A new synthesis of phthalimidines

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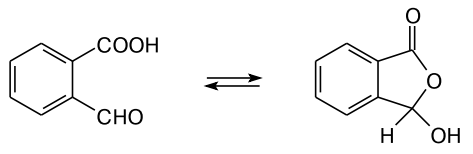
A new synthesis of phthalimidines is described. 3-Acyloxy-2-aryl- and 2-acylamino-3-acyloxyphthalimidines were prepared by the reaction of 3-arylaminophthalides or *o*-formylbenzoic acid acylhydrazones with acetic or propionic anhydrides. Their reactions with O-, N-, S-, and C-nucleophiles were studied. The structure of 2-acetyl(cyanoacetyl)amino-3-acetoxyindolin-1-one was confirmed by X-ray diffraction analysis.

Key words: *o*-formylbenzoic acid, 3-arylaminophthalides, *o*-formylbenzoic acid acylhydrazones, acetic and propionic anhydrides, 3-acyloxy-2-aryl-phthalimidines, 2-acylamino-3-acyloxyphthalimidines, X-ray diffraction analysis.

Phthalimidines descibed for the fist time in 1884 (see Ref. 1) have recently attracted increasing attention of investigators. The essential role in revival of interest in these compounds is the fact that compounds that possess various kinds of biological activity[2—4] are found among them. One of the first method of the synthesis of phthalimidines was the reaction of phthalide (3*H*-1,3-dihydroisobenzofuran-1-one) with ammonia or primary amines that led to replacement of the phthalide oxygen atom by the nitrogen one.[1,5]

The hydroxy analog of phthalide, *i*.e., *o*-formylbenzoic acid, which undergoes ring-chain tautomerism, reacts with amines quite differently. It exists as cyclic 3-hydroxyphthalide form **1b** in the solid state, in aqueous[6] and DMSO[7] solutions (Scheme 1). It affords 3-arylaminophthalides **2** as a result of reactions with primary amines, *i.e.*, the hydroxyl group is replaced by the amino group, the initial phthalide structure being retained.[6,8] Phthalides are easily identified due to intense absorption bands of the carbonyl groups (1715—1750 cm^{-1}), antisymmetric (1050—1096 cm^{-1}) and symmetric (847—900 cm^{-1}) C—O—C vibrations in the IR spectra.[6]

Scheme 1



1a **1b**

At the same time, reaction of *o*-formylbenzoic acid with of anthranilohydrazide affords normal hydrazone, *i.e.*, derivative of the open tautomeric form **1a** (see Ref. 9).

In the present study, we report a new synthesis of phthalimidines from aminophthalides and hydrazones.

It was found that heating of 3-arylaminophthalides **2** in acetic or propionic anhydrides (**3a,b**) leads to recyclization with formation of 3-acyloxy-2-aryl-phthalimidines **6** or **7**. A putative mechanism is given in Scheme 2. It includes N-acylation (structure **4**), addition of a carboxylic acid to the C—O bond followed by phthalide ring opening (**5**) and recyclization followed by elimination of the acid to afford phthalimidines **6**.

The reaction proceeds smoothly only if the anhydride contains some acid, which agrees with the scheme.

It was noted[6] that the reactivity of the cyclic form of *o*-formylbenzoic acid is comparable to that of acid chlorides and anhydrides. 3-Acyloxyphthalimidines **6** are also highly reactive in the reactions with O-, N- and S-nucleophiles. They can be hydrolyzed upon heating in aqueous acid media, therefore, dry and aprotic, where possible, solvents should be used for recrystallization. Our attempt of recrystallization of phthalimidine **6f** from aqueous HOAc led to the corresponding hydroxy derivative **7** (Scheme 3). Compound **6a** was converted into hydroxy derivative **9** under short-term heating in concentrated HCl. Obviously, the reaction proceeds *via*

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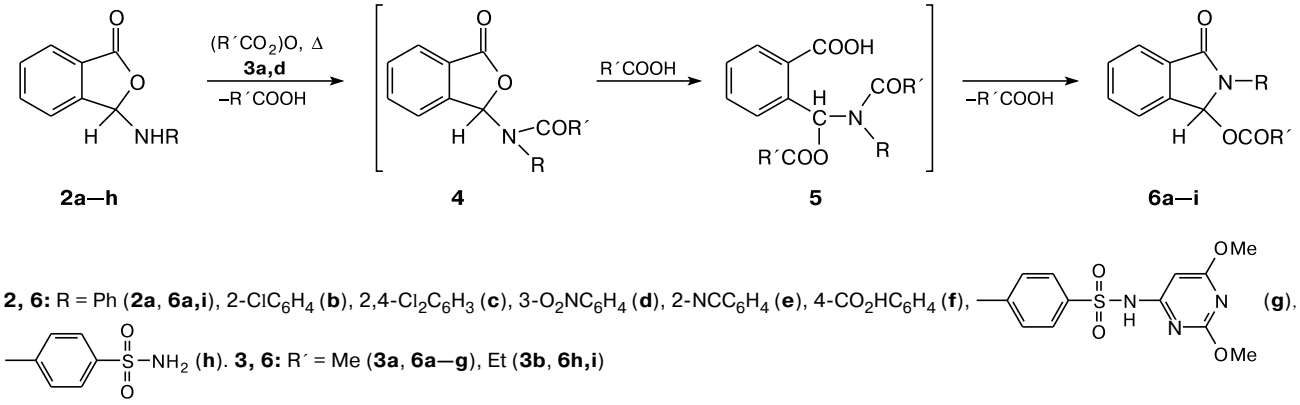
Scheme 2

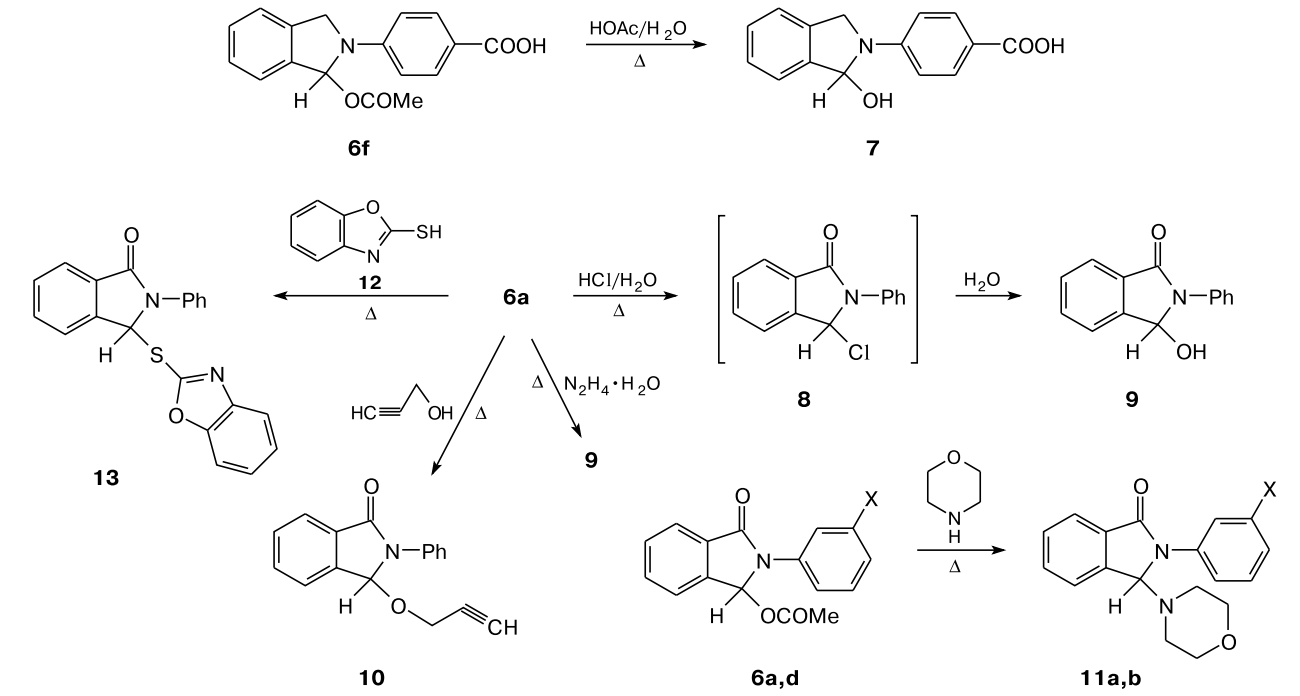


hydrolytically unstable intermediate chlorolactam **8** (see Ref 10). Hydroxy derivative **9** was also obtained in the reaction of **6a** with hydrazine hydrate. Refluxing for 1 h of compound **6a** with propargyl alcohol affords propargyl derivative **10** in almost quantitative yield. With boiling morpholine compound **6a** reacts smoothly as well with formation of morpholine derivative **11a**. The reaction of **6a** with 2-sulfanylbenzoxazole **12** proceeds almost instantly when the mixture was heated to 150 °C (see Scheme 3).

