ISSN 1070-4280, Russian Journal of Organic Chemistry, 2010, Vol. 46, No. 2, pp. 255–259. © Pleiades Publishing, Ltd., 2010.
Original Russian Text © P.S. Silaichev, M.V. Dmitriev, Z.G. Aliev, A.N. Maslivets, 2009, published in Zhurnal Organicheskoi Khimii, 2010, Vol. 46, No. 2, pp. 261–264.

Five-membered 2,3-Dioxoheterocycles: LXVII.* Pyrroledione–Pyrroledion Recyclization of Isopropyl 2-(1-Aryl-4,5-dioxo-2-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)-2-oxoacetates under the Action of Arylamines. Crystal and Molecular Structure of (*Z*)-Isopropyl 2-Hydroxy-4,5-dioxo-1-phenyl-3-[phenyl(phenylamino)-methylene]pyrrolidine-2-carboxylate

P. S. Silaichev[a], M. V. Dmitriev[a], Z. G. Aliev[b], and A. N. Maslivets[a]

[a]*Perm State University, Perm, 614990 Russia*
e-mail: koh2@psu.ru
[b]*Institute of Problems of Chemical Physics, Russian Academy of Sciences, Chernogolovka, Russia*

Received April 6, 20

Abstract—Reactions of isopropyl 2-(1-aryl-4,5-dioxo-2-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)-2-oxoacetates with aromatic amines involve a pyrroledione- pyrroledione recyclization to form isopropyl 1-aryl-2-hydroxy-4,5-dioxo-3-[phenyl(arylamino)methylene]pyrrolidine-2-carboxylates. The crystal and molecular structure of (*Z*)-isopropyl 2-hydroxy-4,5-dioxo-1-phenyl-3-[phenyl(phenylamino)methylene]pyrrolidine-2-carboxylate was proved by XRD analysis.

DOI: 10.1134/S1070428010020193

The reaction of 1-aryl-4-aroyl-5-methoxycarbonyl-1*H*-pyrrole-2,3-diones with arylamines was shown to result in the formation of the products of primary amino group addition to the carbon atom in the position *5* of pyrrolediones, substituted 5-arylamino-3-hydroxy-1*H*-pyrrol-2(5*H*)-ones [2, 3].

In extension of the research on the nucleophilic recyclization of 1*H*-pyrrole-2,3-diones we studied the reactions of the representatives of another class of monocyclic pyrrolediones, isopropyl 2-(1-aryl-4,5-dioxo-2-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)-2-oxoacetates **Ia–Ic** [4] with primary amines **IIa–IId**.

The reaction of compounds **Ia–Ic** with amines **IIa–IId** in a ratio 1:1 performed by keeping the reagents solution in an anhydrous chloroform at room temperature over 8–10 h provided in good yield isopropyl 1-aryl-2-hydroxy-4,5-dioxo-3-[phenyl(arylamino)methylene]-pyrrolidine-2-carboxylates **IIIa–IIIj**. The structure of compound **IIIa** was proved by XRD analysis.

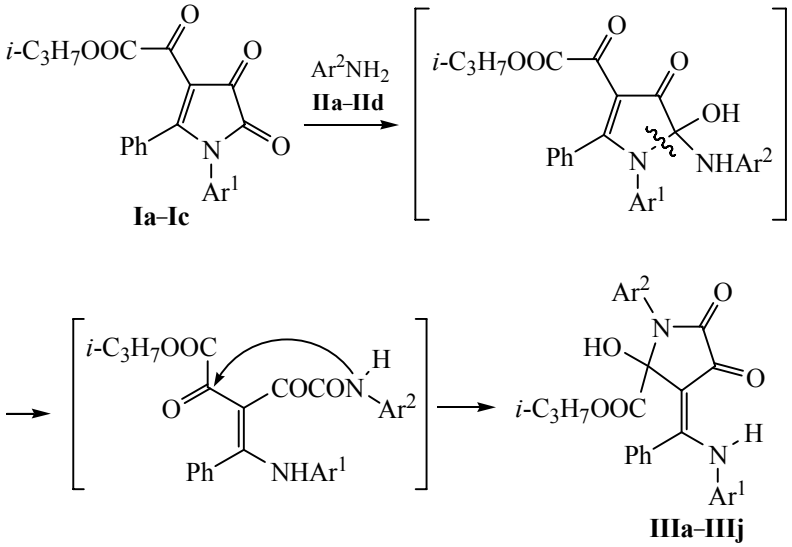
Compounds **IIIa–IIIj** are bright yellow or orange high-melting crystalline substances, readily soluble in DMSO, DMF, and common organic solvents, insoluble in alkanes and water.

