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o-Acetylaminophenylglyoxylic Acid Anil and Its Derivatives

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Abstract—1-Acetyl- and 1-benzoyl-2- and -3-phenyliminooxoindolines were synthesized. *o*-(Acetylamino)-phenylglyoxylic acid anil was prepared from 1-acetyl-3-phenylimino-2-oxoindoline. More stable *o*-(acetyl-amino)phenylglyoxylanilide anil can be prepared not only from *o*-(acetylamino)phenylglyoxylanilide but also from an ester or chloride of *o*-(acetylamino)phenylglyoxylic acid anil. *o*-(Acetylamino)phenylglyoxylothio-semicarbazide was prepared from *o*-(acetylamino)phenylglyoxylic acid anil and from the corresponding anilide.

The stability of the ring in isatin-3-thiosemicarbazones determines their physicochemical properties and biological activity [1, 2]. 1-Acetylisatin 2- and 3-anils **Ia**, **Ib**, **IIa**, and **IIb** are stable. Data on preparation procedures and physicochemical properties of 1-alkyl- and 1-alkoxycarbonylisatins are systematized in [3], whereas data on synthesis and properties of 1-acetyl- and 1-benzoylisatins and their derivatives (in particular, anils) are scarce [4–9]; their preparation procedures were not compared, and physicochemical properties were not reported. Acetylisatin 2- (**IIa**) and 3-anils (**Ia**) and 1-benzoylisatin 3-anil (**Ib**) were not prepared previously. Parisi [10] reported on synthesis of 1-acetylisatin 3-anil (**Ia**) without taking into account the possibility of the isatin ring opening, and this result seems to be erroneous. Actually the compound prepared in [10] is *o*-(acetylamino)phenylglyoxylanilide [11].

The goals of this study were to prepare 1-acetylisatin 2- and 3-anils and to study their structure, hydrolysis products, and derivatives.

We found that the reaction of 1-acetylisatins **IIIa** and **IIIb** with aniline yields the corresponding *o*-(acetylamino)phenylglyoxylanilides **IVa** and **IVb**, which is consistent with the published data on reaction of **IIIa** with primary amines [11]. We were able to prepare 1-acetylisatin 3-anils **Ia** and **Ib** by reaction of acetyl chloride with sodium salt of 3-phenylimino-2-oxoindoline **V**. This salt undergoes slow ring cleavage at the HN–CO bond [12], which can be accompanied by hydrolysis of the anilide group. We took advantage of the fact that the isatin ring is unstable in basic solutions and prepared from **Ia** and **Ib** *o*-(acetylamino)phenylglyoxylic acid anils **VIa** and **VIb**, which is consistent with data of [12, 13]. This result is confirmed by the presence of strong absorption bands at 1570 cm^{-1} in the IR spectra of anils **VIa** and **VIb**, originating from antisymmetric vibrations of the carboxylate ion [14]. *o*-(Acetylamino)phenylglyoxylic acid anils **VIa** and **VIb** are very unstable in aqueous solutions.

By careful evaporation of solutions of *o*-(acetylamino)phenylglyoxylic acid anils **VIa** and **VIb** or of solutions of the initial isatin 3-anils **Ia** and **Ib** in ethanolic sodium ethylate, we obtained sodium salts of *o*-(acetylamino)phenylglyoxylic acid anils **VIIa** and **VIIb**, which were alkylated with methyl iodide or ethyl bromide to give unstable esters **VIIIa** and **VIIIb**. Stefanovic *et al*. [15] reported on synthesis of methyl ester of *o*-(amino)phenylglyoxylic acid hydrazone by methylation of the corresponding hydrazone with diazomethane.

In Table 1 we give the preparation conditions for **Ia**, **Ib**, **IIIb**, and **IIIc** and compare their physicochemical properties with published data. In contrast to anils **Ia** and **Ib**, 1-benzoyl-2-phenylimino-3-oxoindoline **IIb** has already been studied in [17].

For preparing the above-mentioned acylated anils, we developed a general procedure involving acylation of the corresponding salt **IX**; this procedure allows preparation of compounds **IIa** and **IIb** of higher purity.