However, it was of interest to carry out such a reactions with C-nucleophiles.

It would be logical to use in such reactions acylimmonium salts as electrophiles, which could be produced upon reaction of hydroxy lactams (in our case, **7** or **9**) with strong protic acids or Lewis acids,[11] such as $SbCl_5$, $HClO_4$, $BF_3 \cdot OEt_2$, hexachlorophosphoric acid, and trityl perchlorate. Of these salts, only perchlorates were found to be almost insensitive to hydrolysis. Only two such compounds could be isolated in the crystalline form.[10] It turned out that antimony pentachloride was the most convenient reagent for the synthesis of acylimmonium salt. However, toxicity and hydrolytic unstability of both the reagent and acylimmonium hexachloroantimonates

Scheme 3



X = H (**a**), NO_2 (**b**)

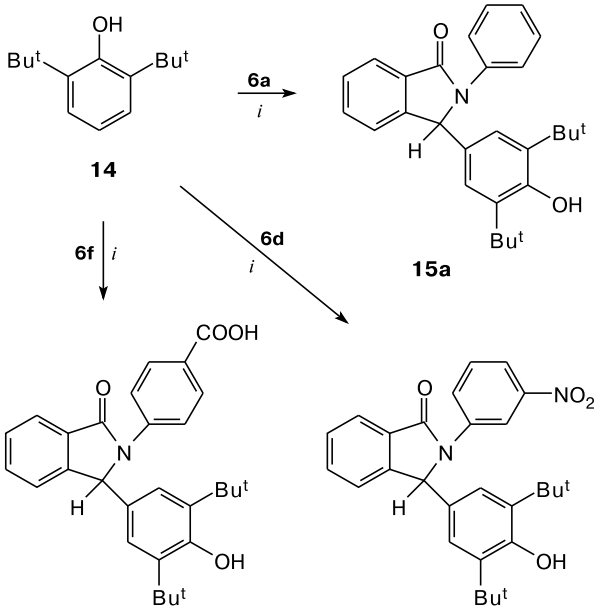
make these compounds inconvenient for carrying out the reactions.

We supposed that trifluoroacetoxyphthalimidine derivatives can be used for this purpose (even if these compounds are not acylimmonium salts but rather highly polarized trifluoroacetates).

It was found that compounds obtained from acetoxyphthalimidines **6** in the presence of CF_3COOH are reactive electrophilic agents. We chose 2,6-di-*tert*-butylphenol as a C-nucleophile. Heterocycles containing 3,5-di-*tert*-butyl-4-hydroxyphenyl substituents are potential bioantioxidants. Such derivatives of isoquinoline[12–14] and indazole[15], which turned out to be low toxic and more effective inhibitors of lipid peroxidation than ionol and natural α-tocopherols, were described by us earlier.

Phthalimidines containing 3,5-di-*tert*-butyl-4-hydroxyphenyl substituents **15a,b,c** were obtained by heating of compounds **6a,d,f**, respectively, with 2,6-di-*tert*-butylphenol **14** in the presence of CF_3COOH (Scheme 4).

Scheme 4

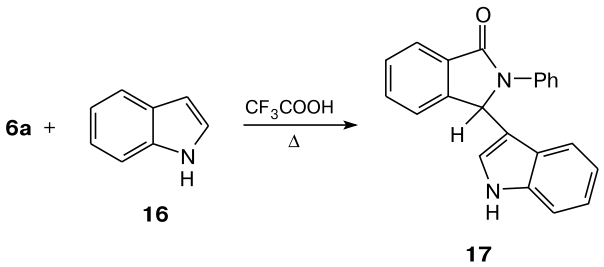


i. CF_3COOH, Δ

The feasibility of using hetrocyclic nucleophiles in this reaction was shown by the example of indole **16** (Scheme 5).

Starting from *o*-formylbenzoic acid and acylhydrazines **18a—c**, acylhydrazones **19a—c** were obtained in high yields upon mixing equimolar amounts of the reactants in hot Pr^{i}OH (Scheme 6). They react with Ac_2O similarly to arylaminophthalides **2**. In contrast to the IR spectra of phthalides, the absorption bands of the carbonyl groups in their IR spectra are always below 1700 cm^{-1}.

Scheme 5



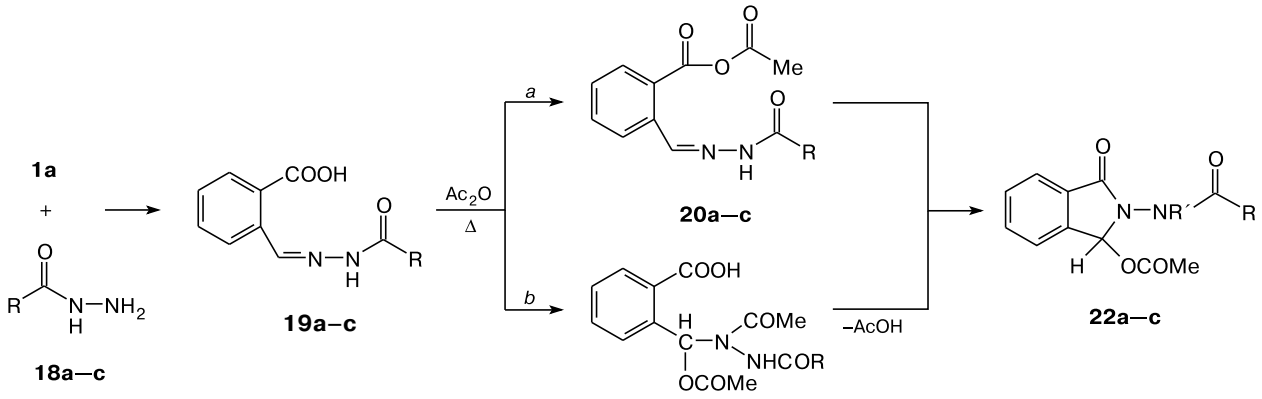
The possible pathways of their reaction with Ac_2O are presented in Scheme 6. The formation of mixed anhydride **20** (path *a*)[16a] followed by its intramolecular addition to the C=N bond could be the first step of the reaction. An alternative possibility (path *b*) supposes the addition of Ac_2O to the C=N bond to produce compound **21** (see Ref. 16b) followed by cyclization with elimination of HOAc. In the course of reaction, the exocyclic NH group can also undergo acylation.

The structure of compound **22a,b** was unambiguously established by IR and ^{1}H NMR spectroscopy and mass spectrometry. The situation with compound **22c** was far more complicated. The total number of protons in the ^{1}H NMR spectrum corresponded to the formula **22c**, however, doubling of signals, which could be considered as a result of the presence of a mixture of two isomers, was observed. Four signals, *viz.*, at δ 2.21, 2.24, 2.33, and 2.66, corresponded to six protons of two methyl groups, and the pattern typical of the AB system (doublets at δ 3.77 and 4.00, J = 19.5 Hz (~40%) and a singlet at δ 4.23 (~60%)) corresponded to two protons of the methylene group (Table 1).

