild conditions may be understood as a nucleophilic attack of the β-nitrogen of the phenylhydrazine on the less spatially shielded C^3 atom of the chloroglycidate giving an α-hydrazinoketone that further undergoes cyclization followed by oxidation into compound **XIV** (Scheme 5).

The reaction product was obtained in an analytically pure state by recrystallization from a 5% methanol solution of DMSO. The transformation of the intermediately formed dihydroderivative of pyrazolidinone resulted either from its autooxidation or from its oxidation by DMSO [25].

The formation of the same final product in reactions of phenylhydrazine with chloropyruvate **Ib** and its isomer chloroglycidate **II** required to check whether the chloroepoxide **II** prior to reaction with phenylhydrazine isomerized into chloropyruvate **Ib**. To this end the behavior of the chloroglycidate was tested under the reaction conditions but in the absence of $PhNHNH_2$. It was shown than neiter long storage (8 h) of the arylchloroglycidate **II** methanol solution at the room temperature and even a short heating did not provide isomerization. This fact shows that the isomerization of chloroglycidate **II** under the reaction conditions is effected first of all by the nucleophile (phenylhydrazine) and not by heating.

Hence the arylchloropyruvates and 3-aryl-2-chloroglycidates in reactions with hydrazines depending on the structural features of the latter and on the experimental conditions form heterocycles operating as synthetic equivalent of two-carbon and three-carbon synthons and supplying into the heterocycle structure two-carbon or three-carbon fragments.

EXPERIMENTAL

Melting points of the crystals were measured on a Boëtius heating block. IR spectra were recorded on a spectrophotometer UR-20 from mulls in mineral oil for all compounds, and for compound **VIIIb** on a spectrometer IFS-113 from solution in $CHCl_3$. ^1H NMR spectra were registered on spectrometers Bruker-250 (250.13 MHz) and Bruker MSL-400 (400.13 MHz). ^{13}C NMR spectra were taken on Bruker MSL-400 instrument (100.6 MHz). Solvent DMSO-d_6. Electron impact mass spectra were obtained on MKh-1310 device (R 1500, ionizing voltage 70 eV, electron collector current 30–60 μA, external heating of the ion source at 80–200°C, direct admission of samples into the ion source through a system SVP-5.

X-ray diffraction studies of compounds were carried out on an automatic four-circle diffractometer Enraf–Nonius CAD-4 ($\lambda Cu K_\alpha$ radiation, graphite monochromator, ω/2θ-scanning).

Crystals of compound **VIIIb** rhombic, $C_{21}N_5O_3H_{15}$. At 20°C *a* 8.889(5), *b* 37.751(9), *c* 5.352(1) Å, *V* 1796(1) Å^3, *Z* 4, d_{calc} 1.43 g/cm^3, space group $Pna2_1$.

Crystals of compound **XII** monoclinic, $C_{31}H_{22}N_6O_5S_2$. At 20°C *a* 22.416(7), *b* 6.463(6), *c* 39.548(2) Å, β 91.93(2) deg, *V* 5726(1) Å^3, *Z* 8, d_{calc} 1.44 g/cm^3, space group *C* 2/*c*.

Unit cell parameters and intensities of 4118 (**VIIIb**) and 8599 (**XII**) reflections, among which 2959 (**VIIIb**)

and 2455 (**XII**) with $I \geq 3\sigma$, were measured at 20°C. No intensity loss in the three control reflections occurred during the data collection.

The absorption was not taken into account [μCu 7.76 (**VIII**) and 20.8 (**XII**) cm^{-1}]. The structures were solved by the direct method with the use of SIR software [26] and were refined first in the isotropic and then in the anisotropic approximation. In compound **XII** the parameters of thermal oscillations of 9 nonhydrogen atoms were taken equal to the corresponding oscillation parameters of the atoms linked thereto. The hydrogen atoms were revealed from the electron density differences and in the final cycles of the least-squares procedure were refined in the isotropic approximation for compound **VIIIb** and were taken into consideration with the fixed positions and temperature parameters for compound **XII**.

The final values of divergence factors are as follows: R 0.044, R_w 0.055 from 2725 independent reflections with $F^2 \geq 3\sigma$ for **VIIIb**, and R 0.088, R_w 0.081 from 1888 independent reflections with $F^2 \geq 3\sigma$ for **XII**. All calculations were performed with the use of program package MolEN [27] on a computer AlphaStation 200. Pictures of the molecules, molecular packing in the crystals, and the calculations of the intramolecular and intermolecular interactions were carried out with the use of PLATON software [28]. The atomic coordinates are available from the authors.

