ISSN 1070-4280, Russian Journal of Organic Chemistry, 2008, Vol. 44, No. 4, pp. 607–611. © Pleiades Publishing, Ltd., 2008.
Original Russian Text © K.S. Bozdyreva, Z.G. Aliev, A.N. Maslivets, 2008, published in Zhurnal Organicheskoi Khimii, 2008, Vol. 44, No. 4, pp. 612–616.

Five-Membered 2,3-Dioxo Heterocycles: LVII.* Recyclization of 3-Pivaloylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones by the Action of *o*-Phenylenediamine. Crystalline and Molecular Structure of 3-[3,3-Dimethyl-2-oxo-1-(3-oxo-3,4-dihydroquinoxalin-2-yl)butyl]-1-phenylquinoxalin-2(1*H*)-one

K. S. Bozdyreva[a], Z. G. Aliev[b], and A. N. Maslivets[a]

[a] *Perm State University, ul. Bukireva 15, Perm, 614990 Russia*
e-mail: koh2@psu.ru

[b] *Institute of Chemical Physics Problems, Russian Academy of Sciences, Chernogolovka, Moscow oblast, Russia*

Received May 16, 2006

Abstract—3-[(*Z*)-3,3-Dimethyl-2-oxobutylidene]-3,4-dihydroquinoxalin-2(1*H*)-one and its 1-phenyl-substituted analog reacted with oxalyl chloride to give the corresponding 3-pivaloylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones. Reactions of the latter with *o*-phenylenediamine led to the formation of 3,3′-(3,3-dimethyl-2-oxobutane-1,1-diyl)di[quinoxalin-2(1*H*)-ones].

