ISSN 1070-4280, Russian Journal of Organic Chemistry, 2012, Vol. 48, No. 10, pp. 1329–1332. © Pleiades Publishing, Ltd., 2012. Original Russian Text © P.S. Silaichev, V.O. Filimonov, P.A. Slepukhin, A.N. Maslivets, 2012, published in Zhurnal Organicheskoi Khimii, 2012, Vol. 48, No. 10, pp. 1334–1337.

Five-Membered 2,3-Dioxo Heterocycles: LXXXIX.* Reaction of Methyl 1-Aryl-3-cinnamoyl-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates with (*E*)-4-Arylaminopent-3-en-2-ones. Crystalline and Molecular Structure of 9-Acetyl-4-cinnamoyl-3-hydroxy-1-(4-methoxyphenyl)-8-methyl-7-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-2,6-dione

P. S. Silaichev^{a, b}, V. O. Filimonov^b, P. A. Slepukhin^c, and A. N. Maslivets^{a, b}

^a Institute of Natural Sciences, Perm State National Research University, ul. Genkelya 4, Perm, 614990 Russia e-mail: koh2@psu.ru

^b Perm State National Research University, Perm, Russia

^c Postovskii Institute of Organic Synthesis, Ural Division, Russian Academy of Sciences, ul. Akademicheskaya/S. Kovalevskoi 22/20, Yekaterinburg, 620990 Russia

Received July 18, 2011

Abstract—Methyl 1-aryl-3-cinnamoyl-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates reacted with 4-benzylamino- and 4-arylaminopent-3-en-2-ones to give 1-aryl-7-benzyl- and 1,7-diaryl-9-acetyl-4-cinnamoyl-3hydroxy-8-methyl-1,7-diazaspiro[4.4]nona-3,8-diene-2,6-diones. The crystalline and molecular structures of 9-acetyl-4-cinnamoyl-3-hydroxy-1-(4-methoxyphenyl)-8-methyl-7-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-2,6-dione were studied by X-ray analysis.

DOI: 10.1134/S1070428012100120

We previously reported on the reaction of methyl 1-aryl-3-cinnamoyl-4,5-dioxo-4,5-dihydro-1H-pyrrole-2-carboxylates with carbocyclic enamines, (Z)-3-amino-5,5-dimethyl-cyclohex-2-en-1-ones, which afforded 1'-aryl-3'-cinnamoyl-4'-hydroxy-6,6dimethyl-6,7-dihydrospiro[indole-3,2'-pyrrole]-2,4,5'(1H,1'H,5H)-triones as a result of attack by the β -CH and NH groups of the enamine on C² and ester carbonyl carbon atom in the dioxopyrrole [2]. Unlike cyclic enamino ketones, their acyclic analogs exist as E isomers stabilized by intramolecular hydrogen bond, which should hamper their reactions as binucleophiles. Nevertheless, methyl 1-aryl-3-benzoyl-4,5-dioxo-4,5dihydro-1H-pyrrole-2-carboxylates reacted with 4-arylaminopent-3-en-2-ones and 3-(4-methyl-phenylamino)-1,3-diphenylprop-2-en-1-one to produce 9-acetyl-1,7-diaryl-4-benzoyl-3-hydroxy-8-methyl-1,7diazaspiro[4.4]nona-3,8-diene-2,6-diones and 9-acetyl-1,7-diaryl-4-benzoyl-3-hydroxy-8-phenyl-1,7-diaza-

By heating equimolar amounts of compounds **Ia–Ic** and **IIa–IId** in boiling anhydrous toluene over a period of 3–4 h (until the bright red color typical of initial pyrrolediones **I** disappeared) we obtained the corresponding 9-acetyl-1,7-diaryl-4-cinnamoyl-3-hydroxy-8-methyl-1,7-diazaspiro[4.4]nona-3,8-diene-2,6-diones **IIIa–IIIg** in good yields (Scheme 1). Compounds **IIIa–IIIg** were isolated as colorless or light yellow high-melting crystalline substances; they are readily soluble in DMF and DMSO, poorly soluble in other common organic solvents, and insoluble in saturated hydrocarbons and water; they showed a positive test for enolic hydroxy group on treatment with an alcoholic solution of iron(III) chloride.

