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Acylation of the Enamino Tautomer of 2-Azaspiro[4.5]deca-1,6,9-trien-8-ones with 5-Arylfuran-2,3-diones. Crystal and Molecular Structure of (2*Z*,5*Z*)-3-Hydroxy-5-(6,9-dimethoxy-3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)-1-phenylpent-2-ene-1,4-dione

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Abstract—5-Arylfuran-2,3-diones reacted with heterocyclic enamines of the 2-azaspiro[4.5]deca-1,6,9-trien-8-one series to give products of β-CH-acylation of the enamino fragment. The structure of (2*Z*,5*Z*)-3-hydroxy-5-(6,9-dimethoxy-3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)-1-phenylpent-2-ene-1,4-dione was proved by X ray analysis.

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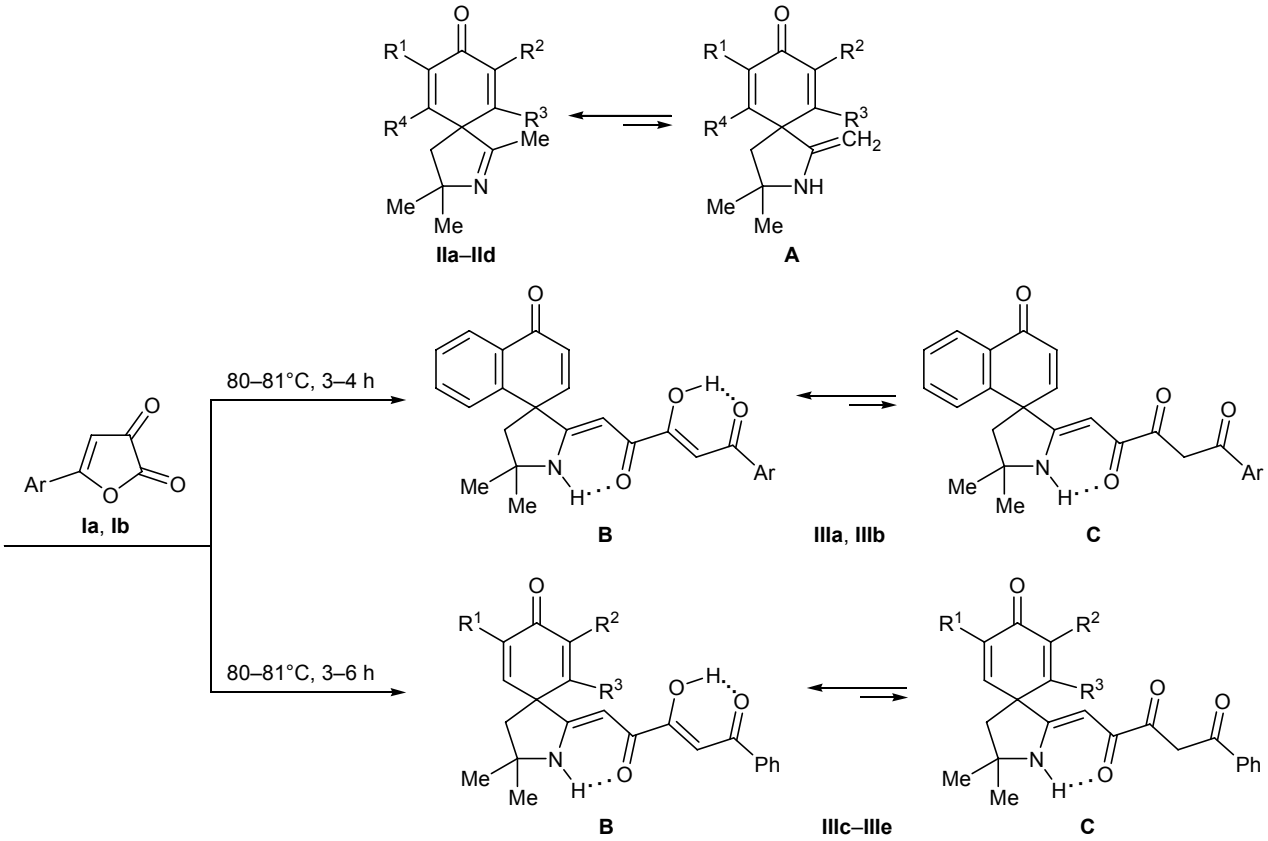
Thermal decarbonylation of 5-arylfuran-2,3-diones generates aroylketenes capable of reacting with active dienophiles according to the Diels–Alder pattern [1, 2] and acylating weak nucleophiles with formation of aroylacetyl derivatives [1, 3]. On the other hand, furandiones themselves can react with nucleophiles to produce aroylpyruvoyl derivatives at a temperature below that required for generation of aroylketenes [1, 4]. We previously showed that some heterocyclic enamines of the 1-methyl-3,4-dihydroisoquinoline, 1-methyl-2-azaspiro[4.5]deca-1,6,9-trien-8-one, and 2-methylidene-1,3,3-trimethyl-2,3-dihydro-1*H*-indole (Fisher's base) series can be acylated with 5-arylfuran-2,3-diones to give the corresponding aroylpyruvoyl derivatives [5–7]. In continuation of our studies on the reactions of 5-arylfuran-2,3-diones with spirans of the 2-azaspiro-[4.5]deca-1,6,9-trien-8-one series in the present work we examined how additional substituents in positions *3* and *6* of the latter affect the direction of their reaction with the former.