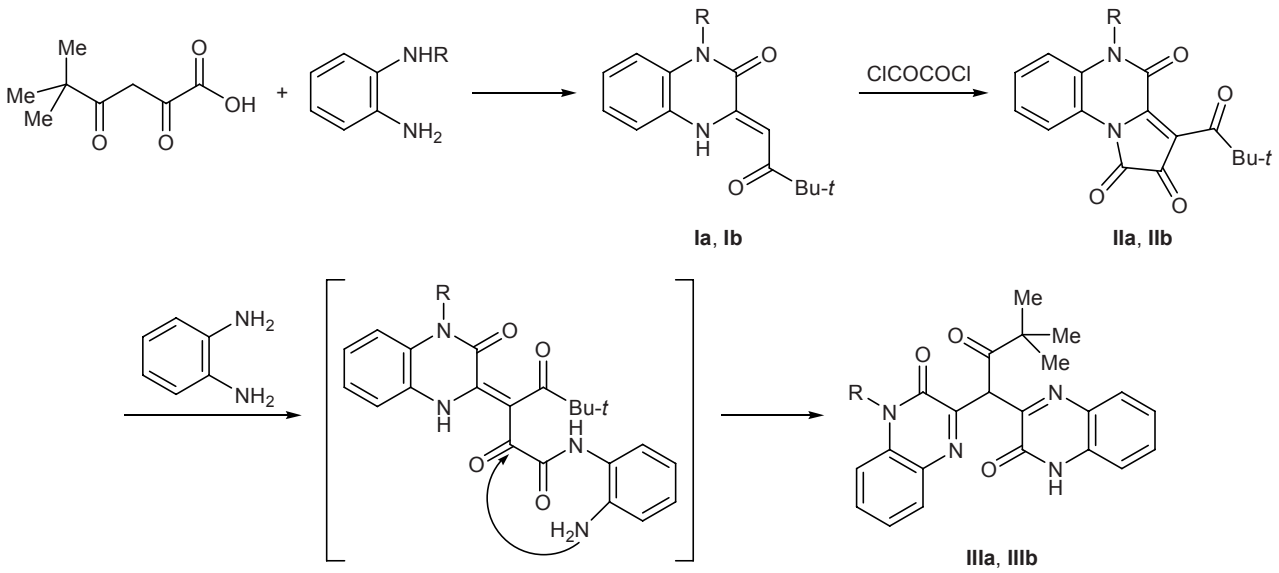
DOI: 10.1134/S1070428008040234

3-Aroyl- and 3-hetaroyl-substituted pyrrolo[1,2-*a*]-quinoxaline-1,2,4(5*H*)-triones were found to be convenient reagents for the synthesis of difficultly accessible polycarbonyl derivatives of nitrogen-containing heterocycles and fused heterocyclic systems. Heterocyclizations of these compounds in reactions with difunctional nucleophiles involve appending of a new heteroring, the original heterocyclic system being retained [2–6]. The present study continues our works on the properties of pyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones; it was aimed at synthesizing new representatives of this class of compounds, namely 3-pivaloylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones and studying their reactions with *o*-phenylenediamine. We believed that introduction of a bulky *tert*-butyl group into the acyl moiety in the 3-position of the pyrroloquinoxaline system could radically affect the direction of their reactions with binucleophiles.

Initial 3-[(*Z*)-3,3-dimethyl-2-oxobutylidene]-3,4-dihydroquinoxalin-2(1*H*)-one (**Ia**) and its 1-phenyl-substituted analog **Ib** were synthesized according to the procedure reported in [7], by reaction of 5,5-dimethyl-2,4-dioxohexanoic acid [8] with *o*-phenylenediamine and *N*-phenyl-*o*-phenylenediamine, respectively, as shown in Scheme 1. Compounds **Ia** and **Ib** are yellow high-melting crystalline substances which are readily soluble in DMF and DMSO, poorly soluble in other common organic solvents, and insoluble in saturated hydrocarbons and water. The IR spectra of **Ia** and **Ib** contain absorption bands due to stretching vibrations of the N^1H group (a sharp peak at 3340 cm^{-1} in the spectrum of **Ia**), N^4H group involved in intramolecular hydrogen bond (a broad band in the region 3130–3150 cm^{-1}), C^2=O amide carbonyl group (1678–1682 cm^{-1}), and pivaloyl carbonyl group involved in intramolecular hydrogen bond (a broad band centered at 1619–1622 cm^{-1}). In the ^1H NMR spectra of quinoxalines **Ia** and **Ib**, recorded from solutions in DMSO-d_6, we observed signals from aromatic protons, a nine-proton singlet from the *tert*-butyl group at δ 1.17–1.18 ppm, a singlet from the exocyclic vinylic proton at δ 6.28–6.33 ppm, a singlet from the N^1H proton at δ 11.91 ppm (**Ia**), and a singlet from the N^4H proton at δ 13.30 ppm; the latter is displaced downfield due to formation of intramolecular hydrogen bond. The doublet signal from the 8-H proton in the quinoxaline ring of compound **Ib** appeared separately from the other aromatic proton signals (δ 6.30 ppm) due to shielding effect produced by π-electron system of the benzene ring on N^1. The spectral parameters of compounds **Ia**

* For communication LVI, see [1].

Scheme 1.



R = H (**a**), Ph (**b**).

and **Ib** indicate that they exist in solution and in the crystalline state as *Z* isomers stabilized by strong intramolecular hydrogen bond between the N^4H proton and side-chain carbonyl oxygen atom, which is typical of structurally related compounds [7].

By reaction of quinoxalines **Ia** and **Ib** with oxalyl chloride in anhydrous benzene (reaction time 1 h) we obtained the corresponding 3-pivaloyl-5-phenylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones **IIa** and **IIb** in almost quantitative yield (Scheme 1). Compounds **IIa** and **IIb** are dark violet (almost black) crystalline substances melting with decomposition at high temperature. They are readily soluble in DMF and DMSO, poorly soluble in other common aprotic organic solvents, and insoluble in saturated hydrocarbons. Pyrroloquinoxalines **IIa** and **IIb** react with alcohols and water; they turn colorless on storage due to hydrolysis by the action of atmospheric moisture. Compounds **IIa** and **IIb** displayed in the IR spectra absorption bands belonging to stretching vibrations of the N^5H group (a narrow peak at 3340 cm^{-1} in the spectrum of **IIa**), lactam carbonyl group (C^1=O, 1760–1763 cm^{-1}), ketone carbonyl group (C^2=O, 1733–1735 cm^{-1}), amide carbonyl group (C^4=O, 1674–1686 cm^{-1}), and pivaloyl carbonyl group (1624–1626 cm^{-1}). The range of carbonyl stretching vibration frequencies, as well as the higher stretching vibration frequency of the lactam carbonyl group compared to the endocyclic ketone carbonyl group, corresponds to published data for monocyclic 1*H*-pyrrole-2,3-diones [9] and isatins [10].