The IR spectra of **IIIa–IIIg** contained absorption bands due to stretching vibrations of enolic hydroxy

spiro[4.4]nona-3,8-diene-2,6-diones [3]. Reactions of methyl 1-aryl-3-cinnamoyl-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates with acyclic enamino ketones were not reported previously.

^{*} For communication LXXXVIII, see [1].



 $\mathbf{I}, Ar = Ph (\mathbf{a}), 4-MeC_{6}H_{4} (\mathbf{b}), 4-MeOC_{6}H_{4} (\mathbf{c}); \mathbf{II}, R = PhCH_{2} (\mathbf{a}), 4-MeC_{6}H_{4} (\mathbf{b}), Ph (\mathbf{c}), 4-BrC_{6}H_{4} (\mathbf{d}); \mathbf{III}, Ar = Ph, R = PhCH_{2} (\mathbf{a}), 4-MeC_{6}H_{4} (\mathbf{b}); Ar = 4-MeC_{6}H_{4} (\mathbf{a}); Ar = 4-Me$

group (3153–3304 cm⁻¹), lactam carbonyl groups $C^6=O$ and $C^2=O$ (1746–1755 and 1707–1725 cm⁻¹), and ketone carbonyl groups in the acetyl and cinnamoyl fragments (1665–1678 and 1642–1647 cm^{-1}). In the ¹H NMR spectra of IIIa–IIIg we observed signals from protons in the aromatic rings and substituents therein, a singlet from the methyl group on C^8 at δ 2.12–2.28 ppm, a singlet from the acetyl protons at δ 2.12–2.15 ppm, doublets from protons at the exocyclic double bond in the cinnamoyl fragment at δ 7.60– 7.74 ppm with a coupling constant ${}^{3}J$ of 15.7–16.2 Hz typical of trans-configured alkenes [4], and a broadened signal from the enolic proton at δ 12.81– 13.13 ppm. Compounds IIIa and IIIe, apart from the above signals, displayed two doublets at δ 4.74– 4.93 ppm from methylene protons in the benzyl fragment with a geminal coupling constant ${}^{2}J$ of 16.7 Hz.

The structure of the synthesized compounds was confirmed by X-ray analysis of IIIf (see figure). Compound IIIf crystallized in centrosymmetric space group, and its molecules are characterized by bond lengths and bond angles approaching the corresponding standard values. The five-membered pyrrole rings are planar within 0.01 Å, and the dihedral angle between their planes is 88.5°. Molecules IIIf in crystal are linked through intermolecular hydrogen bonds $O^{3}-H^{3}\cdots O^{2}$ [-x, -y + 1, -z] [O^{3}-H^{3} 0.85(2), O^{3}\cdots O^{2} 2.713(2) Å, $\angle O^3 H^3 O^2$ 147(1)°]. The observed shortened contact between proton in the benzene ring and the neighboring carbonyl group $C^7 - H^7 \cdots O^4$ [2.638 Å; -1/2 + x, 1.5 - y, -1/2 + z] is likely to be forced. Participation of that carbonyl group in intramolecular hydrogen bond is under discussion, for the $O^3 - N^3 \cdots O^4$ angle is too small [107(1)°].



Structure of the molecule of 9-acetyl-4-cinnamoyl-3-hydroxy-1-(4-methoxyphenyl)-8-methyl-7-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-2,6-dione (**IIIf**) according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

Presumably, compounds **IIIa–IIIg** are formed via initial addition of the β -CH group in the enamine fragment of **IIa–IId** at the C² carbon atom in the pyrrole ring of **Ia–Ic** and subsequent closure of a new pyrrole ring as a result of nucleophilic attack by the secondary amino group on the ester carbonyl carbon atom and elimination of methanol, i.e., according to a scheme analogous to that proposed in [3].