5-Arylfuran-2,3-diones **Ia** and **Ib** reacted with 2-azaspiro[4.5]deca-1,6,9-trien-8-ones **IIa**–**IId** [8–10] at a molar ratio of 1:1 on heating in boiling benzene (3–6 h, TLC monitoring) to afford (2*Z*,5*Z*)-1-aryl-3-hydroxy-5-(5′,5′-dimethyl-4-oxo-2′*H*,4*H*-spiro[naphthalene-1,3′-pyrrolidin]-2′-ylidene)pent-2-ene-1,4-diones **IIIa** and **IIIb** and substituted (2*Z*,5*Z*)-3-hydroxy-5-(3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)-1-phenylpent-2-ene-1,4-diones **IIIc**–**IIIe** (Scheme 1). The structure of compound **IIIe** was confirmed by X-ray analysis.

Compounds **IIIa**–**IIIe** were isolated as light yellow (almost colorless) high-melting crystalline substances which were readily soluble in DMSO and DMF, poorly soluble in alcohols, ethers, and haloalkanes, and insoluble in alkanes and water. They showed a positive test (cherry color) for enolic hydroxy group on treatment with an alcoholic solution of iron(III) chloride.

The IR spectra of **IIIa**–**IIIe** contained absorption bands due to stretching vibrations of enolic hydroxy group and NH group involved in intramolecular hydrogen bonds (broad band at 3150–3261 cm^{-1}), ketone carbonyl group (C^4=O in **IIIa**, **IIIb** or C^8=O in **IIIc**–**IIIe**; 1660–1664 cm^{-1}), and carbonyl groups in posi-

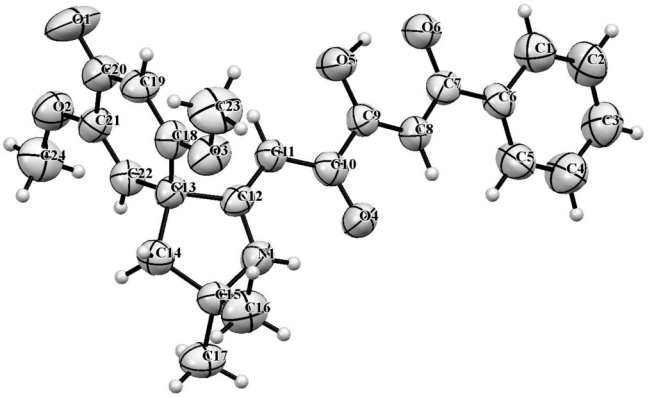
Scheme 1.