The ^{1}H NMR spectra of solutions of **IIa** and **IIb** in DMSO-d_6 contained signals from aromatic protons, a nine-proton singlet from the *tert*-butyl group at δ 1.13 ppm, and a singlet from the N^5H proton at δ 11.77 ppm (**IIa**). The doublet signal from the 9-H proton is displaced downfield (δ 8.30–8.46 ppm) relative to the other aromatic proton signals as a result of deshielding effect produced by the C^1=O carbonyl group. By contrast, the 6-H signal in the spectrum of compound **IIb** appears in a stronger field (δ 6.36 ppm, d) due to shielding by π-electron system of the benzene ring on N^5.

It is known that 4-alkoxalyl- and 4-aroyl-substituted monocyclic 1*H*-pyrrole-2,3-diones react with *o*-phenylenediamine according to a scheme involving successive nucleophilic attacks on the C^5 carbon atom and carbonyl carbon atom in the acyl group on C^4; as a result, substituted pyrrolo[2,3-*b*][1,4]benzodiazepine-2,3-diones are formed [11, 12]. 4-Aroyl- and 4-hetaroyl-substituted 1*H*-pyrrole-2,3-diones fused to a quinoxaline system, namely 3-aroyl- and 3-hetaroylpyrrolo[1,2-*a*]quinoxaline-1,2,4-(5*H*)-triones react with *o*-phenylenediamine in a similar way to produce 8-aryl-(hetaryl)-9,14-dihydroquinoxalino[1′,2′:1,2]pyrrolo-[2,3-*b*][1,5]benzodiazepine-6,7,15(16*H*)-triones [2, 3]. In continuation of our studies on the transformations of 4-acyl-substituted 1*H*-pyrrole-2,3-diones in reactions with nucleophiles, we examined reactions of 3-pivaloylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones **IIa** and **IIb** with *o*-phenylenediamine. The reactions were

carried out in boiling anhydrous benzene using equimolar amounts of the reactants. After 15–25 min, colorless crystalline products **IIIa** and **IIIb** separated from the reaction mixtures on cooling. However, we failed to unambiguously determine their structure on the basis of the IR and NMR data. X-Ray diffraction study of a single crystal of compound **IIIb** showed that it has the structure of 3-[3,3-dimethyl-2-oxo-1-(3-oxo-3,4-dihydroquinoxalin-2-yl)butyl]-1-phenylquinoxalin-2(1*H*)-one.

Compounds **IIIa** and **IIIb** are colorless crystalline substances with high melting points. They are poorly soluble in common organic solvents, except for DMF and DMSO, and insoluble in water and saturated hydrocarbons. The IR spectra of **IIIa** and **IIIb** contained absorption bands assignable to stretching vibrations of NH (3150–3160 cm^{-1}) and carbonyl groups (1664–1665 cm^{-1}). In the ^1H NMR spectra of these compounds in DMSO-d_6, apart from signals in the aromatic region, we observed a nine-proton singlet from the *tert*-butyl group at δ 1.20–1.22 ppm, a singlet from CH proton at δ 6.42–6.44 ppm, and signals from one (**IIIb**) or two (**IIIa**) NH protons in the region δ 12.52–12.57 ppm. In the spectrum of **IIIb**, the 8-H signal (δ 6.64 ppm, d) was displaced upfield due to shielding by π-electron system of the benzene ring on N^1.