3-Hydroxydihydrocinnamic acid hydrazide (V). A mixture of 3.3 g (0.04 mol) of 60% hydrazine hydrate and 2.12 g (0.01 mol) of chloropyruvate **Ia** was heated at reflux in 30 ml of methanol for 8 h. The solution was cooled, the separated precipitate was filtered off, dried, and recrystallized. Yield 73%, mp 160–162°C (*i*-PrOH). IR spectrum, ν, cm^{-1}: 3310 br.s, 3250–2500, 1650, 1625, 1550, 1470, 1380, 1220, 1065, 1010, 715. ^1H NMR spectrum (250 MHz), δ, ppm: signals from the fragment CH_2CH appear as a *ABX* system δ_A 2.42, δ_B 2.45, δ_X 5.05, J_{AB}^{av} 14.02, J_{AX} 8.967, J_{BX} 4.52 Hz; 4.27 br.s (2H, NH_2 or H_2O), 5.46–5.48 m (1H, OH), 7.31–7.42 m (5H, C_6H_5), 9.08 s (1H, HNCO). ^{13}C {^1H} NMR spectrum (22.63 MHz), δ, ppm: 39.44 (CH_2), 64.13 (CH), 126.79 (C_n), 127.24 and 128.02 (C_O) or (Cm), 142.38 (C_{and}), 169.68 (C=O). Found, %: C 59.10; H 6.97; N 15.84. $C_9H_{12}N_2O_2$. Calculated, %: C 60.02; H 6.66; N 15.56.

5-Phenyl-3-pyrazolidone (VII). *a.* Hydrazide **V** (1.00 g, 5.5 mol) was heated to 170–175°C for 5 min. The melt was cooled, the crystalline substance formed was recrystallized. Yield 98%, mp 101–102°C (2-propanol). ^1H NMR spectrum (60 MHz), δ, ppm: 2.43 m (2H, CH_2, $^2J_{gem}$ 16 Hz), 4.50 q (1H, CH, $^3J_{HCNH}$ 8 Hz), 5.52 d (1H, NH, $^3J_{NHNH} < 1$ Hz), 9.17 br.s (1H, NH). ^{13}C {^1H} NMR spectrum (22.63 MHz), δ, ppm: 43.66 (CH_2), 69.46 (CH), 126.65 (C_p), 127.89 and 125.55 (C_O) or (C_m), 145.11 (C_i), 169.48 (C=O). Found, %: C 66.48; H 5.81; N 17.56. $C_9H_{10}N_2O$. Calculated, %: C 66.68; H 6.17; N 17.29. Compound **VII** was also obtained from the methyl cinnamate in a 8% yield [11].

b. To 1.62 g (0.01 mol) of methyl cinnamate was added at cooling dropwise 1.7 g (0.02 mol) of 60% hydrazine hydrate. The mixture at intermittent stirring was heated at 100°C for 40 h. The mixture crystallized at storage. On recrystallization from 2-propanol we obtained 0.12 g (9%) of compound **VII**. From the mother liquor after evaporation we isolated 1.29 g (91%) of dihydrocinnamic acid hydrazide (**VI**) as an oily semicrystalline substance. IR spectrum, ν, cm^{-1}: 3320 br.s, 3250–2600, 1660. ^1H NMR spectrum (250 MHz), δ, ppm: 2.27–2.90 m (3H, $C_6H_5\underline{CH_2CH}$), 3.46 br.s (3H, $NHNH_2$), 4.02 d.d (1H, CHC=O $^2J_{gem}$ 8.15, ^3J 4.03 Hz), 7.19–7.63 m (5H, C_6H_5). Found, %: C 65.79; H 7.38; N 17.11. $C_9H_{12}N_2O$. Calculated, %: C 65.87; H 7.31; N 17.07.

4-Phenylhydrazin-3-oxo-2,5-diphenylpyrazoline (VIIIa). A mixture of 4.0 g (0.037 mol) of phenylhydrazine, 2.12 g (0.01 mol) of chloropyruvate **Ia** was heated at reflux in 35 ml of methanol for 8 h. The solution was cooled, the separated precipitate was filtered off, dried, and recrystallized. Yield 78%, mp 175–176°C (MeCN). IR spectrum, ν, cm^{-1}: 3200–3000, 1680, 1595, 1550, 1495, 1470, 1345, 1279, 1180, 970, 760. ^1H NMR spectrum (400 MHz), δ, ppm: 7.40–8.33 m. ^{13}C {^1H} NMR spectrum (100.6 MHz, DMSO-d_6 + DMSO), δ, ppm: 120.56, 122.521, 120.54, 130.31, 130.62, 131.27, 132.81, 132.95, 133.23, 133.94, 134.03, 141.84 (phenyl), 145.21 (C^3), 150.17 (C^4), 161.16 (C=O). Found, %: C 74.17; H 4.70; N 16.47. $C_{21}H_{16}N_4O$. Calculated, %: C 74.13; H 4.70; N 16.40.