The IR spectra of compounds **IIIa–IIIj** contain the absorption bands of the stretching vibrations of OH and NH group as a broad band in the region 3237–3441 cm^{-1}, of a lactam carbonyl group C^5=O at 1722–1755 cm^{-1}, of an ester carbonyl group in the region 1719–1728 cm^{-1}, and of a ketone carbonyl group involved into the formation of an intramolecular hydrogen bond as a broad band at 1609–1619 cm^{-1}.

In the ^{1}H NMR spectra of compounds **IIIa–IIIj** alongside the signals of the protons of aromatic rings and groups attached thereto appear two doublets of methyl

*For Communication LXVI, see [1].

Scheme 1.



Ar^1 = Ph (**Ia, IIIa, IIIe, IIIh**), C_6H_4Me-4 (**Ib, IIIb, IIIf, IIIi**), C_6H_4OMe-4 (**Ic, IIIc, IIId, IIIg, IIIj**); Ar^2 = Ph (**IIa, IIIa–IIIc**), C_6H_4Me-4 (**IIb, IIId**), C_6H_4OMe-4 (**IIc, IIIe–IIIg**), C_6H_4Br-4 (**IId, IIIh–IIIj**).

groups of the isopropoxycarbonyl substituent at 0.73–0.79 and 0.82–0.85 ppm, a multiplet of the methine proton from the same moiety in the region 4.32–4.34 ppm, and abroadened singlet of the NH group proton (12.62–12.68 ppm). The proton signal of the OH group is located in the region of the aromatic protons signals.

The ^{13}C NMR spectra of compounds **IIIc, IIIe**, and **IIIg** contain characteristic signals in the region 167.17–167.29 and 178.86–179.80 ppm from the carbon atoms of the lactam and ketone carbonyl groups of the pyrroledione ring, and also the signal from the carbon atom in the position *2* (87.62–87.78 ppm). The location of the carbon atoms of the pyrroledione ring is well consistent with the data published for 1*H*-pyrrole-2,3-diones and 5-hydroxy-2,3,4,5-tetrahydro-1*H*-pyrrole-2,3-diones [5].

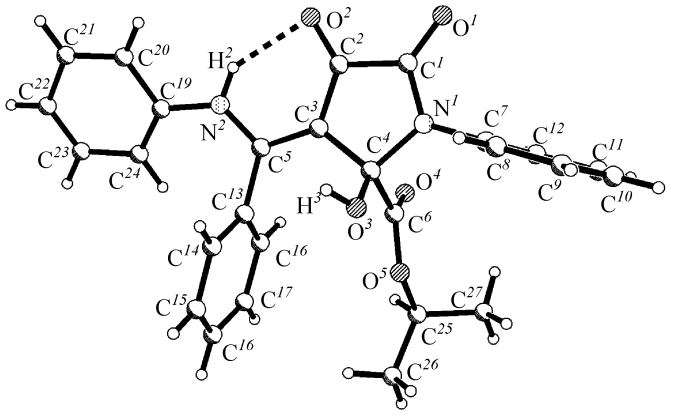


Fig. 1. Molecular structure of (*Z*)-isopropyl 2-hydroxy-4,5-dioxo-1-phenyl-3-[phenyl(phenylamino)methylene]pyrrolidine-2-carboxylate (**IIIa**).