All bond lengths and bond angles in the molecule of compound **IIIb** (Fig. 1) range within the corresponding standard intervals. Interatomic distances in the two quinoxaline fragments are similar; the double $C^2{=}N^2$ (1.295 Å) and $C^4{=}N^3$ bonds (1.303 Å) therein are localized. The quinoxaline ring planes are arranged in a crossed conformation with respect to the C^2–C^3 and C^4–C^3 bonds, and the dihedral angle between them is equal to 75.5°. Molecules **IIIb** in crystal give rise to centrosymmetric dimers formed by strong intermolecular hydrogen bonds N^4–$H^4\cdots O^{2'}$ with the following parameters: $N^4\cdots O^{2'}$ 2.79, $H^4\cdots O^{2'}$ 1.86 Å, $\angle N^4H^4O^{2'}$ 174° (Fig. 2). Presumably, the formation of intermolecular hydrogen bond is responsible for extension of the $C^5{=}O^2$ bond to 1.233 Å. The $C^1{=}O^1$ bond is also extended to 1.239 Å, whereas the $C^{24}{=}O^3$ bond has a standard length (1.199 Å). Probably, the O^1 atom is also involved in hydrogen bonding with crystallization water molecule. The $O^1\cdots O^{29}$ distance equal to 3.17 Å is too large for a strong hydrogen bond; however, the accuracy in the localization of the oxygen atom in the crystallization water molecule is not high due to large thermal vibration amplitude and small number of experimental reflections.

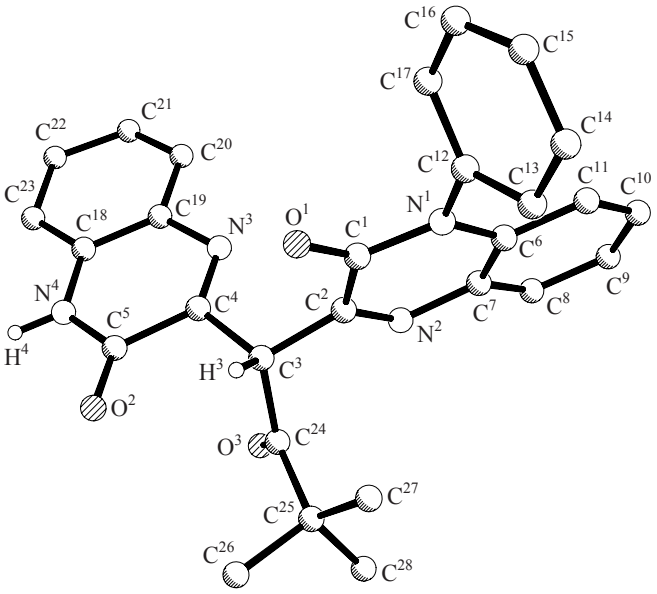


Fig. 1. Structure of the molecule of 3-[3,3-dimethyl-2-oxo-1-(3-oxo-3,4-dihydroquinoxalin-2-yl)butyl]-1-phenylquinoxalin-2(1*H*)-one (**IIIb**) according to the X-ray diffraction data.

Compounds **IIIa** and **IIIb** are likely to be formed via successive attacks by the amino groups of *o*-phenylenediamine on the carbon atoms in positions *1* and *2* of pyrroloquinoxalinetriones **Ia** and **Ib** with intermediate cleavage of the C^1–N^{10} bond. The reaction of 3-pivaloylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones **IIa** and **IIb** with *o*-phenylenediamine follows a different path than that reported for 3-aroyl(hetaroyl)pyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones [2, 3]. Probable reasons are steric hindrances to nucleophilic attack on the pivaloyl carbonyl group, created by the bulky *tert*-butyl group and different electron density distribution in molecules **Ia** and **Ib** due to strong electron-donating effect of the *tert*-butyl group.

It should be noted that the described reaction provides a new example of formation of difficultly accessible bis-quinoxaline heterocyclic systems with functional substituents in both quinoxaline fragments.

EXPERIMENTAL

The IR spectra were recorded in mineral oil on a UR-20 spectrophotometer. The ^1H and ^{13}C NMR spectra were obtained on a Bruker AM-400 spectrometer (400 MHz for ^1H) from solutions in DMSO-d_6 containing tetramethylsilane as internal reference. The purity of the products was checked by thin-layer chromatography on Silufol plates (eluent benzene–ethyl acetate, 5:1; spots were visualized by treatment with iodine vapor or under UV light).