The molecular weight of compound **22c** is 315, however, its mass spectrum contains a peak with a maximum m/z of 273. It should also be noted that we faced a rare case where elemental analysis cannot help with solution of the problem. The percentage of C and H in the compound containing an acetyl group or a hydrogen atom at the nitrogen atom coincided to within one tenth of percent, and the difference in the percentage of N was only 2% (13.33 and 15.38, respectively). Although the results of the analysis (percentage of nitrogen) were in favor of the structure **22c**, this structure was unambiguously established by X-ray diffraction analysis. The abnormal character of the mass spectrum of compound **22c** can be explained by the electron-impact-induced elimination of the acetyl group. The mass spectrum shows a peak with m/z 43 with 100% intensity, which corresponds to the mass of the acetyl group.

The overall view of molecule **22c** is presented in Figure 1. The five-membered ring has a flattened envelope conformation with the deviation of N(1) by 0.162(2) Å. The acetyl(cyanoacetyl)amine substituent is orthogonal to the plane of the bicycle (interplane angle is 87.05(2)°),

Scheme 6



18—22: R = 4-$MeOC_6H_4$ (**a**), $PhOCH_2$ (**b**), CH_2CN (**c**); **22:** R′ = H (**a**, **b**), MeCO (**c**)

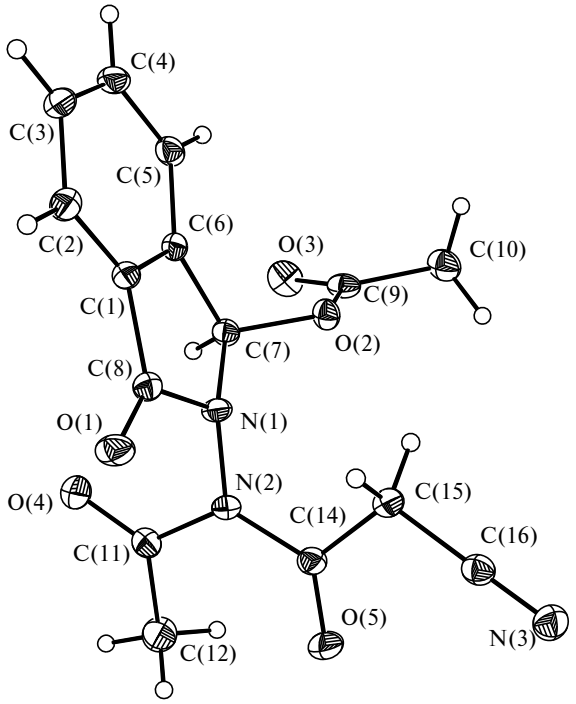
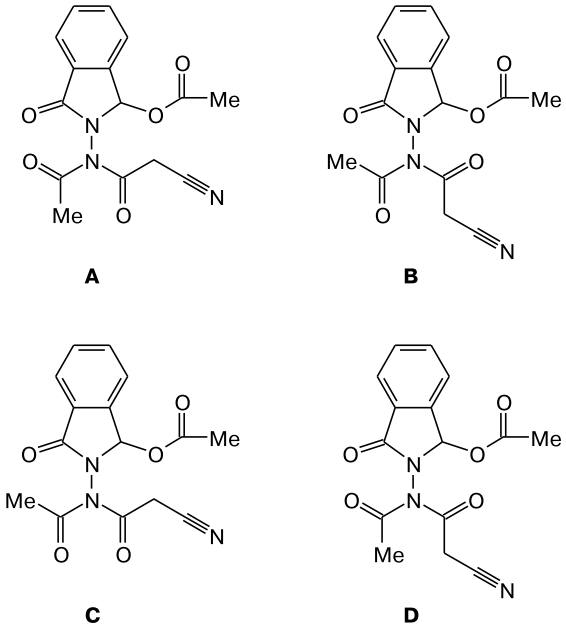


Fig. 1. Overall view of molecule **22c** (atoms are represented as thermal ellipsoids at the 50% probability level).



Conformers of compound **22c**	**A**	**B**	**C**
Total energy*/kcal·mol^{-1}	0	3.5	7.4
Contribution of energy of conjugation of acetyl(cyanoacetyl)amine substituent and energy of nonvalence intraatomic contacts to the total energy*/kcal·mol^{-1}	0	2.8	10.4

which could obviously be explained by steric repulsion from the substituent at the C(7) and C(8) atoms, and the perpendicular orientation is apparently stabilized by anomeric interaction of a lone electron pair of the N(1) atom and the antibonding orbitals of the N(2)—C(11) and N(2)—C(14) bonds. The acetyl(cyanoaceyl)amine substituent is planar, which suggests the conjugation of the C=O groups and the lone electron pair of the N(2) atom.

In order to investigate the possibility of existence of compound **22c** in another conformations and to find out if the conformation observed in the crystal meets the energy minimum in the isolated molecule, we carried out quantum chemical calculations (in a PBE0/6-311G(d,p) approximation using the Gaussian03[17] program) of tree

* The energy of the most favorable conformer **A** set to be zero.