I, Ar = Ph (**a**), 4-MeC$_6$H$_4$ (**b**); **II**, R^{1}R^4 = benzo, R^2 = R^3 = H (**a**); R^1 = R^2 = Me, R^3 = R^4 = H (**b**); R^1 = MeO, R^2 = R^4 = H, R^3 = Me (**c**); R^1 = R^3 = MeO, R^2 = R^4 = H (**d**); **III**, Ar = Ph (**a**), 4-MeC$_6$H$_4$ (**b**); R^1 = R^2 = Me, R^3 = H (**c**); R^1 = MeO, R^2 = H, R^3 = Me (**d**); R^1 = R^3 = MeO, R^2 = H (**e**).

tions *1* and *4* of the side chain (H-bonded; broad band at 1595–1611 cm^{-1}).

Compounds **IIIa**–**IIIe** displayed in the ^{1}H NMR spectra (DMSO-d_6) signals from aromatic substituents,



Structure of the molecule of (2*Z*,5*Z*)-3-hydroxy-5-(6,9-dimethoxy-3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)-1-phenylpent-2-ene-1,4-dione (**IIIe**) according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

two three-proton singlets from geminal methyl groups in the pyrrolidine fragment (δ 1.30–1.65 ppm), a doublet of doublets from two methylene protons in the pyrrolidine ring (δ 2.16–2.46 ppm), singlets from 5-H (δ 5.06–6.61 ppm), 2-H (δ 6.90–7.16 ppm), and NH (δ 10.75–10.83 ppm), and a broadened singlet from the enolic hydroxy proton (δ 15.66–16.10 ppm), which belong to major tautomer **B**. In addition, minor signals assignable to diketone tautomer **C** were present; in particular, protons of the CH$_2$ group in the β-dicarbonyl fragment resonated as a singlet at δ 4.31–5.42 ppm, and the 5-H and NH signals were located at δ 4.84–6.03 and 10.42–10.61 ppm, respectively. The **B**/**C** tautomer ratio was estimated at ~5:1 from the signal intensity ratio.

Figure shows the structure of molecule **IIIe** according to the X-ray diffraction data. Compound **IIIe** crystallized in centrosymmetric point symmetry group. The spiro-fused cyclohexadiene and pyrrolidine rings are planar within 0.04 Å, and they form a dihedral angle of 89.4° with respect to each other. The bis-

enone fragment has *s-cis-s-cis-s-cis* configuration fixed by intramolecular hydrogen bonds. The bond lengths therein indicate rupture of conjugation at the C^9–C^{10} bond whose length (1.505 Å) approaches that typical of standard single bond. As a result, two conjugated enone fragments can be distinguished in the open-chain moiety with the C–C bond lengths in each enone fragment ranging from 1.365 to 1.405 Å, which is quite typical of such systems. Localization of the OH proton and C–O bond lengths in the open-chain moiety confirm structure **B**. A short C^4–$H^4\cdots O^6$ contact [$-x$, $-0.5 + y$, $1.5 - z$] was found in the crystal packing of **IIIe**; the H···O distance is shorter by ~0.3 Å than the sum of the corresponding van der Waals radii (2.417 Å). Insofar as this contact may be regarded as both forced and arising from specific interaction C–H···O=C, its nature could be identified only by quantum chemical calculations.

The mechanism of formation of compounds **III** is likely to involve acylation of the $=CH_2$ group in enamino tautomer **A** of spiro compound **II** by the C^2=O carbonyl group of 5-arylfuran-2,3-dione **I**, followed by cleavage of the furan ring at the O^1–C^2 bond, as described previously for the reactions of 5-arylfuran-2,3-diones with such heterocyclic enamines as 1-methyl-3,4-dihydroisoquinolines [5] and Fischer base [6]. Considerable steric hindrances created by geminal methyl groups in the pyrrolidine fragment and spiro-fused naphthalene ring in molecule **IIa**, as well as by additional substituents in positions *3* and *6* of molecules **IIb** and **IIc**, do not prevent them from reacting with 5-arylfuran-2,3-diones.