To prepare stable derivatives of *o*-(acetylamino)-phenylglyoxylic acid anils, we attempted to perform the reaction of esters **VIIIa** and **VIIIb** with thiosemicarbazide; however, we found that virtually no reaction occurs in aqueous alcohol at room temperature, and in acidic buffer solutions an intractable mixture is formed. Therefore, we prepared *o*-(acetylamino)phenylglyoxylothiosemicarbazide anil **Xa** (the chemical

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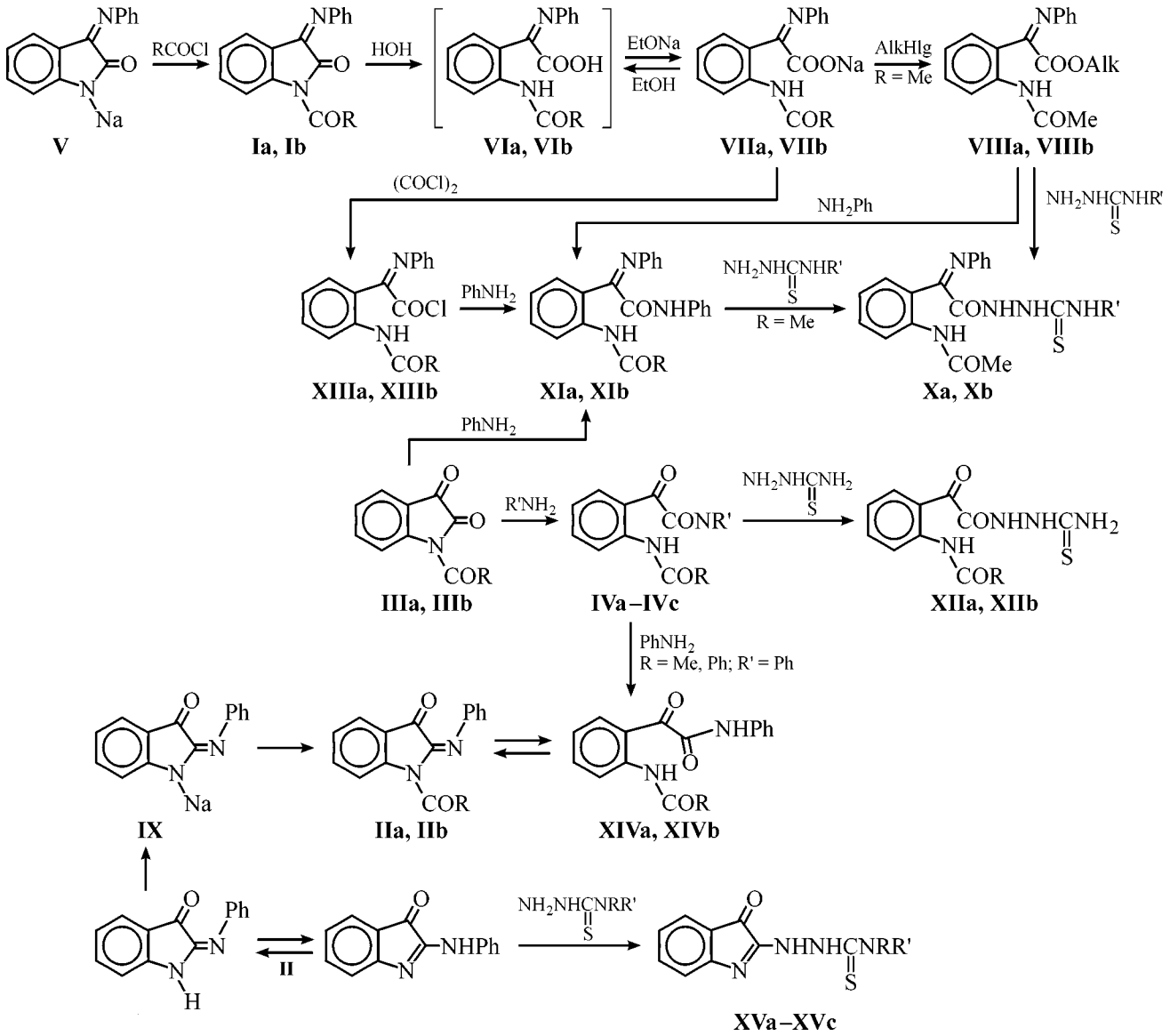

I–**III**, **VI**, **VII**, **XI**, **XIII**, R = Me (**a**), Ph (**b**); **IV**, R = Me, R' = Ph (**a**), R = R' = Ph (**b**); R = Me, R' = Et (**c**); **VIII**, Alk = Me (**a**), Et (**b**); X, R' = H (**a**), R' = CH_2Ph (**b**); **XIV**, R = Me (**a**), Ph (**b**); **XV**, R = R' = H (**a**), R = H, R' = Me (**b**), R = R' = Me (**c**).

form convenient for identification) from *o*-(acetylamino)phenylglyoxylanilide anil **XIa**. The synthesis of *o*-(acetylamino)phenylglyoxylic acid alkylamides from 1-acetylisatin was reported in [11], and their structure was proved.