Table 1. ^{1}H NMR spectra of phthalimidines obtained

Compound	Solvent	^{1}H NMR spectra, δ, (*J*/Hz)
6a	$CDCl_3$	2.07 (s, 3 H, Me); 7.27 (m, 1 H, CH_{arom}); 7.45 (m, 2 H, CH, CH_{arom}); 7.55—7.70 (m, 6 H, CH_{arom}); 7.92 (m, 1 H, C(7)H)
6b	$CDCl_3$	2.04 (s, 3 H, Me); 7.30—7.45 (m, 4 H, CH, CH_{arom}); 7.50—7.75 (m, 4 H, CH_{arom}); 7.94 (m, 1 H, C(7)H)
6c	$CDCl_3$	2.07 (s, 3 H, Me); 7.30—7.55 (m, 4 H, CH, CH_{arom}); 7.55—7.75 (m, 3 H, CH_{arom}); 7.93 (m, 1 H, C(7)H)
6d	$CDCl_3$	2.11 (s, 3 H, Me); 5.16 (s, 1 H, CH); 7.50—7.80 (m, 4 H, CH_{arom}); 7.94 (m, 1 H, C(7)H); 8.01 (dd, 1 H, C(6′)H, ^3J = 8.2, ^4J = 2.2); 8.11 (dd, 1 H, C(4′)H, ^3J = 8.2, ^4J = 2.2); 8.57 (two d, 1 H, C(2′)H, J = 2.2)
6e	$CDCl_3$	2.04 (s, 3 H, Me); 7.40—7.56 (m, 3 H, CH, CH_{arom}); 7.56—7.76 (m, 4 H, CH_{arom}); 7.80 (dd, 1 H, CH_{arom}, ^3J = 7.7, ^4J = 1.1); 7.95 (m, 1 H, C(7)H)
6f	DMSO-d_6	2.05 (s, 3 H, Me); 7.80—8.10 (m, 9 H, CH, CH_{arom}); 12.60 (br.s, 1 H, OH)
6g	DMSO-d_6	2.05 (s, 3 H, Me); 3.77, 3.81 (both s, 6 H, OMe); 5.94 (s, 1 H, $CH_{pyrimid}$); 7.50—8.20 (m, 9 H, CH, CH_{arom}); 11.30 (br.s, 1 H, NH)
6h	DMSO-d_6	1.06 (t, 3 H, Me, J = 7.6); 2.33 (m, 2 H, CH_2); 7.20 (s, 2 H, NH_2); 7.50—8.00 (m, 9 H, CH, CH_{arom})
6i	$CDCl_3$	1.07 (t, 3 H, Me, J = 7.5); 2.32 (q, 2 H, CH_2, J =7.5); 7.28 (m, 1 H, CH_{arom}); 7.44 (m, 2 H, CH_{arom}); 7.60 (m, 6 H, CH, CH_{arom}); 7.92 (m, 1 H, C(7)H)
7	DMSO-d_6	6.47 (br.d, 1 H, CH); 6.82 (br.d, 1 H, OH); 7.40—7.85 (m, 4 H, CH_{arom}); 7.99 (m, 4 H, CH_{arom}); 11.00—13.60 (br.s, 1 H, OH)
9	DMSO-d_6	6.37 (d, 1 H, OH, J = 10.0); 6.71 (d, 1 H, CH, J = 10.0); 7.15 (m, 1 H, CH_{arom}); 7.39 (m, 2 H, CH_{arom}); 7.45—7.90 (m, 6 H, CH_{arom})
10	$CDCl_3$	2.34 (t, 1 H, ≡CH, J = 2.4); 3.77, 3.90 (both dd, 2 H, CH_2, ^2J = 15.0, ^4J = 2.4); 6.56 (s, 1 H, CH); 7.26 (m, 1 H, CH_{arom}); 7.40—7.75 (m, 5 H, CH_{arom}); 7.80 (d, 2 H, CH_{arom}, J = 7.8); 7.92 (d, 1 H, C(7)H, J = 7.2)
11a	$CDCl_3$	2.36 (m, 2 H, NCH_2); 2.66 (m, 2 H, NCH_2); 3.53 (m, 4 H, OCH_2); 7.28 (m, 1 H, CH_{arom}); 7.45 (m, 2 H, CH_{arom}); 7.50—7.70 (m, 5 H, CH_{arom}); 7.91 (d, 1 H, C(7)H, J = 7.5)
11b	$CDCl_3$	2.48 (m, 2 H, NCH_2); 2.71 (m, 2 H, NCH_2); 3.57 (t, 4 H, OCH_2, J = 4.7); 5.95 (s, 1 H, CH); 7.45—7.80 (m, 4 H, CH_{arom}); 7.94 (d, 1 H, C(7)H, J = 7.95); 8.10 (m, 1 H, CH_{arom}); 8.22 (m, 1 H, CH_{arom}); 8.53 (t, 1 H, C(2′)H, ^4J = 2.1)
13	$CDCl_3$	6.52 (d, 1 H, CH_{arom}, J = 8.1); 6.85—7.80 (m, 11 H, CH_{arom}); 8.10 (dd, 1 H, C(7)H, ^3J = 6.0, ^4J = 2.4); 8.19 (s, 1 H, CH)
15a	DMSO-d_6	1.28 (s, 18 H, Bu^t); 6.26 (s, 1 H, CH); 6.57 (s, 1 H, OH); 6.90 (s, 2 H, CH_{arom}); 7.06 (m, 1 H, CH_{arom}); 7.30 (m, 3 H, CH_{arom}); 7.40—7.70 (m, 4 H, CH_{arom}); 7.80 (d, 1 H, C(7)H, J = 7.9)
15b	$CDCl_3$	1.32 (s, 18 H, Bu^t); 5.20 (s, 1 H, CH); 6.7 (s, 1 H, OH); 6.95 (s, 2 H, CH_{arom}); 7.31 (br.d, 1 H, CH_{arom}); 7.40—7.70 (m, 3 H, CH_{arom}); 7.34 (br.d, 1 H, CH_{arom}); 7.98 (br.d, 1 H, CH_{arom}); 8.32 (two d, 1 H, CH_{arom}, J = 2.1)
15c	DMSO-d_6	1.29 (s, 18 H, Bu^t); 6.38 (s, 1 H, CH); 6.62 (s, 1 H, OH); 6.94 (s, 2 H, CH_{arom}); 7.00—8.00 (m, 8 H, CH_{arom}); 12.5 (br.s, 1 H, OH)
17	$CDCl_3$	6.40 (s, 1 H, CH); 6.85—7.70 (m, 13 H, CH_{arom}); 8.03 (m, 1 H, C(7)H); 8.12 (br.s, 1 H, NH)
22a	$CDCl_3$	2.17 (s, 3 H, Me); 3.84 (s, 3 H, OMe); 6.88 (d, 2 H, CH_{arom}, J = 8.6); 7.18 (s, 1 H, CH); 7.45—7.55 (m, 3 H, CH_{arom}); 7.82 (d, 2 H, CH_{arom}, J = 8.6); 7.87 (d, 1 H, CH_{arom}, J = 7.15); 8.62 (s, 1 H, NH)
22b	$CDCl_3$	2.14 (s, 2 H, Me); 4.71 (s, 2 H, CH_2); 6.98 (d, CH_{arom}, J = 7.8); 7.07 (t, 1 H, CH_{arom}, J = 7.4); 7.15 (s, 1 H, CH); 7.36 (m, 2 H, CH_{arom}); 7.50—7.80 (m, 3 H, CH_{arom}); 7.88 (d, 1 H, CH_{arom}, J = 7.4); 8.51 (s, 1 H, NH)
22c	$CDCl_3$	2.21, 2.24, 2.33, 2.66 (all s, 6 H, Me); 3.77 (d, 0.5 H, CH_2, J = 19.5); 4.00 (d, 0.5 H, CH_2, J = 19.5); 4.23 (s, 1 H, CH_2); 7.01, 7.04 (both s, 1 H, CH); 7.50—7.85 (m, 3 H, CH_{arom}); 7.93 (m, 1 H, C(7)H)

conformations that differ from one other in the turn of the C(12)—C(11)—O(4) and O(5)—C(14)—C(15)—C(16)—N(3) fragments relative to the N(2)—C(11) and N(2)—C(14) bonds (of the four possible conformations **A—D**, conformation **D** should be the least stable due to repulsion of hydrogen atoms at the C(12) and C(15) atoms; this conformation was not considered).

The estimation of the energy of intramolecular interactions was carried out in the framework of natural analysis of populations, which is included in the Gaussian program, and of the R. Bader theory «Atoms in molecules».[18—20] The calculations carried out has shown that all three conformations correspond to minimas on the potential energy surface, conformer **A** observed in the crystal being the

most favorable. For the explanation of obtained energy values of conformers, we used a relatively simple scheme that takes into account the energy of conjugation of the acetyl(cyanoacetyl)amino fragment and the energy of nonvalence intraatomic contacts appeared as a result of the turn relative to the N(2)—C(11) and N(2)—C(14) bonds. The scheme proposed explains the difference in the energy at a semiquantitative level. The acetyl(cyanoacetyl)amine substituent is planar in conformers **A** and **B**. The O(2) atom participates in C(15)—H(15A)...O(2) nonvalence contact in conformer **A** and in O(2)...O(5) nonvalence contact in conformer **B**, both of the contacts being similar in energy, and the difference is caused by slightly greater conjugation in conformer **A**. Probably, the anomaly in the ^{1}H NMR spectrum of compound **22c** can be explained by the presence in the solution of these similar in energy conformers with different orientation of the CH_2 group regarding the chiral center of the molecule. The acetyl(cyanoacetyl)amine substituent in conformer **C** is deviates to some extent from the plane (the conjugation energy is 16 kcal • mol^{-1} smaller). However, this structure is favorable for the interaction between oxygen atoms O(4) and O(5): the lone electron pair of the O(4) atom is directed to the area of local vacuum of the electron density of the O(5) atom, which leads to the appearance of the critical point (3, −1) between these atoms. Two additional weak contacts C(15)—H(15A)...O(2) and C(15)—H(15B)...O(1) also are realized in conformer **C**.

In the crystal structure, molecules are linked by the van der Waals interactions and weak C—H...O contacts (commensurable in energy with the van der Waals contacts).