EXPERIMENTAL

The IR spectra were recorded in mineral oil on a Bruker IFS 66v spectrometer with Fourier transform. The ^{1}H NMR spectra were measured on a Varian Mercury-300BB (300 MHz) in DMSO-d_6 or $CDCl_3$ using hexamethyldisiloxane as internal reference. The purity of the isolated compounds was checked by TLC on Sorbfil plates (ethyl acetate–benzene, 1:5, or ethyl acetate; development with a 0.5% solution of chloranil in toluene).

(2*Z*,5*Z*)-3-Hydroxy-5-(5′,5′-dimethyl-4-oxo-2′*H*,4*H*-spiro[naphthalene-1,3′-pyrrolidin]-2′-ylidene)-1-phenylpent-2-ene-1,4-dione (IIIa). A solution of 1.0 mmol of 5-phenylfuran-2,3-dione (**Ia**) and 1.0 mmol of compound **IIa** in 20 mL of anhydrous benzene was heated for 4 h under reflux. The mixture was cooled, and the precipitate was filtered off. Yield 82%, mp 194–195°C (decomp.; from EtOH). IR spectrum, ν, cm^{-1}: 3150 br (OH, NH), 1660 ($C=O_{naphth.}$), 1595 br (C=O, assoc.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: **B**: 1.59 s and 1.65 s (3H each, Me), 2.46 m (2H, 4′-H, *AB*), 5.08 s (1H, 5-H), 6.45 d (1H, 3-H, naphth.), 6.92 s (1H, 2-H), 7.26 d (1H, 2-H, naphth.), 7.41–8.06 m (9H, H_{arom}), 10.77 s (1H, NH), 16.04 br.s (1H, OH); **C**: 1.53 s and 1.60 s (3H each, Me), 2.41 m (2H, 4′-H, *AB*), 4.31 s (2H, 2-H), 4.85 s (1H, 5-H), 6.43 d (1H, 3-H, naphth.), 7.22 d (1H, 2-H, naphth.), 7.37–8.05 m (9H, H_{arom}), 10.57 s (1H, NH). Found, %: C 75.46; H 5.63; N 3.24. $C_{26}H_{23}NO_4$. Calculated, %: C 75.53; H 5.61; N 3.39.

Compounds **IIIb**–**IIIe** were synthesized in a similar way.

(2*Z*,5*Z*)-3-Hydroxy-5-(5′,5′-dimethyl-4-oxo-2′*H*,4*H*-spiro[naphthalene-1,3′-pyrrolidin]-2′-ylidene)-1-(4-methylphenyl)pent-2-ene-1,4-dione (IIIb). Yield 79%, mp 183–185°C (decomp.; from EtOH). IR spectrum, ν, cm^{-1}: 3180 br (OH, NH), 1660 ($C=O_{naphth.}$), 1598 br (C=O, assoc.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: **B**: 1.59 s and 1.64 s (3H each, Me), 2.41 s (3H, **Me**C_6H_4), 2.45 m (2H, 4′-H, *AB*), 5.06 s (1H, 5-H), 6.44 d (1H, 3-H, naphth.), 6.90 s (1H, 2-H), 7.25 d (1H, 2-H, naphth.), 7.49–8.04 m (8H, H_{arom}), 10.82 s (1H, NH), 16.10 br.s (1H, OH); **C**: 1.53 s and 1.58 s (3H each, Me), 2.39 s (3H, **Me**C_6H_4), 2.41 m (2H, 4′-H, *AB*), 4.33 s (2H, 2-H), 4.84 s (1H, 5-H), 6.40 d (1H, 3-H, naphth.), 7.21 d (1H, 2-H, naphth.), 7.43–8.00 m (8H, H_{arom}), 10.52 s (1H, NH). Found, %: C 75.69; H 5.95; N 3.17. $C_{27}H_{25}NO_4$. Calculated, %: C 75.86; H 5.89; N 3.28.