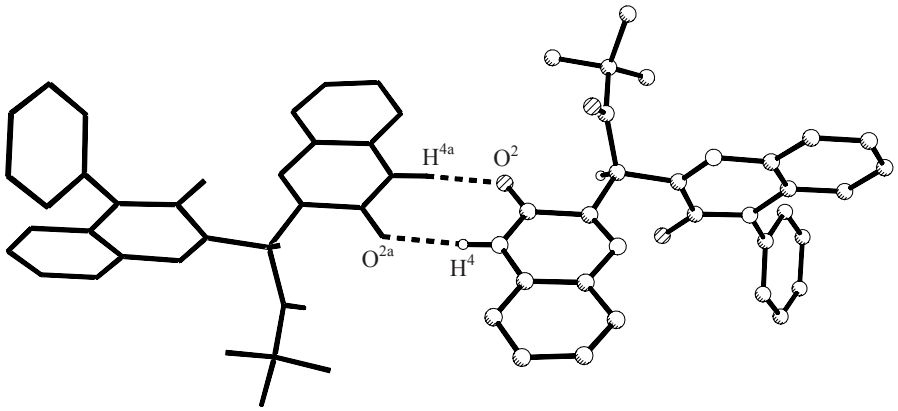


Fig. 2. Fragment of the crystalline structure of 3-[3,3-dimethyl-2-oxo-1-(3-oxo-3,4-dihydroquinoxalin-2-yl)butyl]-1-phenylquinoxalin-2(1*H*)-one (**IIIb**) according to the X-ray diffraction data.

3-[(*Z*)-3,3-Dimethyl-2-oxobutylidene]-3,4-dihydroquinoxalin-2(1*H*)-one (Ia). A suspension of 1.60 g (9.3 mmol) of 5,5-dimethyl-2,4-dioxohexanoic acid and 1.01 g (9.3 mmol) of *o*-phenylenediamine in 40 ml of ethanol was heated for 60 min under reflux. The mixture was cooled, and the precipitate was filtered off and recrystallized from ethanol. Yield 1.63 g (72%), mp 242–243°C. IR spectrum, ν, cm^{-1}: 1622 br (*t*-BuCO), 1682 (C^2=O), 3130 br (N^4–H), 3340 (N^1–H). ^{1}H NMR spectrum, δ, ppm: 1.17 s (9H, CMe_3), 6.28 s (1H, C^3=CH), 7.09–7.43 m (4H, 5-H–8-H), 11.91 s (1-H), 13.30 s (4-H). ^{13}C NMR spectrum, δ_C, ppm: 27.09 (Me), 41.84 (**C**Me_3), 88.23 (C^3=**C**H), 115.12–144.39 (C_{arom}), 155.12 (C^2=O), 205.16 (*t*-Bu**C**O). Found, %: C 68.88; H 6.61; N 11.47. $C_{14}H_{16}N_2O_2$. Calculated, %: C 68.83; H 6.60; N 11.47.

3-[(*Z*)-3,3-Dimethyl-2-oxobutylidene]-1-phenyl-3,4-dihydroquinoxalin-2(1*H*)-one (Ib) was synthesized in a similar way. Yield 2.75 g (86%), mp 158–160°C (from ethanol). IR spectrum, ν, cm^{-1}: 1619 br (*t*-BuC=O), 1678 (C^2=O), 3150 br (N^4–H). ^{1}H NMR spectrum, δ, ppm: 1.18 s (9H, CMe_3), 6.30 d (1H, 8-H, J = 7.6 Hz), 6.33 s (1H, C^3=CH), 6.96–7.65 m (8H, C_6H_5, 5-H, 6-H, 7-H), 13.30 s (4-H). Found, %: C 74.92; H 6.26; N 8.73. $C_{20}H_{20}N_2O_2$. Calculated, %: C 74.98; H 6.29; N 8.74.