Reaction of equimolar amount of aniline with **IIIa** and **IIIb** yields anilides **IVa** and **IVb**, and from the reaction of **IIIa** with a tenfold excess of aniline we obtained *o*-(acetylamino)phenylglyoxylanilide anil **XIa**. When treated with thiosemicarbazide in a methanolic solution of anhydrous HCl, compound **XIa** transforms into thiosemicarbazide **Xa** identified by ^{1}H NMR and IR spectra.

The IR spectrum of the product formed by reaction of **XIa** with thiosemicarbazide contains, along with a broadened carbonyl absorption band shifted toward longer waves, also a strong "amide II" band originating from interaction of the bending vibrations of the NH group of the thiosemicarbazide fragment bonded to the carboxy group with the NH stretching vibrations of the thioamide moiety.

The ^{1}H NMR spectrum of the presumed thiosemicarbazide **Xa** contains, along with two proton signals of the thioamide group, also signals from protons at the N^1 and N^2 atoms of the thiosemicarbazide chain at δ 7.92 and 12.72 ppm. Splitting of the acetylamide

Table 1. Yields, melting points, UV and IR spectra, and elemental analyses of 1-acyl-3-phenylimino-2-oxoindolines **Ia** and **Ib** and of 1-acyl-2-phenylimino-3-oxoindolines **IIa** and **IIb**

Comp. no.	Yield, %	mp, °C (solvent for crystallization)	UV spectrum ($CHCl_3$), λ_{max}, nm (log ε)	IR spectrum (CCl_4), ν, cm^{-1}			Found, %			Formula	Calculated, %		
				C=O	C=N	N–C(=O)R	C	H	N		C	H	N
Ia	20	138–144 (benzene–cyclohexane, 3 : 1)	259 (4.01), 308 (3.61), 455 (1.64)	1755	1650	1702	70.29, 70.21	4.72, 4.82	10.22, 10.03	$C_{16}H_{14}N_2O_2$	68.12	5.03	10.16
Ib	26	137 (*m*-xylene–methylene chloride, 2 : 1)	237 (2.97), 263 (3.04), 591 (3.92)	1755	1640	1704	47.01, 46.92	4.34, 4.45	8.55, 8.60	$C_{21}H_{14}N_2O_3$	46.64	4.32	8.68
IIa	22	133.5 [16]	282 (3.22), 352 (3.81), 461 (3.77)	1760	1655	1702	70.33, 69.97	4.74, 4.77	10.21, 10.13	$C_{16}H_{14}N_2O_2$	68.12	5.03	10.16
IIb	14	134.5–135 (benzene) [6]	–	1760	1652	1704							

Table 2. IR and ^1H NMR spectra of thiosemicarbazides **Xa**, **XIIa**, and **XIIb**

Comp. no.	IR spectrum (CCl_4), ν, cm^{-1}			^1H NMR spectrum (DMSO-d_6), δ, ppm										
	C(=O)NH	C–N	C(=O)R	COMe	phenyl substituent			*o*-acylaminophenyl ring			NH			
					H_o	H_m	H_p	3	4, 5	6	$C(S)NH_2$	C(=O)NH	NHC(S)	NHCOR
Xa	1545, 1505	1625	1670	2.10 s	6.98 t	7.26 t	8.88 q	8.52 t	6.62 t, 7.22 t	7.48 d, 7.55 s	9.74 s, 10.14 s	7.98 s	12.72 s	10.68 s, 12.56 s
XIIa	1545, 1500		1645	1.83 s	–	–	–	9.02 q	7.11 s, 7.37 q	7.33 d	8.60 s	7.66 d	12.11 s	10.10 s, 9.67 s
XIIb	1545, 1500		1670		7.72 d, 7.74 d	7.93 t	7.99 d	8.76 d	7.20 t, 7.60 t	7.40 t	8.31 s	8.00 m	12.75 s	11.19 s

proton signal in the ^1H NMR spectrum of **Xa** (δ 10.68 and 12.56 ppm) suggests the presence of the *Z* and *E* isomers of **Xa** with respect to the N–C=O bond in the acetylamino group.

To confirm the structure of the product formed by the reaction of **XIa** with thiosemicarbazide, we examined the possibility of preparing *o*-(acetylamino)phenylglyoxylic acid derivatives **VIIIa** and **VIIIb** from anilides **IVa** and **IVb** under conditions of synthesis of **Xa**. Anilides **IVa** and **IVb** were prepared according to [11]; compound **IVb** was unknown previously. Reactions of **IVa** and **IVb** with thiosemicarbazide yield individual compounds whose IR spectra contain absorption bands of carbonyl groups at 1690 cm^{-1} and of the C=O bond in the amide group of the thiosemicarbazide chain at 1625 cm^{-1}, and also the bands of the carbonyl groups in the acylamide moieties at 1660–1665 cm^{-1}.