(2*Z*,5*Z*)-3-Hydroxy-5-(3,3,7,9-tetramethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)-1-phenylpent-2-ene-1,4-dione (IIIc). Yield 75%, mp 173–175°C (decomp.; from EtOAc). IR spectrum, ν, cm^{-1}: 3243 br (OH, NH), 1662 (C^8=O), 1610 br (C=O, assoc.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: **B**: 1.30 s and 1.51 s (3H each, 3-Me), 2.11 s (6H, Me), 2.16 m (2H, 4-H, *AB*), 6.61 s (1H, 5-H), 6.67 s (1H, 6-H), 6.90 s (1H, 10-H), 7.16 s (1H, 2-H), 7.56–8.06 m (5H, Ph), 10.78 s (1H, NH), 16.07 br.s (1H, OH); **C**: 1.23 s and 1.45 s (3H each, 3-Me), 2.09 s (6H, Me), 2.15 m (2H, 4-H, *AB*), 5.38 s (2H, 2-H), 6.59 s (1H, 5-H), 6.64 s (1H, 6-H), 6.85 s (1H, 10-H), 7.54–8.04 m (5H, Ph), 10.57 s (1H, NH). Found, %: C 73.56; H 6.52; N 3.57. $C_{24}H_{25}NO_4$. Calculated, %: C 73.64; H 6.44; N 3.58.

(2*Z*,5*Z*)-3-Hydroxy-5-(9-methoxy-3,3,6-trimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)-1-

phenylpent-2-ene-1,4-dione (IIId). Yield 78%, mp 132–134°C (decomp.; from EtOAc). IR spectrum, ν, cm^{-1}: 3261 br (OH, NH), 1664 (C^8=O), 1611 br (C=O, assoc.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: **B**: 1.56 s and 1.62 s (3H each, 3-Me), 1.97 s (3H, Me), 2.30 m (2H, 4-H, *AB*), 3.64 s (3H, OMe), 6.07 s (1H, 5-H), 6.32 s (1H, CH), 6.59 s (1H, CH), 7.03 s (1H, 2-H), 7.59–8.03 m (5H, Ph), 10.83 s (1H, NH), 16.09 br.s (1H, OH); **C**: 1.50 s and 1.60 s (3H each, 3-Me), 1.94 s (3H, Me), 2.21 m (2H, 4-H, *AB*), 3.61 s (3H, OMe), 5.36 s (2H, 2-H), 6.03 s (1H, 5-H), 6.30 s (1H, CH), 6.58 s (1H, CH), 7.56–8.01 m (5H, Ph), 10.61 s (1H, NH). Found, %: C 70.62; H 6.20; N 3.31. $C_{24}H_{25}NO_5$. Calculated, %: C 70.74; H 6.18; N 3.44.

(2*Z*,5*Z*)-3-Hydroxy-5-(6,9-dimethoxy-3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)-1-phenylpent-2-ene-1,4-dione (IIIe). Yield 80%, mp 183–184°C (decomp.; from EtOAc). IR spectrum, ν, cm^{-1}: 3207 br (OH, NH), 1661 (C^8=O), 1604 br (C=O, assoc.). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: **B**: 1.53 s and 1.55 s (3H each, 3-Me), 2.32 m (2H, 4-H, *AB*), 3.69 s and 3.76 s (3H each, OMe), 5.73 s (1H, 5-H), 7.05 s (1H, 2-H), 7.26 s (1H, CH), 7.36 s (1H, CH), 7.44–7.99 m (5H, Ph), 10.75 s (1H, NH), 15.66 br.s (1H, OH); **C**: 1.48 s and 1.50 s (3H each, 3-Me), 2.29 m (2H, 4-H, *AB*), 3.64 s and 3.72 s (3H each, OMe), 5.42 s (2H, 2-H), 5.68 s (1H, 5-H), 7.21 s (1H, CH), 7.31 s (1H, CH), 7.42–7.96 m (5H, Ph), 10.42 s (1H, NH). Found, %: C 67.95; H 6.15; N 3.29. $C_{24}H_{25}NO_6$. Calculated, %: C 68.07; H 5.95; N 3.31.