3-Pivaloylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-trione (IIa). A solution of 1.00 g (4 mmol) of compound **Ia** and 0.37 ml (4.3 mmol) of oxalyl chloride in 20 ml of anhydrous benzene was heated for 60 min under reflux (until the originally yellow mixture turned dark violet). The mixture was cooled, and the precipitate was filtered off. Yield 1.12 g (92%), mp 242–243°C (decomp., from benzene). IR spectrum, ν, cm^{-1}: 1626 (*t*-BuC=O), 1686 (C^4=O), 1733 (C^2=O), 1760 (C^1=O), 3340 (N–H). ^{1}H NMR spectrum, δ, ppm: 1.13 s (9H, CMe_3), 7.07–7.19 m (3H, H_{arom}), 8.30 d (1H, 9-H, J = 6.9 Hz), 11.77 s (1H, NH). Found, %: C 64.45; H 4.74; N 9.35. $C_{16}H_{14}N_2O_2$. Calculated, %: C 64.42; H 4.73; N 9.39.

5-Phenyl-3-pivaloylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-trione (IIb) was synthesized in a similar way. Yield 2.29 g (98%), mp 233–235°C (decomp., from benzene). IR spectrum, ν, cm^{-1}: 1624 (*t*-BuC=O), 1674 (C^4=O), 1735 (C^2=O), 1763 (C^1=O). ^{1}H NMR spectrum, δ, ppm: 1.13 s (9H, CMe_3), 6.36 d (1H, 6-H, J = 8.2 Hz), 7.07–7.84 m (7H, H_{arom}), 8.46 d (1H, 9-H, J = 8.2 Hz). Found, %: C 70.53; H 4.86; N 7.42. $C_{22}H_{18}N_2O_4$. Calculated, %: C 70.58; H 4.85; N 7.48.

3,3′-(3,3-Dimethyl-2-oxobutane-1,1-diyl)di[quinoxalin-2(1*H*)-one] (IIIa). A solution of 0.36 g (3.4 mmol) of *o*-phenylenediamine in 30 ml of anhydrous benzene was added to 1.00 g (3.4 mmol) of compound **IIa** in 40 ml of anhydrous benzene, and the mixture was heated for 15 min under reflux until the original dark violet color disappeared. The mixture was cooled, and the precipitate was filtered off. Yield 1.08 g (83%), mp 279–280°C (from propan-2-ol). IR spectrum, ν, cm^{-1}: 1664 (C=O, *t*-BuC=O), 3160 (N–H). ^{1}H NMR spectrum, δ, ppm: 1.20 s (9H, CMe_3), 6.42 s (1H,), 7.26–7.63 m (8H, H_{arom}), 12.52 br.s (2H, NH). Found, %: C 68.03; H 5.17; N 14.42. $C_{22}H_{20}N_4O_3$. Calculated, %: C 68.03; H 5.19; N 14.42.

3-[3,3-Dimethyl-2-oxo-1-(3-oxo-3,4-dihydroquinoxalin-2-yl)butyl]-1-phenylquinoxalin-2(1*H*)-one (IIIb) was synthesized in a similar way. Yield 0.59 g (92%), mp 198–200°C (from acetonitrile). IR spectrum, ν, cm^{-1}: 1665 (C=O, *t*-BuC=O), 3150 (N–H).

^{1}H NMR spectrum, δ, ppm: 1.22 s (9H, CMe_3), 6.44 s (1H), 6.64 d (1H, 8-H, J = 7.4 Hz), 7.29–7.73 m (12H, H_{arom}), 12.57 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 26.88 (Me), 44.44 (**C**Me_3), 54.00 (CH), 115.25–135.37 (C_{arom}), 153.00 ($C^{3'}$=O), 153.69 (C^2=O), 157.61 (C^3), 157.87 ($C^{2'}$), 209.52 (*t*-BuCO). Found, %: C 72.41; H 5.28; N 12.00. $C_{28}H_{24}N_4O_3$. Calculated, %: C 72.40; H 5.21; N 12.06.