The final conclusion on the structure of compounds synthesized was done based on the XRD analysis on a single crystal of compound **IIIa** (Fig.. 1).

Compound **IIIa** crystallized with a molecule of water in an equimolar ratio. The molecule is stabilized in the crystal by the intramolecular hydrogen bond $N^2–H^{2\cdots}O^2$ 2.756(4) Å forming a flat "bicycle". The longer bond of the carbonyl group $C^2=O^2$ (1.238 Å) compared to the bond $C^1=O^1$ (1.224 Å) indicates the involvement of the group $C^2=O^2$ in the intramolecular hydrogen bond and the existence of the **IIIa** molecule in the crystalline state in the enaminoketone form. All bond distances in the five-membered ring and in its substituents are virtually identical to analogous bond lengths in the similar in structure molecule of (*Z*)-3-(1-benzyl-2-hydroxy-4,5-dioxo-2-*p*-tolyltetrahydropyrrol-3-idene)-3,4-dihydro-2*H*-1,4-benzoxazin-2-one [6]. The planes of the phenyl rings at the atoms N^1 and C^5 are orthogonal to each other and to the plane of the "bicycle". The orientation of the phenylamine fragment is characterized by the torsion angle $C^5N^2C^{19}C^{20}$ of 153.8 deg. In the crystal **IIIa**

molecules are connected through the water molecule into dimeric associates (Fig. 2).

Unlike [6] where the formation of the analogous dimeric associate was shown to involve two oxygen atoms of the carbonyl groups of the pyrroledione ring, in this study the water molecule is connected by the hydrogen bond with a carbonyl (O^6–H···O^1) and a hydroxy (O^6···H^3–O^3) groups. Dimeric associates multiplied by the glide reflection plane are connected by a weaker hydrogen bond O^6–H···O^1 into an infinite chain. The parameters of the hydrogen bonds in the crystal are given below.

D–H···A	*d*(D–H), Å	*d*(H···A), Å	*d*(D···A), Å	Angle DHA, deg
O^3–H^3···O^6	0.83(4)	1.90(4)	2.733(4)	177(4)
N^2–H^2···O^2	0.84(4)	2.05(4)	2.756(4)	141(3)
O^6–H^{6A}···O^{1*}	0.80(6)	2.03(6)	2.822(4)	171(6)
O^6–H^{6B}···O^{4**}	0.70(5)	2.29(5)	2.939(4)	156(5)

The formation of compounds **IIIa–IIIj** occurs apparently by initial addition of the primary amino group of arylamines **IIa–IId** to the carbon atom in the position *2* of pyrroledione **Ia–Ic**, the cleavage of the pyrroledione ring at the N^1–C^2 bond and the subsequent closure of a "new" pyrroledione ring by intramolecular nucleophilic addition of the NH group of the oxamoyl fragment to the keto carbonyl groyp of the isopropoxalyl substituent.

The reaction described is an example of pyrrolediones recyclization under the action of anilines, namely, the cleavage of a pyrroledione ring with the closure of a "new" pyrroledione ring.

EXPERIMENTAL

IR spectra of compounds obtained were recorded on a spectrophotometer FSM-1201from mulls in mineral oil. ^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker AM-400 (operating frequency 400 MHz) in DMSO-d_6, internal reference TMS. The homogeneity of compounds synthesized was proved by TLC on Silufol plates, eluates benzene–ethyl acetate, 5 : 1, ethyl acetate. Elemental analysis was performed using samples preliminary dried at 100–105°C.