Experimental

The IR spectra were recorded on a Specord IR-75 instrument in Nujol mulls for compounds **2a,b**, **6a,b,c,f—i**, **9**, and **22a,c** and in $CHCl_3$ for compound **15a**. The IR spectra of compounds **2c—h**; **6d,e**; **7**; **10**; **11a,b**; **13**; **15b,c**; **17**; **19a—c**; **22b** were recorded on a Varian Excalibur 3100 FT-IR instrument by the method of frustrated total internal reflection. The ^{1}H NMR spectra were recorded on a Varian UNITY-300 spectrometer. Mass spectra were obtained on a Finnigan MAT INCOS 50 spectrometer with direct sample inlet into the ion source, and mass spectra of compound **11b** was obtained on an Agilrut 1200 Bruker Daltonius mir OTOFQ spectrometer.

3-Anilinophthalide (2a). Aniline (1 mL, 10.5 mmol) was added to a hot solution of *o*-formylbenzoic acid (1.5 g, 10 mmol) in Pr^{i}OH (15 mL), the reaction mixture was heated to boiling and cooled with ice. The precipitate that formed was filtered off, washed with Pr^{i}OH and petroleum ether and dried. A colorless substance was obtained, m.p. 182—185 °C (*cf.* Ref. 6: m.p. 180—181 °C). The yield was 2.15 g (95%). IR, ν/cm^{-1}: 3327 (NH), 1727, 1715 (CO), 1600 (arom.), 1060, 855 (C—O—C).

3-(2-Chloroanilino)phthalide (2b). A mixture of *o*-formylbenzoic acid (0.5 g, 3.3 mmol) and *o*-chloroaniline (0.4 mL, 3.8 mmol) was heated to fusion, which followed by instant solidification. The reaction product was recrystallized from Pr^{i}OH, cooled on ice, the precipitate was filtered off, washed with Pr^{i}OH and petroleum ether and dried. A colorless substance was obtained, m.p. 170 °C (*cf.* Ref. 6: m.p. 170—171 °C). The yield was 0.59 g (68%). IR, ν/cm^{-1}: 3327 (NH), 1747, 1727 (CO), 1595 (arom.), 1060, 855 (C—O—C).

3-(2,4-Dichloroanilino)phthalide (2c). A hot solution of 2,4-dichloroaniline (0.9 g, 5.5 mmol) in MeOH (10 mL) was added to a hot solution of *o*-formylbenzoic acid (0.75 g, 5 mmol) in MeOH (10 mL). The reaction mixture was refluxed for 2—3 min and cooled in ice water triturating with a glass rod. The precipitate that formed was filtered off, washed with cold MeOH and dried. A colorless substance was obtained, m.p. 160—165 °C (BuOH). The yield was 1 g (68%). Found (%): C, 57.11; H, 3.23; N, 4.82. $C_{14}H_9NO_2Cl_2$. Calculated (%): C, 57.17; H, 3.08; N, 4.76. IR, ν/cm^{-1}: 3395 (NH), 1759 (CO), 1063, 888 (C—O—C).

3-(3-Nitroanilino)phthalide (2d). A hot solution of *m*-nitroaniline (1.4 g, 10 mmol) in MeOH (10 mL) was added to a hot solution of *o*-formylbenzoic acid (1.5 g, 10 mmol) in MeOH (20 mL). The precipitate that formed after short induction period was cooled in ice water, filtered off, washed with MeOH, and dried. A light yellow substance was obtained, m.p. 228 °C. The yield was 2.55 g (94%). Found (%): C, 61.97; H, 3.92; N, 10.18. $C_{14}H_{10}N_2O_4$. Calculated (%): C, 62.22; H, 3.73; N, 10.37. IR, ν/cm^{-1}: 3379 (NH), 1738 (CO), 1530, 1352 (NO_2), 1080, 867 (C—O—C).

3-(2-Cyanoanilino)phthalide (2e) was prepared analogously to **2d** from *o*-formylbenzoic acid (0.75 g, 5 mmol) in Pr^{i}OH (5 mL) and anthranilonitrile (0.65 g, 5.5 mmol) in Pr^{i}OH (5 mL). A colorless substance was obtained, m.p. 188—190 °C. The yield was 0.4 g (32%). An additional amount (0.13 g) of this substance with the same melting point was precipitated with petroleum ether from the mother liquor. Total yield was 0.53 g (42%). Found (%): C, 72.12; H, 4.21; N, 11.03. $C_{15}H_{10}N_2O_2$. Calculated (%): C, 71.99; H, 4.03; N, 11.19. IR, ν/cm^{-1}: 3355 (NH), 2220 (CN), 1763, 1740 (CO), 1073, 888 (C—O—C).

3-(4-Carboxyanilino)phthalide (2f) was prepared analogously to **2d** from *p*-aminobenzoic acid (1.4 g, 10 mmol) in EtOH (10 mL) and *o*-formylbenzoic acid (1.5 g, 10 mmol) in EtOH (5 mL). This reaction was exothermic. After cooling, the precipitate was filtered off and dried. A colorless substance was obtained, m.p. 280—282 °C. The yield was 2.45 g (91%). Found (%): C, 66.57; H, 4.43; N, 4.97. $C_{15}H_{11}NO_4$. Calculated (%): C, 66.91; H, 4.12; N, 5.20. IR, ν/cm^{-1}: 3321 (NH), 1752, 1663 (CO), 1070, 881 (C—O—C).

3-[4-(*N*-(2,6-Dimethoxypyrimidine-4-yl)sulfamoyl)anilino]-phthalide (2g). A hot solution of *o*-formylbenzoic acid (0.25 g, 1.65 mmol) was added to a hot solution of Sulfadimethoxine (0.5 g, 1.6 mmol) in Pr^{i}OH (10 mL). The reaction mixture was refluxed for 1—2 min, cooled, the oil that formed was triturated with a glass rod with cooling in ice water. The precipitate was filtered off, washed with cold Pr^{i}OH and petroleum ether and dried. A colorless substance was obtained, m.p. 198—200 °C. An additional amount of this substance with the same melting point was precipitated with petroleum ether from the filtrate. Total yield was 0.45 g (63%). Found (%): C, 54.03; H, 4.37; N, 12.41. $C_{20}H_{18}N_4O_6S$. Calculated (%): C, 54.29; H, 4.10; N, 12.66. IR, ν/cm^{-1}: 3340, 3307 (NH), 1748 (CO), 1590 (arom.), 1064, 868 (C—O—C).

3-(4-Sulfamoylanilino)phthalide (2h). *o*-Formylbenzoic acid (0.45 g, 3 mmol) in EtOH (5 mL) was added to a hot solution of Streptocide White (0.55 g, 3 mmol) in EtOH (10 mL). The reaction mixture was heated to boiling and cooled to room temperature. The precipitate was filtered off, washed with EtOH, and dried. A colorless substance was obtained, m.p. 256—260 °C. The yield was 2.1 g (67%). Found (%): C, 55.11; H, 4.27; N, 9.00. $C_{14}H_{12}N_2O_4S$. Calculated (%):C, 55.26; H, 3.97; N, 9.21. IR, ν/cm^{-1}: 3340, 3242 (NH), 1729 (CO), 1325, 1150 (SO_2), 1094, 868 (C—O—C).

3-Acetoxy-2-phenylisoindolin-1-one (6a). A mixture of phthalide **2a** (0.95 g, 4.2 mmol) and Ac_2O (2.5 mL) was heated up to dissolution, refluxed for 3 min, cooled, and quenched with a mixture of MeOH (5 mL) and H_2O (15 mL). The oily precipitate that formed was cooled on ice, triturated using a glass rod until solidification, filtered off, washed with H_2O, and dried. A colorless substance was obtained. The yield was 1.05 g (93%). After recrystallization from isooctane (30 mL), compound **6a** was obtained in a yield of 0.85 g (75 %), m.p. 97—99 °C. Found (%): C, 71.76; H, 5.11; N, 5.32. $C_{16}H_{13}NO_3$. Calculated (%):C, 71.90; H, 4.90; N, 5.24. IR, ν/cm^{-1}: 1735, 1714 (CO), 1595, 1495 (arom.). $M^+ = 276$.