The ^1H NMR spectra of thiosemicarbazides **XIIa** and **XIIb**, along with the signals of two protons of the thioamide group at δ 8.83 and 9.11 ppm (for **XIIb**), contain the signals originating from the protons at the amide nitrogen atom of the acylamide group (δ 8.47 and 8.34 ppm, respectively, for **XIIa** and **XIIb**). In the ^1H NMR spectrum of **XIIb**, the proton signal of the acetylamino group is also split owing to the *Z*–*E* isomerism (Table 2).

The ^{13}C NMR spectrum of **XIIa**, along with six signals of the aromatic carbon atoms, contains signals originating from the carbon atoms of the acetylamino group (δ_C 161.17 and 161.47 ppm, *Z* and *E* isomers),

carbonyl group of the carbonylamide fragment (δ_C 158.89 ppm), and carbonyl and thiocarbonyl groups (see Experimental).

o-(Acetylamino)phenylglyoxylanilide anil **XIa**, which is an intermediate in synthesis of **Xa**, is formed in a higher yield from chlorides of *o*-(acetylamino)-phenylglyoxylic acid anils **XIIIa** and **XIIIb**, which are prepared by reaction of oxalyl chloride with **VIIa** and **VIIb** (see Experimental).

Reaction of *o*-(acetylamino)phenylglyoxylothiosemicarbazide **XIIa** with an equimolar amount of aniline does not yield **Xa**.

We have also examined the possibility of preparing the structural isomer of *o*-(acetylamino)phenylglyoxylic acid, *o*-(acetylamino)phenylglyoxylanilide **XIVa**, which can be prepared by hydrolysis of 1-acetyl-2-phenylimino-3-oxoindoline **IIa**. In contrast to 1-acyl-3-phenylimino-2-oxoindolines **Ia** and **Ib**, anil **IIa**, when heated in aqueous acetone, does not undergo cleavage of the isatin ring. The absorption band at 3060–3430 cm^{-1}, assignable to the acetylamino group [16] in **XIVa**, appears only on treatment of **IIa** with weakly alkaline aqueous solutions. The compound obtained from hydrolysis of **IIa** is similar in the physicochemical properties to the structural isomer, *o*-(acetylamino)phenylglyoxylanilide **IVa**.

From the reaction of anil **II** with thiosemicarbazide and its alkyl derivatives under standard conditions of synthesis of thiosemicarbazones [18], we prepared thiosemicarbazides **XVa**–**XVc**, stable without heating in neutral solutions. The ^{13}C NMR spectrum of **XIIa**, along with six signals of aromatic carbon atoms, contains two signals belonging to the carbon atoms in acetylamino group of the *Z* and *E* isomers (see Experimental).

EXPERIMENTAL

The IR spectra were taken on Specord-75, UR-10, and SF-22 spectrophotometers (KBr pellets or solutions in CCl_4 or CF_3Cl). The ^1H NMR spectra were recorded on a Tesla-497 spectrometer (100.1 MHz) in DMSO-d_6 and $CDCl_3$, and also on a Bruker CXP-300 spectrometer (300 MHz); internal reference HMDS. The ^{13}C NMR spectra were taken on a Bruker CXP-300 spectrometer (75 MHz), internal reference DMSO-d_6. The product purity was checked by TLC on Silufol UV-254 plates (UV development).

1-Acetyl-3-phenylimino-2-oxoindoline Ia. A solution of 10 g of 3-phenylimino-2-oxoindoline [19], dried over P_2O_5, in 90 ml of absolute methanol was added to a solution of sodium methylate, prepared from 1.17 g of sodium metal and 70 ml of dry methanol. The resulting suspension was shaken for 15 min with cooling on a water bath. The suspension was filtered, and the precipitate was dried in a vacuum at 70°C over granulated KOH; yield of dark violet crystalline salt **V** 7.7 g (70%).

A 6.5-g portion of **V** was suspended in 80 ml of anhydrous benzene, with protection from atmospheric moisture. To this suspension, 2.5 ml of freshly distilled acetyl chloride was added dropwise with cooling on an ice bath. The mixture was warmed up to 55°C over a period of 40 min and stirred at this temperature for 2.5 h. To the resulting solution, 32 ml of anhydrous benzene was added, and the mixture was quickly filtered while hot. The precipitate was treated with dry ethyl acetate (2 × 15 ml), and the crystalline product was separated and vacuum-dried at 70°C; R_f 0.23 (cyclohexane–methyl acetate, 3 : 1).