(*Z*)-Isopropyl 2-hydroxy-4,5-dioxo-1-phenyl-3-[phenyl(phenylamino)methylene]pyrrolidine-2-carboxylate (IIIa). A solution of 1.0 mmol of compound

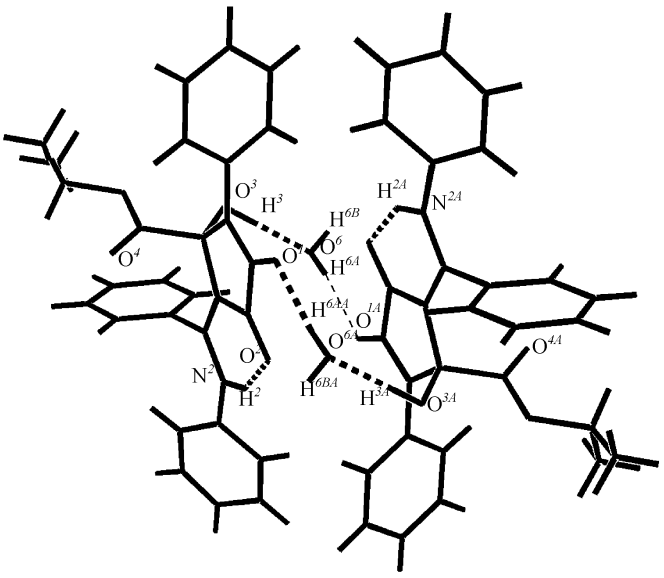


Fig. 2. Dimeric associate of molecules of compound **IIIa** in the crystal.

Ia and 1.0 mmol of aniline (**IIa**) in 15 ml of anhydrous chloroform was maintained at 20°C for 8 h, then the solvent was removed, and the residue was ground with ethanol. Yield 83%, mp 182–183°C (from toluene). IR spectrum, ν, cm^{-1}: 3252 br (OH, NH), 1754 (C^5=O), 1723 (COO), 1614 (C^4=O in internal H-bond). ^{1}H NMR spectrum, δ, ppm: 0.73 d (3H, Me, *J* 6.4 Hz), 0.82 d (3H, Me, *J* 6.4 Hz), 4.32 m (1H, OCH, *J* 6.4 Hz), 6.88–7.43 group of signals (16H, 3Ph, OH), 12.67 br.s (1H, NH). Found, %: C 74.04; H 5.27; N 6.24. $C_{27}H_{24}N_2O_5$. Calculated, %: C 74.04; H 5.30; N 6.14.

Compounds **IIIb–IIIj** were prepared similarly.

(*Z*)-Isopropyl 2-hydroxy-3-[4-methylphenylamino(phenyl)methylene]-4,5-dioxo-1-phenylpyrrolidine-2-carboxylate (IIIb). Yield 79%, mp 192–193°C (from ethyl acetate). IR spectrum, ν, cm^{-1}: 3246 br (OH, NH), 1755 (C^5=O), 1724 (COO), 1616 (C^4=O in internal H-bond). ^{1}H NMR spectrum, δ, ppm: 0.73 d (3H, Me, *J* 6.4 Hz), 0.82 d (3H, Me, *J* 6.4 Hz), 2.18 s (3H, Me), 4.32 m (1H, OCH, *J* 6.4 Hz), 6.77–7.42 group of signals (15H, 2Ph + C_6H_4 + OH), 12.67 br.s (1H, NH). Found, %: C 71.49; H 5.63; N 6.02. $C_{28}H_{26}N_2O_5$. Calculated, %: C 71.47; H 5.57; N 5.95.