3-Acetoxy-2-(2-chlorophenyl)isoindolin-1-one (6b) was prepared analogously to **6a** from phthalide **2b** (0.55 g, 2.1 mmol) and Ac_2O (1 mL). It was precipitated with a mixture of HOAc (3 mL) and H_2O (20 mL). The emulsion that formed was cooled on ice and triturated with a glass rod until solidification. A colorless substance was obtained, m.p. 99—102 °C. The yield was 0.64 g (~100%). Found (%): C, 63.42; H, 4.27; N, 4.72. $C_{16}H_{12}NClO_3$. Calculated (%): C, 63.69; H, 4.01; N, 4.64. IR, ν/cm^{-1}: 1727, 1700 пл. (CO), 1607, 1580 (arom.). $M^+ = 301.5$.

3-Acetoxy-2-(2,4-dichlorophenyl)isoindolin-1-one (6c) was prepared analogously to **6a** from phthalide **2c** (0.5 g, 1.7 mmol) and Ac_2O (1 mL). It was precipitated with a mixture of MeOH (5 mL) and H_2O (25 mL). The oil that formed gradually hardened with cooling on ice and trituration with a glass rod. The yield was ~0.6 g (~100%). A colorless substance was obtained, m.p. 95—97 °C. Found (%): C, 56.93; H, 3.57; N, 4.28. $C_{16}H_{11}NCl_2O_3$. Calculated (%):C, 57.17; H, 3.30; N, 4.17. IR, ν/cm^{-1}: 1760, 1735, 1725 (CO), 1607, 1595, 1580 (arom.).

3-Acetoxy-2-(3-nitrophenyl)isoindolin-1-one (6d) was prepared analogously to **6a** from phthalide **2d** (2.55 g, 9.4 mmol) and Ac_2O (2.5 mL). 50% MeOH (15 mL) was added to the reaction mixture hardened after cooling, the precipitate was filtered off, washed with 50% MeOH and dried. A colorless substance was obtained, m.p. 160 °C (from toluene). The yield was 2.65 g (98%). Found (%): C, 61.56; H, 3.92; N, 8.80. $C_{16}H_{12}N_2O_5$. Calculated (%): C, 61.54; H, 3.87; N, 8.97. IR, ν/cm^{-1}: 1729 (CO), 1522, 1355 (NO_2).

3-Acetoxy-2-(4-cyanophenyl)isoindolin-1-one (6e) was prepared analogously to **6a** from phthalide **2e** (0.24 g, 1 mmol) and Ac_2O (1 mL). The reaction mixture was refluxed for 5 min, MeOH (3 mL) and H_2O (10 mL) were added to a cooled solution, the oil that formed hardened with cooling on ice (~1 h) and triturating with a glass rod. A colorless substance was obtained, m.p. 130—132 °C (fromisooctane). The yield was 0.27 g (93%). Found (%): C, 70.21; H, 4.47; N, 9.32. $C_{17}H_{12}N_2O_3$. Calculated (%): C, 69.86; H, 4.14; N, 9.58. IR, ν/cm^{-1}: 2227 (CN), 1753, 1721 (CO).

3-Acetoxy-2-(4-carboxyphenyl)isoindolin-1-one (6f) was prepared analogously to **6a** from phthalide **2f** (0.95 g, 3.5 mmol) and Ac_2O (3.5 mL). The reaction mixture was refluxed (~10 min) until complete homogenization, cooled, and quenched with a mixture of MeOH (5 mL) and H_2O (25 mL). The oil that formed was cooled on ice and triturated with a glass rod until complete solidification. The preciritate was filtered off, washed with H_2O and 50% EtOH and dried. A colorless substance was obtained, m.p. 193—195 °C. The yield was 1 g (91%). Found (%): C, 65.24; H, 4.43; N, 4.35. $C_{17}H_{13}NO_5$. Calculated (%): C, 65.59; H, 4.21; N, 4.50. IR, ν/cm^{-1}: 1735, 1715, 1680 (CO), 1595, 1500 (arom.). $M^+ = 311$.

3-Acetoxy-2-[4-(*N*-(2,6-dimethoxypyrimidin-4-yl)-sulfamoyl)phenyl]isoindolin-1-one (6g) was prepared analogously to **6a** from phthalide **2g** (0.45 g, 1 mmol) and Ac_2O (1.5 mL). After cooling, EtOH (3 mL) was added, and the oil was precipitated with water, which was separated and triturated with small amount of Pr^{i}OH with ice cooling. The crystalls that formed were filtered off, washed with cold Pr^{i}OH and dried. A colorless substance was obtained, m.p. 150—154 °C. The yield was 0.07 g (14%). Found (%): C, 54.25; H, 4.30; N, 11.42. $C_{22}H_{20}N_4SO_7$. Calculated (%): C, 54.54; H, 4.16; N, 11.56. IR, ν/cm^{-1}: 3365, 3170 (NH), 1740, 1715 (CO), 1600, 1580 (arom.), 1155, 1355 (SO_2). MS (EI): 64 (SO_2, 100%), $M^+ = 484$ (weak signal).

3-Propionyloxy-2-(4-sulfamoylphenyl)isoindolin-1-one (6h). A mixture of phthalide **2h** (0.3 g, 1 mmol) and propionic anhydride (1 mL) was refluxed for 4 min. A mixture of MeOH (2 mL) and H_2O (8 mL) was added, the mixture obtained was heated to boiling and cooled. A part of the oily precipitate that formed was triturated with MeOH, and solidified substance was added to the remaining mass with cooling on ice and trituration with a glass rod. The solid was filtered off, washed with cold MeOH and dried. A colorless crystalline substance was obtained in a yield of 2 g (55%), m.p. 198—200 °C. Found (%): C, 56.27; H, 4.72; N, 7.63. $C_{17}H_{16}N_2SO_5$. Calculated (%): C, 56.66; H, 4.47; N, 7.77. IR, ν/cm^{-1}: 3300, 3220 (NH_2), 1727, 1707 (CO), 1595, 1495 (arom.), 1340, 1155 (SO_2).

3-Propionyloxy-2-phenylisoindolin-1-one (6i). A mixture of phthalide **2a** (0.41 g, 1.8 mmol) and propionic anhydride (1 mL) was refluxed until complete dissolution (3 min), cooled, and quenched with a mixture of MeOH (2 mL) and H_2O (8 mL). The mixture obtained was kept on ice and triturated with a glass rod for 30 min. The precipitate that formed was filtered off, washed with 50% EtOH and dried. A colorless substance was obtained, m.p. 93—96 °C. The yield was 0.42 g (80%). Found (%): C, 72.49; H, 5.43; N, 5.11. $C_{17}H_{15}NO_3$. Calculated (%): C, 72.58; H, 5.37; N, 4.98. IR, ν/cm^{-1}: 1740, 1700 (CO), 1595, 1495 (arom.).

3-Hydroxy-2-(4-carboxyphenyl)isoindolin-1-one (7). A suspension of phthalimidine **6f** (0.31 g, 1 mmol) in 12 mL of a mixture of AcOH and H_2O (1 : 1) was refluxed for 30 min, then cooled. H_2O (10 mL) was added to the reaction mixture, the precipitate was filtered off, washed with H_2O and dried. A colorless substance was obtained, m.p. 244—247 °C. The yield was 0.19 g (70%). Found (%): C, 66.82; H, 4.37; N, 5.24. $C_{15}H_{11}NO_4$. Calculated (%): C, 66.91; H, 4.12; N, 5.20. IR, ν/cm^{-1}: 3223 (OH), 1677 (CO), 1604, 1573, 1513 (arom.). $M^+ = 269$.