1-Benzoyl-3-phenylimino-2-oxoindoline Ib. Salt **V** was prepared as described above for **Ia** from 1 g of 3-phenylimino-2-oxoindoline. The product (0.7 g, 63%) was suspended in 10 ml of dry benzene, with protection from atmospheric moisture. To this suspension, 0.84 ml of purified and distilled benzoyl chloride was added with cooling on a water bath. The mixture was warmed up to room temperature over a period of 10 min. To the resulting precipitate, 3 ml of toluene was added, and the precipitate was filtered off and vacuum-dried over granulated NaOH at 70°C; R_f 0.98 (butanol–acetic acid–water, 4 : 5 : 1).

1-Acetyl-2-phenylimino-3-oxoindoline IIa. Sodium salt **IX** was prepared as described above from 1.31 g of 2-phenylimino-3-oxoindoline. The product (0.9 g, 72%) was suspended in 10 ml of dry benzene. The suspension was cooled on an ice bath, and 0.36 ml of acetyl chloride was added. The mixture was stirred at 0°C for 20 min, gradually warmed up to 55°C, and kept at this temperature for 80 min. To the hot solution, 10 ml of dry boiling benzene was added. The solution was filtered, allowed to cool to room temperature, and then carefully evaporated at a bath temperature of 35°C. The resulting dark brown oily mass crystallized on treatment with pentane (3 × 6 ml). The dark brown crystalline product was filtered off and vacuum-dried at 50°C; yield of **IIa** 0.08 g (15%). The pentane extract was evaporated to dryness and treated with CCl_4 (2 × 2.5 ml); the crystalline precipitate was filtered off and dried. An additional crop of **IIa** (0.02 g, 4%) was obtained. IR spectrum (CCl_4), ν, cm^{-1}: 1655 (C=N), 1702 (C=O in $COCH_3$), 1760 (C=O).

1-Benzoyl-2-phenylimino-3-oxoindoline IIb was prepared similarly according to [6].

1-Acetylisatin IIIa and 1-benzoylisatin IIIb were prepared according to [5, 7] from sodium isatin [20].

***o*-(Acetylamino)phenylglyoxylanilide IVa** was prepared according to [11]; mp 177°C [11]. R_f 0.34 (cyclohexane–ethyl acetate, 5 : 2). IR spectrum (KBr), ν, cm^{-1}: 1675 (C=O of carbonylanilide moiety), 1685 (C=O of the phenylglyoxyl moiety), 3240 (NH of the anilide group).

***o*-(Benzoylamino)phenylglyoxylanilide IVb.** *a*. To a solution of 0.1 g of 1-benzoylisatin **IIIb** in 4 ml of dry methanol was added 0.36 ml of aniline; the mixture was refluxed with stirring for 2 h, the solution was cooled, and the precipitate was collected; yield of **IVb** 0.04 g (53%), mp 177.5°C.

b. A 0.34-g portion of sodium salt of *o*-(benzoylamino)phenylglyoxylic acid [21] dried in a vacuum desiccator over granulated NaOH was suspended in 7 ml of benzene dried over sodium metal. To the fine suspension of the salt, 0.41 ml of freshly distilled oxalyl chloride was added dropwise with cooling on a bath with ice-cold water over a period of 5 min, and then a mixture of 0.4 ml of freshly distilled aniline and 4 ml of diethyl ether was added dropwise at 10°C. The suspension was stirred for 15 min. The resulting thick precipitate was filtered off and dried for 2 h at 70°C. Yield of *o*-(benzoylamino)phenylglyoxylanilide hydrochloride 0.31 g (53%); mp 177.5–179°C. Found, %: C 39.96; H 4.24; N 7.23. *M* 330.86.[1] $C_{21}H_{17}Cl_2N_2O_2$. Calculated, %: C 39.96; H 4.23; N 7.35. *M* 380.88.

Neutralization of this hydrochloride with 0.5 M aqueous Na_2CO_3 gave **IVb**; yield 0.14 g (41%).