(*Z*)-Isopropyl 2-hydroxy-3-[4-methoxyphenylamino(phenyl)methylene]-4,5-dioxo-1-phenylpirrolidine-2-carboxylate (IIIc). Yield 85%, mp 189–190°C (from toluene). IR spectrum, ν, cm^{-1}: 3237 br (OH, NH), 1755 (C^5=O), 1726 (COO), 1609 (C^4=O in internal H-bond). ^{1}H NMR spectrum, δ, ppm: 0.73 d (3H, Me,

J 6.4 Hz), 0.82 d (3H, Me, *J* 6.4 Hz), 3.66 s (OMe), 4.32 m (1H, OCH, *J* 6.4 Hz), 6.72–7.40 group of signals (15H, 2Ph + C_6H_4 + OH), 12.66 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 20.81 (Me), 55.12 (OMe), 69.27 (OCH), 87.78 (C^2), 108.38 (C^3), 113.79–161.60 (C^{Ar} + C^3=C–NH), 161.89 (COO), 167.17 (C^5), 178.86 (C^4). Found, %: C 69.24; H 5.43; N 5.71. $C_{28}H_{26}N_2O_6$. Calculated, %: C 69.12; H 5.39; N 5.76.

(*Z*)-Isopropyl 2-hydroxy-1-(4-methylphenyl)-3-[4-methoxyphenylamino(phenyl)-methylene]-4,5-dioxopyrrolidine-2-carboxylate (IIId). Yield 74%, mp 187–189°C (from toluene). IR spectrum, ν, cm^{-1}: 3237 br (OH, NH), 1753 (C^5=O), 1721 (COO), 1619 (C^4=O in internal H-bond). ^1H NMR spectrum, δ, ppm: 0.76 d (3H, Me, *J* 6.4 Hz), 0.85 d (3H, Me, *J* 6.4 Hz), 2.28 C (3H, Me), 3.66 C (OMe), 4.33 m (1H, OCH, *J* 6.4 Hz), 6.71–7.40 group of signals (14H, Ph + $2C_6H_4$ + OH), 12.64 br.s (1H, NH). Found, %: C 69.54; H 5.52; N 5.56. $C_{29}H_{28}N_2O_6$. Calculated, %: C 69.59; H 5.64; N 5.60.

(*Z*)-Isopropyl 2-hydroxy-1-(4-methoxyphenyl)-4,5-dioxo-3-[phenyl(phenylamino)methylene]-pyrrolidine-2-carboxylate (IIIe). Yield 79%, mp 192–193°C (from toluene). IR spectrum, ν, cm^{-1}: 3261 br (OH, NH), 1753 (C^5=O), 1722 (COO), 1613 (C^4=O in internal H-bond). ^1H NMR spectrum, δ, ppm: 0.79 d (3H, Me, *J* 6.4 Hz), 0.85 d (3H, Me, *J* 6.4 Hz), 3.74 s (OMe), 4.34 m (1H, OCH, *J* 6.4 Hz), 6.88–7.43 group of signals (15H, 2Ph + C_6H_4 + OH), 12.67 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 20.86 (Me), 20.92 (Me), 55.20 (OMe), 69.32 (OCH), 87.62 (C^2), 108.80 (C^3), 113.80–160.90 (C^{Ar} + C^3=C–NH), 161.71 (COO), 167.17 (C^5), 179.80 (C^4). Found, %: C 69.17; H 5.43; N 5.72. $C_{28}H_{26}N_2O_5$. Calculated, %: C 69.12; H 5.39; N 5.76.

(*Z*)-Isopropyl 2-hydroxy-1-(4-methoxyphenyl)-3-[4-methylphenylamino(phenyl)methylene]-4,5-dioxopyrrolidine-2-carboxylate (IIIf). Yield 80%, mp 195–196°C (from toluene). IR spectrum, ν, cm^{-1}: 3441 br (OH, NH), 1722 (C^5=O, COO), 1618 (C^4=O in internal H-bond). ^1H NMR spectrum, δ, ppm: 0.79 d (3H, Me, *J* 6.4 Hz), 0.85 d (3H, Me, *J* 6.4 Hz), 2.18 s (3H, Me), 3.74 s (OMe), 4.34 m (1H, OCH, *J* 6.4 Hz), 6.75–7.42 group of signals (14H, Ph + $2C_6H_4$ + OH), 12.64 br.s (1H, NH). Found, %: C 69.55; H 5.52; N 5.73. $C_{29}H_{28}N_2O_6$. Calculated, %: C 69.59; H 5.64; N 5.60.