3-Hydroxy-2-phenylisoindolin-1-one (9). ***A.*** Isoindolinone **6a** (0.2 g, 0.75 mmol) was dissolved in EtOH (3 mL) with heating. This solution was cooled to room temperature, hydrazine hydrate (0.1 g) was added and the mixture obtained was refluxed for

1 min and then cooled on ice. A few drops of the solution was triturated with water until formation of hard flakes, and H_2O (6 mL) was added. The suspension obtained was added to a cooled solution with trituration with a glass rod. The precipitate that formed was filtered off, washed with 50% EtOH and dried. A colorless substance was obtained, m.p.160—162 °C. The yield was 0.1 g (59%).

B. The analogous transformation of **6a** occured on heating with concentrated HCl to boiling. At first the substance melted and then hardened. The yield of crude product was quantitative. The IR spectra of this product coincides with that obtained from the reaction with hydrazine hydrate, and the melting point of the mixed sample does not display depression. Found (%): C, 74.53 H, 5.13; N, 6.37. $C_{14}H_{11}NO_2$. Calculated (%): C, 74.65; H, 4.92; N, 6.22. IR, ν/cm^{-1}: 3380 (OH), 1695 (CO), 1595, 1500 (arom.).

3-Propargyloxy-2-phenylisoindolin-1-one (10). A mixture of phthalimidine **6a** (0.53 g, 2 mmol) and propargyl alcohol (1 mL) was refluxed for 30 min, then cooled, and H_2O (10 mL) was added. The oily precipitate that formed was cooled on ice and triturated with a glass rod until complete solidification. The precipitate was filtered off, washed with H_2O and dried. The yield of the crude product was 0.496 g (94%). After recrystallization from petroleun ether, a colorless substance was obtained in a yield of 0.325 g (62%), m.p. 122—124 °C. Found (%): C, 77.62; H, 5.11; N, 5.43. $C_{17}H_{13}NO_2$. Calculated (%): C, 77.55; H, 4.98; N, 5.32. IR, ν/cm^{-1}: 3265 (≡CH), 2127 (C≡C), 1705 (CO), 1596, 1501 (arom.).

3-Morpholino-2-phenylisoindolin-1-one (11a). A mixture of phthalimidine **6a** (0.27 g, 1 mmol) and morpholine (0.5 mL) was refluxed for 7 min, then cooled, and EtOH (3 mL) was added. The solution was triturated under cooling on ice until complete solidification. The precipitate was filtered off, washed with cold EtOH and dried. The yield was 0.173 g (59%). Analytically pure product was obtained after recrystallization from Pr^{i}OH (5 mL), the yield of colorless crystals was 80 mg, m.p. 177—178 °C. Found (%): C, 73.12; H, 6.42; N, 9.24. $C_{18}H_{18}N_2O_2$. Calculated (%): C, 73.45; H, 6.16; N, 9.52. IR, ν/cm^{-1}: 1680 (CO), 1595, 1498 (arom.).

3-Morpholino-2-(3-nitrophenyl)isoindolin-1-one (11b). A mixture of phthalimidine **6d** (0.31 g, 1 mmol) and morpholine (0.5 mL) was refluxed for 10 min, then cooled and dissolved in Pr^{i}OH (5 mL), a precipitate and resin were precipitated with water. The resin was separated, triturated with MeOH, and the solid together with MeOH was poured into the remaining mass. The suspension was cooled on ice and triturated with a glass rod, the precipitate was filtered off, washed with H_2O and dried. A colorless substance that easily crystallized from Pr^{i}OH was obtained in a yield of 0.29 g (85%), m.p. 130—132 °C (Pr^{i}OH). Found (%): C, 63.52; H, 5.12; N, 12.54. $C_{18}H_{17}N_3O_4$. Calculated (%): C, 63.71; H, 5.05; N, 12.38. IR, ν/cm^{-1}: 1709 (CO), 1611 (arom.), 1520, 1363 (NO_2). $[M + H]^+$ = 340.139; M = 339.131.

3-(Benzoxazol-2-ylsulfanyl)-2-phenylisoindolin-1-one (13). A mixture of phthalimidine **6a** (0.27 g, 1 mmol) and 2-mercaptobenzoxazole (0.16 g, 1 mmol) was ground in a mortar and fused at 150 °C. The solid foam was cooled, dissolved under reflux in CH_3CN (8 mL), filtered while hot and cooled on ice. The precipitate that formed was filtered off, washed with cold CH_3CN and dried. A colorless substance was obtained, m.p 240 °C (petroleum ether). The yield was 0.166 g (46.5%). It was recrystallized from toluene (3 mL), washed with cold toluene and petroleum ether, and analytically pure compound **13** was obtained in a yield of 0.054 g, m.p. 243—250 °C. Found (%): C, 70.22; H, 4.17; N, 8.00. $C_{21}H_{14}N_2SO_2$. Calculated (%): C, 70.37; H, 3.94; N, 7.82. IR, ν/cm^{-1}: 1713 (CO), 1595, 1500, 1476 (arom.).

3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-phenylisoindolin-1-one (15a). A mixture of phthalimidine **6a** (0.27 g, 1 mmol), CF_3COOH (0.2 mL) and 2,6-di-*tert*-butylphenol (0.25 g, 1.2 mmol) was heated until boiling and refluxed for 1 min, then cooled, and Pr^{i}OH (3 mL) was added. The solution was cooled on ice and triturated with a glass rod. The crystalline precipitate that formed was filtered off, washed with Pr^{i}OH and petroleun ether and dried. A colorless substance was obtained, m.p 229—230 °C (isooctane—toluene, 1 : 1). The yield was 0.32 g (77%). Found (%): C, 81.28; H, 7.84; N, 3.67. $C_{28}H_{31}NO_2$. Calculated (%): C, 81.32; H, 7.55; N, 3.39. IR, ($CHCl_3$), ν/cm^{-1}: 3635 (OH), 2960, 2905, 2865 (Bu^t), 1687 (CO). M^+ = 413.

3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-(3-nitrophenyl)-isoindolin-1-one (15b). A mixture of phthalimidine **6d** (0.312 g, 1 mmol) and 2,6-di-*tert*-butylphenol (0.3 g, 1.5 mmol) was fused, CF_3COOH (0.2 mL) was added, the mixture obtained was refluxed for 1 min, cooled, Pr^{i}OH (7 mL) was added, and the mixture was cooled on ice. The precipitate that formed was filtered off, washed with Pr^{i}OH and petroleun ether and dried. A colorless substance was obtained, m.p 183—185 °C. The yield was 0.421 g (92%). Found (%): C, 73.42; H, 6.80; N, 6.44. $C_{28}H_{30}N_2O_4$. Calculated (%): C, 73.34; H, 6.59; N, 6.11. IR, ν/cm^{-1}: 3568 (OH), 2959, 2915, 2874 (*t*-Bu), 1691 (CO), 1525, 1349 (NO_2).

3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-(4-carboxyphenyl)-isoindolin-1-one (15c). A mixture of phthalimidine **6c** (0.31 g, 1 mmol) and CF_3COOH (0.3 mL) was heated until boiling. After complete homogenization, 2,6-di-*tert*-butylphenol (0.3 g, 1.5 mmol) was added. Pr^{i}OH (10 mL) was added to almost instantaneously solidified reaction mixture, it was refluxed and triturated with a glass rod until complete dissolution. Clear solution was cooled on ice, triturated with a glass rod until complete precipitation. The precipitate was filtered off, washed with Pr^{i}OH and petroleum ether and dried. A colorless substance was obtained, m.p 290—295 °C (CH_3CN). The yield was 0.28 g (61%). Found (%): C, 75.93; H, 6.98; N, 3.27. $C_{29}H_{31}NO_4$. Calculated (%): C, 76.12; H, 6.83; N, 3.06. IR, ν/cm^{-1}: 3623 (OH), 2954, 2909, 2870 (Bu^t), 1711, 1673 (CO).