X-Ray analysis of compound IIIb. Triclinic crystals, $C_{28}H_{24}N_4O_3 \cdot H_2O$, with the following unit cell parameters: a = 13.640(3), b = 11.573(2), c = 8.540(2) Å; α = 73.94(3), β = 88.96(3), γ = 83.97(3)°; V = 1288.1(5) Å^3; M 482.53; d_{calc} = 1.244 g/cm^3; Z = 2; space group P-1. The unit cell parameters and the set of experimental reflections were measured on a Kuma Diffraction KM-4 automatic four-circle diffractometer (χ-geometry, monochromatized MoK_α irradiation, ω/2Θ scanning, 2Θ ≤ 50.2°). The crystals were weakly reflecting. Among 4226 independent reflections, only 1071 were with $I \geq 2\sigma(I)$ (R_{int} = 0.0787). No correction for absorption was introduced (μ = 0.085 mm^{-1}). The structure was solved by the direct method using SIR92 program [13], followed by a series of calculations of electron density maps. The positions of hydrogen atoms (except for those in the crystallization water molecule, which were not localized) were determined from the geometry considerations, and only their positional parameters were refined by the least-squares procedure. Full-matrix least-squares refinement of the positions of non-hydrogen atoms was performed in anisotropic approximation using SHELXL 97 software [14] and was complete at R_1 = 0.0840, wR_2 = 0.2026 [for reflections with $I \geq 2\sigma(I)$]; goodness of fit 0.800.

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 07-03-960366).

REFERENCES

1. Racheva, N.L., Belova, M.A., and Maslivets, A.N., *Russ. J. Org. Chem*., 2008, vol. 44, p. 582.
2. Tolmacheva, I.A., Mashevskaya, I.V., and Maslivets, A.N., *Russ. J. Org. Chem*., 2002, vol. 38, p. 281.
3. Maslivets, A.N., Mashevskaya, I.V., Kol'tsova, S.V., Duvalov, A.V., and Feshin, V.P., *Russ. J. Org. Chem*., 2002, vol. 38, p. 738.
4. Mashevskaya, I.V., Kol'tsova, S.V., Duvalov, A.V., and Maslivets, A.N., *Khim. Geterotsikl. Soedin*., 2000, p. 1281.
5. Maslivets, A.N. and Bozdyreva, K.S., *Khim. Geterotsikl. Soedin*., 2002, p. 1735.
6. Bozdyreva, K.S., Maslivets, A.N., and Aliev, Z.G., *Mendeleev Commun*., 2005, p. 163.
7. Bozdyreva, K.S., Smirnova, I.V., and Maslivets, A.N., *Russ. J. Org. Chem*., 2005, vol. 41, p. 1081.
8. Berezina, E.S., Koz'minykh, V.O., Idigov, N.M., Shirinkina, S.S., Koz'minykh, E.N., Makhmudov, R.R., and Bukanova, E.V., *Russ. J. Org. Chem*., 2001, vol. 37, p. 539.
9. Andreichikov, Yu.S., Maslivets, A.N., Smirnova, L.I., Krasnykh, O.P., Kozlov, A.P., and Perevozchikov, L.A., *Zh. Org. Khim*., 1987, vol. 23, p. 1534.
10. Zhungietu, R.I. and Rekhter, M.A., *Izatin i ego proizvodnye* (Isatin and Its Derivatives), Kishinev: Shtiintsa, 1977, p. 228.
11. Terpetschnig, E., Ott, W., Kollenz, G., Peters, K., Peters, E.-M., and von Schnering, H.G., *Monatsh. Chem*., 1988, vol. 119, p. 367.
12. Maslivets, A.N., Smirnova, L.I., Ivanenko, O.I., and Andreichikov, Yu.S., *Russ. J. Org. Chem*., 1995, vol. 31, p. 563.
13. Altomare, A., Cascarano, G., Giacovazzo, C., and Gualardi, A., *J. Appl. Crystallogr*., 1993, vol. 26, p. 343.
14. Sheldrick, G.M., *SHELXL 97. Programs for Crystal Structure Analysis*, Gottingen, Germany: Univ. of Gottingen, 1998, p. 2332.