X-Ray analysis of compound IIIe. The X-ray diffraction data for compound **IIIe** were acquired on an Xcalibur E automatic diffractometer equipped with a CCD detector according to standard procedure [ω-scanning through a step of 1°; MoK_α irradiation, λ 0.71073 Å; 295(2) K] [11]. The data were obtained from a 0.25×0.20×0.15-mm fragment of a yellow prismatic single crystal. Monoclinic crystal system, space group $P2_1/c$; $C_{24}H_{25}NO_6$; unit cell parameters: a = 16.534(2), b = 13.514(2), c = 9.9331(12) Å; β = 96.761(13)°; V = 2204.1(6) $Å^3$; Z = 4; d_{calc} = 1.276 g×cm^{-3}. Total of 9774 reflection intensities were measured in the range $-16 < h < 20$, $-15 < k < 16$, $-12 < l < 12$; 4506 reflections were independent (R_{int} = 0.0791), and 1625 reflections were characterized by $I > 2\sigma(I)$; completeness 99.9% for the range $2.84 < \Theta < 26.00$. The structure was solved using SHELXS-97 and was refined using SHELXL-97 [12] against F^2 in anisotropic approximation for non-hydrogen atoms. The positions of hydrogen atoms were refined according to the riding model in isotropic approximation with dependent thermal parameters, and the positions of the NH and OH hydrogen atoms were refined independently in isotropic approximation. A correction for absorption was applied empirically (μ = 0.092 mm^{-1}). Final divergence factors: R_1 = 0.0617, wR_2 = 0.0887 [for reflections with $I > 2\sigma(I)$] and R_1 = 0.1947, wR_2 = 0.1251 (for all reflections); goodness of fit S = 0.991. The maximum and minimum electron density peaks were 0.155 and –0.149 $\bar{e}/Å^3$, respectively. The set of crystallographic data for compound **IIIe** was deposited to the Cambridge Crystallographic Data Centre (entry no. CCDC 1032763) and is available at *www.ccdc.cam.ac.uk/data_request/cif*.

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REFERENCES

1. Andreichikov, Yu.S., Gein, V.L., Zalesov, V.V., Kozlov, A.P., Kollents, G., Maslivets, A.N., Pimenova, E.V., and Shurov, S.N., *Khimiya pyatichlennykh 2,3-dioksogeterotsiklov* (Chemistry of Five-Membered 2,3-Dioxo Heterocycles), Perm: Perm. Gos. Univ., 1994, p. 5.
2. Nekrasov, D.D. and Shurov, S.N., *Chem. Heterocycl. Compd*., 2005, vol. 41, no. 10, p. 1245.
3. Novikov, A.A., Vostrov, E.S., and Maslivets, A.N., *Russ. J. Org. Chem*., 2005, vol. 41, p. 1234.
4. Andreichikov, Yu.S., Voronova, L.A., and Milyutin, A.V., *Zh. Org. Khim*., 1979, vol. 15, p. 847.
5. Khalturina, V.V., Shklyaev, Yu.V., Aliev, Z.G., and Maslivets, A.N., *Russ. J. Org. Chem*., 2009, vol. 45, p. 728.
6. Khalturina, V.V., Shurov, S.N., and Maslivets, A.N., *Russ. J. Org. Chem*., 2009, vol. 45, p. 953.
7. Konovalova, V.V., Shklyaev, Yu.V., and Maslivets, A.N., *Russ. J. Org. Chem*., 2011, vol. 47, p. 1119.
8. Nifontov, Yu.V., Glushkov, V.A., and Shklyaev, Yu.V., *Russ. Chem. Bull., Int. Ed*., 2003, vol. 52, no.2, p. 437.
9. Rozhkova, Yu.S., Khmelevskaya, K.A., Shklyaev, Yu.V., Ezhikova, M.A., and Kodess, M.I., *Russ. J. Org. Chem*., 2012, vol. 48, p. 69.
10. Glushkov, V.A., Stryapunina, O.G., Gorbunov, A.A., Maiorova, O.A., Slepukhin, P.A., Ryabukhina, S.Ya., Khorosheva, E.V., Sokol, V.I., and Shklyaev, Yu.V., *Tetrahedron*, 2010, vol. 66, p. 721.
11. *CrysAlisPro, Version 1.171.36.32* (release 02-08-2013 CrysAlis171.NET), Agilent Technologies.
12. Sheldrick, G.M., *Acta Crystallogr., Sect. A*, 2008, vol. 64, p. 112.