3-(Indol-3-yl)-2-phenylisoindolin-1-one (17). Phthalimidine **6a** (0.27 g, 1 mmol) and indole (0.13 g, 1.1 mmol) were mixed and CF_3COOH (0.1 mL) was added. The mixture obtained was heated until boiling, cooled, dissolved in EtOH (5 mL) with heating, cooled, the oil precipitated with water. This gradually solidified upon cooling on ice and trituration. The precipitate was filtered off and recrystallized from toluene (15 mL). A white-pink substance was obtained in a yield of 0.18 g (56%). After recrystallization from a toluene—isooctane mixture, colorless crystals were obtained, m.p. 230—235 °C. Found (%): C, 81.32; H, 5.11; N, 8.56. $C_{22}H_{16}N_2O$. Calculated (%): C, 81.46; H, 4.97; N, 8.64. IR, ν/cm^{-1}: 3188 (NH), 1663 (CO). M^+ = 324.

***o*-Formylbenzoic acid anisoylhydrazone (19a).** A hot solution of anisohydrazide (0.55 g, 3.3 mmol) in Pr^{i}OH (5 mL) was added to a hot solution of *o*-formylbenzoic acid (0.5 g, 3.3 mmol) in Pr^{i}OH (5 mL). Pr^{i}OH (5 mL) was added to a thick mass formed as a result of the exothermic reaction. The mixture was

filtered while hot, washed with Pr^iOH and petroleun ether and dried. A colorless substance **19a** was obtained in a yield of 0.83 g (84%), m.p. 200—202 °C. Found (%): C, 64.32; H, 4.68; N, 9.27. $C_{16}H_{13}N_2O_4$. Calculated (%): C, 64.64; H, 4.41; N, 9.42. IR, ν/cm^{-1}: 3251—3005 (NH), 1681 (CO), 1624, 1603, 1570 (arom.).

***o*-Formylbenzoic acid phenoxyacetylhydrazone (19b)** was prepared analogously to **19a** by mixing hot solutions of *o*-formylbenzoic acid (0.5 g) and phenylacetohydrazide (0.55 g) in Pr^iOH (5 mL each). The mixture was heated until boiling. After cooling to room temperature, the precipitate was filtered off, washed with Pr^iOH and petroleum ether and dried. A colorless substance (**19b**) was obtained in a yield of 0.95 g (96%), m.p. 192—194 °C. Found (%): C, 64.17; H, 5.02; N, 9.28. $C_{16}H_{14}N_2O_4$. Calculated (%): C, 64.43; H, 4.73; N, 9.39. IR, ν/cm^{-1}: 3028 (NH), 1684 (CO), 1599, 1559, 1495 (arom.).

***o*-Formylbenzoic acid cyanoacetylhydrazone (19c)** was prepared analogously to **19a** by mixing hot solutions of *o*-formylbenzoic acid (1.5 g) in Pr^iOH (10 mL) and cyanoacetohydrazide (1 g) in Pr^iOH (15 mL). After completion of exothermic reaction, Pr^iOH (10 mL) was added to the solid mass, then the mixture was cooled to room temperature, the precipitate was filtered off, washed with Pr^iOH and petroleum ether and dried. Compound **19c** was obtained in a yield of 2.1 g (91%), m.p. 186—188 °C. Found (%): C, 56.93; H, 4.15; N, 18.32. $C_{11}H_9N_3O_3$. Calculated (%): C, 57.14; H, 3.92; N, 18.17. IR, ν/cm^{-1}: 3171—3078 (NH), 2260 (C≡ N),1674, 1649 (CO), 1606, 1566 (arom.). $M^+ = 231$.

3-Acetoxy-2-(*p*-methoxybenzoylamino)isoindolin-1-one (22a). A mixture of hydrazone **19a** (0.3 g, 1 mmol) and Ac_2O (2 mL) was heated until dissolution and refluxed for 5 min, cooled, and quenched with MeOH (3 mL) and H_2O (10 mL). The mixture was cooled on ice and triturated with a glass rod. The crystalline precipitate that formed was filtered off, washed with H_2O and 50% EtOH and dried. A colorless substance was obtained in a yield of 0.28 g (81%), m.p. 159—161 °C. The analytically pure product was obtained by recrystallization from Pr^iOH or toluene. Found (%): C, 63.42; H, 7.85; N, 8.27. $C_{18}H_{16}N_2O_5$. Calculated (%): C, 63.53; H, 4.74; N, 8.23. IR, ν/cm^{-1}: 3113 (NH), 1755, 1730, 1675 (CO), 1615, 1500 (arom.). $M^+ = 340$.

3-Acetoxy-2-(phenoxyacetylamino)isoindolin-1-one (22b). A mixture of hydrazone **19b** (0.3 g, 1 mmol) and Ac_2O (2 mL) was refluxed for 5 min, cooled, and quenched with MeOH (3 mL) and H_2O (20 mL). The liquid was decanted and cooled on ice, the oily residue was dissolved in small amount of MeOH, the solution obtained was poured to the cooled liquid with trituration with a glass rod, crystallization occured gradually. The precipitate was filtered off, washed with H_2O and 50% EtOH and dried. A colorless substance was obtained in a yield of 0.26 g (76%), m.p. 165—168 °C (Pr^iOH or toluene). The analytically pure product was obtained by recrystallization from Pr^iOH and then from toluene. Found (%): C, 63.38; H, 4.85; N, 8.30. $C_{18}H_{16}N_2O_5$. Calculated (%): C, 63.53; H, 4.74; N, 8.23. IR, ν/cm^{-1}: 3241 (NH), 1768, 1737, 1695 (CO), 1596, 1491 (arom.). $M^+ = 340$.

3-Acetoxy-2-acetyl(cyanoacetyl)aminoisoindolin-1-one (22c). A mixture of hydrazone **19c** (0.23 g, 1 mmol) and Ac_2O (2 mL) was refluxed until dissolution of the hydrazone and for 5 min more, cooled, and quenched with MeOH (3 mL) and H_2O (25 mL). The oily precipitate that formed was cooled on ice and triturated with a glass rod until solidification, filtered, washed with H_2O and 50% MeOH and dried. The yield was 0.22 g (69%). After twofold recrystallization from Pr^iOH, a colorless substance was obtained, m.p. 145 °C. Its structure was established by X-ray diffraction analysis. IR, ν/cm^{-1}: 2256 (C≡N), 1755 pl., 1730, 1715 (CO), 1620 (arom.). MS (EI): 273, 43 (about 100%, CH_3CO).

X-ray diffraction analysis. Crystals of **22c** ($C_{15}H_{13}N_3O_5$) at 100 K are monoclinic, $a = 8.6329(4)$ Å, $b = 17.4658(9)$ Å, $c = 9.6957(5)$ Å, $V = 1457.05(13)$ Å^3, $Z = 4$, space group $P2_1/c$, $\mu = 0.11$ mm^{-1}, $d_{calc} = 1.437$ g·cm^{-3}. Intensities of 16383 reflections were measured on a SMART APEX2 CCD diffractometer (λ(Mo-Kα) = 0.71073 Å, graphite monochromator, ω scanning technique, scan step was 0.5°, $2\theta < 58°$). The initial array of measured intensities were processed using the SAINT[21], SADABS[22] programs. The structure was solved by the direct method and refined by the full-matrix least-squares method in the anisotropic approximation for nonhydrogen atoms against F^2_{hkl}. Hydrogen atoms were placed at the calculated positions and refined using the riding model ($U_{iso}(H) = nU_{eq}(C)$, where $n = 1.5$ for C atoms of the methyl groups, $n = 1.2$ for the remaining C atoms). 3858 independent reflections were included in the refinement ($R_{int} = 0.0274$, the number of refined parameters was 210). The accuracy of the refinement on all independent reflections (wR_2) was 0.0840 ($R_1 = 0.0357$ on 3192 reflections with $I > 2\sigma(I)$). All calculations were carried out on an IBM PC AT using the SHELXTL[23] complex program. The atomic coordinates and thermal parameters were deposited with the Cambridge Crystallographic Data Centre (CCDC 753793).*

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