(*Z*)-Isopropyl 2-hydroxy-1-(4-methoxyphenyl)-3-[4-methoxyphenylamino(phenyl)methylene]-4,5-dioxopyrrolidine-2-carboxylate (IIIg). Yield 79%, mp 195–196°C (from toluene). IR spectrum, ν, cm^{-1}: 3242 br (OH, NH), 1752 (C^5=O), 1719 (COO), 1612 (C^4=O in internal H-bond). ^1H NMR spectrum, δ, ppm: 0.79 d (3H, Me, *J* 6.4 Hz), 0.85 d (3H, Me, *J* 6.4 Hz), 3.66 s (OMe), 3.74 s (OMe), 4.34 m (1H, OCH, *J* 6.4 Hz), 6.75–7.44 group of signals (14H, Ph + $2C_6H_4$ + OH), 12.62 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 20.88 (Me), 20.91 (Me), 55.12 (OMe), 55.19 (OMe), 69.27 (OOCH), 87.67 (C^2), 108.35 (C^3), 113.77–161.41 (C^{Ar} + C^3=C–NH), 161.98 (COO), 167.29 (C^5), 179.26 (C^4). Found, %: C 67.31; H 5.37; N 5.35. $C_{29}H_{28}N_2O_7$. Calculated, %: C 67.43; H 5.46; N 5.42.

(*Z*)-Isopropyl 1-(4-bromophenyl)-2-hydroxy-4,5-dioxo-3-[phenyl(phenylamino)methylene]pyrrolidine-2-carboxylate (IIIh). Yield 88%, mp 183–184°C (ethyl acetate). IR spectrum, ν, cm^{-1}: 3264 br (OH, NH), 1753 (C^5=O), 1725 (COO), 1611 (C^4=O in internal H-bond). ^1H NMR spectrum, δ, ppm: 0.73 d (3H, Me, *J* 6.4 Hz), 0.85 d (3H, Me, *J* 6.4 Hz), 4.33 m (1H, OCH, *J* 6.4 Hz), 6.83–7.62 group of signals (15H, 2Ph + C_6H_4 + OH), 12.68 br.s (1H, NH). Found, %: C 60.65; H 4.35; N 5.23. $C_{27}H_{23}BrN_2O_5$. Calculated, %: C 60.57; H 4.33; N 5.23.

(*Z*)-Isopropyl 1-(4-bromophenyl)-2-hydroxy-3-[4-methylphenylamino(phenyl)methylene]-4,5-dioxopyrrolidine-2-carboxylate (IIIi). Yield 85%, mp 193–194°C (from toluene). IR spectrum, ν, cm^{-1}: 3255 br (OH, NH), 1754 (C^5=O), 1728 (COO), 1619 (C^4=O in internal H-bond). ^1H NMR spectrum, δ, ppm: 0.73 d (3H, Me, *J* 6.4 Hz), 0.85 d (3H, Me, *J* 6.4 Hz), 2.18 s (3H, Me), 4.33 m (1H, OCH, *J* 6.4 Hz), 6.68–7.62 group of signals (14H, Ph + $2C_6H_4$ + OH), 12.67 br.s (1H, NH). Found, %: C 61.12; H 4.49; N 5.07. $C_{28}H_{25}BrN_2O_5$. Calculated, %: C 61.21; H 4.59; N 5.10.