***o*-(Acetylamino)phenylglyoxylethylamide IVc** was described in [11].

***o*-(Acetylamino)phenylglyoxylic acid anil VIa.** *a*. A solution of 0.13 g of 1-acetyl-3-phenylimino-2-oxoindoline **Ia** in 5 ml of 30% aqueous ethanol was refluxed for 1.5 h. The precipitate was filtered off and dried in a vacuum desiccator over granulated KOH; yield of **VIa** 0.1 g (65%); mp 164–165°C. ^{1}H NMR spectrum (CD_3OD), δ, ppm: 2.10 s (3H, COMe), 6.40, 6.50 m (1H, Ar–H), 6.92 s (1H, Ar–H), 7.10–7.30 m (3H, Ar–H), 7.53–7.66 m (4H, Ar–H), 8.07 d (1H, NH).

b. A 0.42-g portion of 1-acetyl-3-phenylimino-2-oxoindoline **Ia** was dissolved in 2.5 ml of 1.6 N aqueous K_2CO_3, and the solution was heated on a boiling water bath for 10 min. Then the solution was cooled with ice-cold water and neutralized with 2 ml of 2 N HCl to pH 6. The precipitate was filtered off and vacuum-dried at 70°C over granulated KOH; yield of **VIa** 0.2 g (54%). The product is identical to that prepared by method *a*.

[1] The molecular weight was determined by comparing the heats of vaporization of dioxane solutions.

***o*-(Benzoylamino)phenylglyoxylanilide IVb.** A 0.26-g portion of 1-benzoyl-3-phenylimino-2-oxoindoline **Ib** was dissolved in 1 ml of 1 M aqueous K_2CO_3 with heating on a water bath for 15 min. The resulting suspension was cooled to room temperature and then with ice-cold water, after which it was neutralized with 0.8 ml of 2 N HCl. The yellow-green precipitate was filtered off and dried in a vacuum desiccator. Yield of **IVb** 0.04 g (24%); mp 166–167°C.

***o*-(Acetylamino)phenylglyoxylic acid anil, methyl ester VIIIa.** A solution of 0.27 g of 1-acetyl-3-phenylimino-2-oxoindoline **Ia**, dried in a vacuum desiccator over P_2O_5, in 6 ml of absolute methanol was gradually added to a sodium methylate solution prepared from 0.057 g of sodium metal and 3 ml of methanol. The mixture was evaporated to dryness, 2 ml of DMF and 0.15 ml of methyl iodide were added, and the mixture was kept at 0°C for 12 h. The resulting precipitate was filtered off; yield of **VIIIa** 0.05 g (16%). Crystallization from ethyl acetate gave a sample with mp 86–87°C. IR spectrum ($CHCl_3$), ν, cm^{-1}: 1400–1410 [C(=O)Me], 1660 [C=O in C(=O)Me]. The compound is insufficiently stable for recording the UV spectrum.

***o*-(Acetylamino)phenylglyoxylic acid anil, ethyl ester VIIIb.** A solution of sodium methylate prepared from 0.057 g of sodium metal and 3 ml of methanol was added to a solution of 0.65 g of 1-acetyl-2-phenylimino-2-oxoindoline **Ia**, dried over P_2O_5, in 10 ml of anhydrous ethanol. The mixture was quickly filtered with protection from atmospheric moisture. The filtrate was allowed to stand at room temperature for 4 min and then evaporated to dryness; 2 ml of DMF and 0.65 ml of ethyl bromide were added. The mixture was kept at 0°C, and the precipitate was filtered off. Yield of **VIIIb** 0.18 g (21%). After crystallization from toluene–hexane–cyclohexane (3 : 4 : 1), mp 163°C. IR spectrum (CF_3Cl–$CHCl_3$, 3 : 1), ν, cm^{-1}: 1450 (C=O in COOEt), 1670 (C=O in COMe). The compound is insufficiently stable for recording the UV spectrum.

***o*-(Acetylamino)phenylglyoxylothiosemicarbazide anil Xa.** *a*. A solution of 0.36 g of thiosemicarbazide in 3 ml of methanol was added to a solution of 0.55 g of *o*-(acetylamino)phenylglyoxylanilide anil **IXa** in 6 ml of absolute methanol containing 0.5% HCl. The mixture was heated for 3 h with protection from atmospheric moisture on a water bath at a temperature no higher than 50°C. A part of the solvent was vacuum-evaporated, and the mixture was cooled on an ice bath. The precipitate was filtered off and dried in a vacuum desiccator over $CaCl_2$. *o*-(Acetylamino)phenylglyoxylothiosemicarbazide anil hydrochloride was obtained; yield 0.43 g (68%), mp 180–183°C. Neutralization with aqueous Na_2CO_3 and drying gave **XIa**;

mp 160–164°C, R_f 0.53 (ethyl acetate–chloroform, 7 : 1). ^{1}H NMR spectrum (CD_3CN), δ, ppm: 1.82 s (6H, Me in COMe, *Z* and *E* isomers), 6.56 d, 6.62 d (1H, Ar–H), 7.05–7.48 m (7H, Ar–H), 7.84 s [1H, NHC(=O) in thiosemicarbazide moiety], 8.20 s (1H, Ar–H), 8.50 s [1H, $NH_2C(S)$], 9.00–9.12 m [1H, $NH_2C(S)$ in thiosemicarbazide moiety], 12.58 s [1H at N^2H in NHC(S)]. Found, %: C 57.22; H 4.86; N 20.22. $C_{17}H_{17}N_5O_2$. Calculated, %: C 57.40; H 4.76; N 19.96.