4-Phenylhydrazono-3-oxo-2-phenyl-5-(3-nitrophenyl)pyrazoline (VIIIb) was prepared similarly from 4.00 g (0.037 mol) of phenylhydrazine and 2.57 g (0.01 mol) of chloropyruvate **Ia**. Yield 64%, mp 211–212°C (DMSO). IR spectrum, ν, cm^{-1}: 3240–3000, 1675, 1600, 1560, 1490, 1470, 1380, 1350, 1280, 1190, 990, 920, 765. ^1H NMR spectrum (400 MHz), δ, ppm: 7.41–7.64 m (7H), 7.79 d (2H, *J* 7.92 Hz), 7.95 d.d (1H, *J* 7.99, *J* 7.98 Hz), 8.11 d (2H, *J* 7.99 Hz), 8.43 d (1H, *J* 8 Hz), 8.67 d (1H, *J* 8.04 Hz) – прОtОνы γрσпп $2C_6H_5$ + C_6H_4, 9.13 C (1H, NH). Found, %: C 65.38; H 4.25; N 18.43. $C_{21}H_{15}N_5O_3$. Calculated, %: C 65.47; H 3.89;

N 18.18. Compound **VIIIb** was also obtained from pyrazolinedione **XIV** in a 91% yield.

2-(4'-Methoxycarbonyl-5'-phenyl)thiazolyl-3-oxo-4-(4'-methoxycarbonyl-5'-phenyl)thiazolylhydrazono-5-phenylpyrazoline (XII) was likewise prepared from 2.8 g (0.01 mol) of 2-hydrazinothiazole (**X**) and 0.64 g (0.03 mol) of chloropyruvate **Ia**. Yield 67%, mp 263–265°C (MeCN). IR spectrum, ν, cm^{-1}: 3180 br.s, 3080–2500 st, 1720, 1670, 1550, 1520, 1480, 1460, 1380, 1290, 1260, 1200, 1150, 900. ^1H NMR spectrum (250 MHz), δ, ppm: 3.75 s (3H, CH_3CO_2), 3.79 s (3H, CH_3CO_2), 7.51–8.17 br.s (15H, $3C_6H_4$), 9.06 br.s (1H, NH). Found, %: C 60.04; H 3.41; N 13.78; S 10.21. $C_{31}H_{22}N_6O_5S_2$. Calculated, %: C 59.81; H 3.53; N 13.50; S 10.30.

2-(4'-Methoxycarbonyl-5'-phenyl)thiazolyl-3-oxo-4-(4'-methoxycarbonyl-5'-phenyl)-*N*-thiazolyl-*N*-acetylhydrazono-5-phenylpyrazoline (XIII). A mixture of 2.8 g (0.01 mol) of 2-hydrazinothiazole (**X**) and 64 g (0.03 mol) of chloropyruvate **Ia** was heated at reflux in 15 ml of acetic acid for 10 h. On cooling the solution the separated precipitate was filtered off, dried, and recrystallized. Yield 61%, mp 259–260°C (MeCN). IR spectrum, ν, cm^{-1}: 1720, 1715, 1675, 1545, 1520, 1480, 1465, 1380, 1295, 1260, 1200, 1145, 910. ^1H NMR spectrum (250 MHz), δ, ppm: 3.71 s (3H, CH_3CO_2), 3.76 s (3H, CH_3CO_2), 2.13 br.s (3H, CH_3CO), 7.45–8.12 m (15H, $3C_6H_5$). Found, %: C 59.43; H 3.87; N 12.68; S 9.59. $C_{33}H_{24}N_6O_6S_2$. Calculated, %: C 59.65; H 3.61; N 12.65; S 9.65.

2-Phenyl-5-(3-nitrophenyl)-3,4-pyrazolinedione (XIV). A mixture of 0.02 mol of chloroglycidate **II** and 0.02 mol of phenylhydrazine was stirred in 5 ml of methanol at room temperature for 3 h, then the solution was heated to boiling, and the reaction was continued at reflux for 5 h more. On cooling the separated precipitate was filtered off, dried, and recrystallized from a 5% methanol solution of DMSO.

Reaction of pyrazolinedione XIV with phenylhydrazine. A mixture of 1.5 g (0.005 mol) of pyrazolinedione **XIV** and 0.64 g (0.006 mol) of phenylhydrazine was heated at reflux in 10 ml of methanol for 3 h. On cooling the solution the separated precipitate was filtered off and recrystallized.

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