(*Z*)-Isopropyl 1-(4-bromophenyl)-2-hydroxy-4,5-dioxo-3-[4-methoxyphenylamino(phenyl)methylene]pyrrolidine-2-carboxylate (IIIj). Yield 73%, mp 190–191°C (from toluene). IR spectrum, ν, cm^{-1}: 3269 br (OH, NH), 1750 (C^5=O), 1720 (COO), 1612 (C^4=O in internal H-bond). ^1H NMR spectrum, δ, ppm: 0.73 d (3H, Me, *J* 6.4 Hz), 0.85 d (3H, Me, *J* 6.4 Hz), 3.66 s (OMe), 4.34 m (1H, OCH, *J* 6.4 Hz), 6.72–7.62 group of signals (14H, Ph + $2C_6H_4$ + OH), 12.68 br.s (1H, NH). Found, %: C 59.40; H 4.37; N 4.92. $C_{28}H_{25}BrN_2O_6$. Calculated, %: C 59.48; H 4.46; N 4.95.

X-ray diffraction analysis of compound IIIa. Yellow clear edged crystals $C_{27}H_{24}N_2O_5 \cdot H_2O$ belong to monoclinic crystal system: *a* 21.763(5), *b* 13.452(3), *c* 16.622(4) Å, β 96.46(2) deg, *V* 4835.3(19) $Å^3$, *M* 474.50, d_{calc} 1.304 g/cm^3, *Z* 8, space group *C*2/C. The set of

experimental reflections was obtained on an automatic four-circle diffractometer QM-4 of χ-geometry by the method of ω/2Θ scanning on monochromated MoK_α-radiation. $2\Theta_{max}$ 49.98° (86.6%). Overall measured independent reflections 3677 (R_{int} 0.0411) among them 2425 with $I \le 2\sigma(I)$. No correction for extinction was used (μ 0.093 mm^{-1}). The structure was solved by the direct method by the program SIR92 [7] followed by a series of calculations of electron density maps. The hydrogen atoms of the hydroxy and amino groups and of water molecule were localized from the difference synthesis. The other hydrogen atoms were located geometrically. The full-matrix anisotropic refinement of nonhydrogen atoms by least-squares method was performed using SHELXL-97 program [8, 9] and was completed at R_1 0.0647 and wR_2 0.1765 for 2425 reflections with $I \le 2\sigma(I)$. *GOOF* 0.992.

The study was carried out under a financial support of the Russian Foundation for Basic Research (grants nos. 07-03-96036, 08-03-01032).

REFERENCES

1. Khalturina, V.V., Shklyaev, Yu.V., Aliev, Z.G., and Maslivets, A.N., *Zh. Org. Khim.,* 2009, vol. 45, p. 1535.
2. Maslivets, A.N., Smirnova, L.I., and Andreichikov, Yu.S., *Zh. Org. Khim.,* 1989, vol. 25, p. 1748.
3. Maslivets, A.N., Smirnova, L.I., and Andreichikov, Yu.S., *Zh. Org. Khim.,* 1992, vol. 28, p. 2141.
4. Maslivets, A.N., Smirnova, L.I., Ivanenko, O.I., and Andreichikov, Yu.S., *Zh. Org. Khim.,* 1995, vol. 31, p. 610.
5. Sano, T., Horiguchi, Y., and Tsuda, Y., *Chem. Pharm. Bull*., 1985, vol. 33, p. 110.
6. Aliev, Z.G., Maslivets, A.N., Mashevskaya, I.V., Andreichikov, Yu.S., and Atovmyan, L.O., *Izv. Akad. Nauk, Ser. Khim.,* 1997, p. 566.
7. Allen, F.H., Kennard, O., Watson, D.G., Brammer, L., Orpen, G., and Taylor, R., *J. Chem. Soc., Perkin Trans. 2,* 1987, vol. 12, p. 1.
8. Altomare, A., Cascarano, G., Giacovazzo, C., and Gualardi, A., *J. Appl. Cryst*., 1993, vol. 26, p. 343.
9. Sheldrick, G.M., *SHELX 97. Programs for Crystal Structure Analysis,* University of Gottingen, Germany, 1998, p. 2332.