b. A 1.2-g portion of ethyl ester of *o*-(acetylamino)-phenylglyoxylic acid anil **VIIIb** was mixed with 1.76 g of finely divided thiosemicarbazide, and 16 ml of ethanol was added. After a day, the resulting suspension was filtered. The filtrate was vacuum-evaporated at a temperature not exceeding 45°C. The residue, according to TLC and ^{1}H NMR spectra, was a mixture of three compounds. The precipitate was washed with hot chloroform and treated with hot acetone; the extract was vacuum-evaporated, and 0.21 g (14%) of **Xa** was obtained.

***o*-(Acetylamino)phenylglyoxylo(4-benzyl)thio-semicarbazide anil Xb** was prepared similarly to **Xa** by procedure *b* from **VIIIb**. Benzylthiosemicarbazide was prepared according to [22]. Along with ethanol, the reaction of **VIIIb** with benzylthiosemicarbazide can also be performed in ethyl acetate. The reaction occurs within 1.5 h on heating; yield of **Xb** 2.6 g (40%), mp 198–204°C. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 2.10 s (3H, Me in NHCOMe), 4.97 d (2H, CH_2Ph), 6.90–7.10 m (2H, Ar–H), 7.15–7.37 t (10H, Ar–H), 7.91 s [1H, NH(C=O) in thiosemicarbazide moiety], 9.13 d (1H, Ar–H), 9.98–10.00 m (1H, Ar–H), 10.12 d (1H, $NHCH_2Ph$), 12.72 s (1H, $NHCOCH_3$, *Z* isomer), 12.79 s (1H, N^2H of thiosemicarbazide moiety).

***o*-(Acetylamino)phenylglyoxylanilide anil XIa.** *a*. Oxalyl chloride (0.3 ml) was added dropwise with shaking and cooling on an ice bath to a solution of 0.09 g of **VIIa** in 2 ml of dry methylene chloride. The solution was shaken while cooling in ice. Chloride of *o*-(acetylamino)phenylglyoxylic acid anil **VIIIa** was obtained, to which a mixture of 0.07 ml of aniline in 0.05 ml of diethyl ether was immediately added dropwise. The resulting precipitate was filtered off and dried in a vacuum desiccator over granulated alumina. Yield of **XIa** 0.05 g (48%); mp 157–158°C.

b. A 0.29-g portion of **IIIa** was dissolved in 3.5 ml of absolute methanol with heating and stirring, and 1.4 ml of aniline was added. The mixture was refluxed for 2.5 h with protection from atmospheric moisture; after cooling, the thick precipitate was filtered off and dried in a vacuum desiccator over granulated KOH; yield of **XIa** 0.14 g (43%), mp 157–158°C.

c. A 0.42-g portion of **IVa** was dissolved in 35 ml of absolute methanol with heating and stirring, and a mixture of 1.8 ml of aniline and 2 ml of absolute methanol was added. The mixture was refluxed for 2.5 h with protection from atmospheric moisture. After cooling to room temperature, the precipitate was filtered off and dried in a vacuum desiccator over granulated KOH. Yield of **XIa** 0.14 g (43%), mp 157–158°C (from 1-butanol). IR spectrum (CCl_4), ν, cm^{-1}: 1640 (C=N), 1680 [C=O in C(=O)NHPh], 1693 [C=O in C(=O)Me], 3190 (N^1H). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm (the signal of the carbon atom of the solvent is not given): 29.10 (1C, Me), 116.03 (1C, Ar–C), 116.96 (1C, Ar–C), 128.33 (2C, Ar–C), 129.44 (2C, Ar–C), 129.65 (1C, Ar–C), 131.88 (1C, Ar–C), 134.53 (1C, Ar–C), 135.07 (1C, Ar–C), 136.71 (1C, Ar–C), 136.82 (1C, C=N), 161.03 [1C, C=O in C(=O)Me]. Found, %: C 92.84; H 4.57; N 11.08. $C_{27}H_{21}N_3O_2$. Calculated, %: C 92.99; H 4.87; N 11.28.

***o*-(Benzoylamino)phenylglyoxylanilide anil XIb.** First, anil **VIb** was prepared: 0.42 g of **Ib** was heated with a solution of 0.2 g of Na_2CO_3 in 2 ml of water on a boiling water bath for 10 min, and the mixture was cooled on an ice bath and neutralized with 1.6 ml of 2 M HCl. The precipitate was filtered off, and compound **VIb** was obtained. The product (0.08 g, 18%) was dissolved in a sodium methylate solution prepared as described for **V**. The resulting solution was evaporated, and the residue containing sodium *o*-(benzoylamino)phenylglyoxylate **VIIb** was dried in a vacuum desiccator over NaOH and treated with dry benzene (6 × 1 ml). The resulting product [**VIIb**, yield 0.03 g (36%)] was dissolved in 1.5 ml of benzene, and 0.15 ml of freshly distilled oxalyl chloride was added, which resulted in precipitation of chloride **XIIIb**. The precipitate was filtered off and vacuum-dried at 60°C. Transformation into **XIb** was performed as described above for **XIa** (procedure *a*); **XIb**, mp 148–149.5°C.

***o*-(Acetylamino)phenylglyoxylothiosemicarbazide XIIa.** A 0.42-g portion of *o*-(acetylamino)phenylglyoxylanilide was dissolved in 15 ml of a 3% solution of HCl in absolute methanol. The solution was heated with protection from atmospheric moisture for 3 h at a bath temperature not exceeding 50°C. The solution was vacuum-evaporated to a volume of 3 ml and cooled. The precipitate was filtered off and dried in a vacuum desiccator over $CaCl_2$. The thiosemicarbazide was obtained in the form of hydrochloride; yield 0.36 g (58%), mp 187–188°C; melting point after neutralization with 1.5 ml of 1 M of aqueous Na_2CO_3 and vacuum drying 182–184°C (Table 2). UV spec-

trum ($CHCl_3$), λ_{max}, nm ($\log\varepsilon$): 242 (4.70), 306 (3.81). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm (the signal of the solvent carbon atom is not given): 23.17 (1C, Me, *Z* isomer), 26.58 (1C, *E* isomer), 121.0 (1C, Ar–C), 124.7 (1C, Ar–C), 129.9 (1C, Ar–C), 139.35 (1C, Ar–C), 161.17 (1C, NHCO), 161.43 (1C, NHCO), 169.89 (1C, C=O), 178.69 (1C, CONH), 181.41 (1C, $CSNH_2$). Found, %: C 43.11; H 4.25; N 18.34. $C_{11}H_{13}ClN_4O_3$. Calculated, %: C 43.06; H 4.26; N 18.26.

***o*-(Benzoylamino)phenylglyoxylothiosemicarbazide XIIb** was prepared similarly to **XIIa**. Neutralization of the hydrochloride with 1 M aqueous Na_2CO_3 gave **XIIb**; mp 180–181°C. UV spectrum (ethanol), λ_{max}, mn ($\log\varepsilon$): 244 (4.10), 306 (3.77).

***o*-(Acetylamino)phenylglyoxylanilides XIVa and XIVb.** A 0.15 g portion of **IIa** or 0.11-g portion of **IIb** was dissolved in 2 or 1 ml, respectively, of 1 M aqueous Na_2CO_3. The mixture was heated on a boiling water bath for 30 min and, after cooling, neutralized with 2 M HCl to pH 7.0. The precipitated crystals were dried in a vacuum desiccator over granulated $CaCl_2$. **XIVa**: yield 0.03 g (31%), mp 197°C; IR spectrum (CCl_4), ν, cm^{-1}: 1545 (C=O), 1665 (C=O in COMe), 3080 (Me in C(=O)NHMe]. **XIVb**: yield 0.04 g (43%), mp 214°C; IR spectrum (CCl_4), ν, cm^{-1}: 1545 (C=O), 1660 (C=O in COPh), 3100 (NH).

1-(3-Oxoindol-2-yl)thiosemicarbazide XVa was prepared according to [23].

1-(3-Oxoindol-2-yl)(4′-methyl)thiosemicarbazide XVb and 1-(3-oxoindol-2-yl)(4′,4″-dimethyl)thiosemicarbazide XVc, along with the synthesis from isatin methyl ether [24], can also be prepared from 2-phenylimino-3-oxoindoline **II**; the UV and IR data for these compounds are given in [24]. 4-Methylthiosemicarbazide was prepared according to [25].

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