EXPERIMENTAL

The IR spectra were recorded on an FSM-1201 spectrometer from samples dispersed in mineral oil. The ¹H NMR spectra were run on a Bruker AM-400 spectrometer at 400 MHz using DMSO- d_6 as solvent and tetramethylsilane as internal reference.

9-Acetyl-7-benzyl-4-cinnamoyl-3-hydroxy-8methyl-1-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-2,6-dione (IIIa). Compound Ia, 1.0 mmol, was dissolved in 15 ml of anhydrous toluene, 1.0 mmol of enamino ketone IIa in 5 ml of anhydrous toluene was added, and the mixture was heated for 3 h under reflux. The mixture was cooled, and the precipitate was filtered off, and recrystallized from ethyl acetate. Yield 81%, mp 215–217°C. IR spectrum, v, cm⁻¹: 3179 (OH), 1754 (C⁶=O), 1721 (C²=O), 1678 (9-C=O), 1645 (4-C=O). ¹H NMR spectrum, δ, ppm: 2.13 s (3H, COMe), 2.28 s (3H, Me), 4.77 d and 4.92 d (1H each, J = 16.7 Hz), 6.88–7.69 m (15H, H_{arom}), 7.60 d (1H, COCH=CHPh, J = 16.0 Hz), 7.73 d (1H, COCH=CHPh, J = 16.0 Hz), 13.08 br.s (1H, OH). Found, %: C 74.08; H 5.02; N 5.35. C32H26N2O5. Calculated, %: C 74.12; H 5.05; N 5.40.

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

9-Acetyl-4-cinnamoyl-3-hydroxy-8-methyl-7-(4-methylphenyl)-1-phenyl-1,7-diazaspiro[4.4]nona-**3,8-diene-2,6-dione (IIIb).** Yield 77%, mp 209–210°C (from ethyl acetate). IR spectrum, v, cm⁻¹: 3170 (OH), 1748 (C⁶=O), 1725 (C²=O), 1665 (9-C=O), 1645 (4-C=O). ¹H NMR spectrum, δ , ppm: 2.12 s (6H, Me, COMe), 2.38 s (3H, C₆H₄Me), 7.09–7.72 m (14H, H_{arom}), 7.66 d (1H, COCH=CHPh, J = 16.2 Hz), 7.74 d (1H, COCH=CHPh, J = 16.2 Hz), 12.97 br.s (1H, OH). Found, %: C 74.05; H 5.01; N 5.36. C₃₂H₂₆N₂O₅. Calculated, %: C 74.12; H 5.05; N 5.40.

9-Acetyl-4-cinnamoyl-3-hydroxy-8-methyl-1-(4-methylphenyl)-7-phenyl-1,7-diazaspiro[4.4]nona-**3,8-diene-2,6-dione (IIIc).** Yield 76%, mp 229–230°C (from ethyl acetate). IR spectrum, v, cm⁻¹: 3153 (OH), 1748 (C⁶=O), 1717 (C²=O), 1673 (9-C=O), 1644 (4-C=O). ¹H NMR spectrum, δ , ppm: 2.12 s (3H, Me), 2.13 s (3H, COMe), 2.34 s (3H, C₆H₄**Me**), 7.00– 7.71 m (14H, H_{arom}), 7.66 d (1H, COC**H**=CHPh, *J* = 16.2 Hz), 7.74 d (1H, COCH=C**H**Ph, *J* = 16.2 Hz), 12.88 br.s (1H, OH). Found, %: C 74.16; H 5.01; N 5.44. C₃₂H₂₆N₂O₅. Calculated, %: C 74.12; H 5.05; N 5.40.

9-Acetyl-7-(4-bromophenyl)-4-cinnamoyl-3-hydroxy-8-methyl-1-(4-methylphenyl)-1,7-diazaspiro-[4.4]nona-3,8-diene-2,6-dione (IIId). Yield 81%, mp 222–223°C (from ethyl acetate). IR spectrum, v, cm⁻¹: 3310 (OH), 1753 (C⁶=O), 1713 (C²=O), 1672 (9-C=O), 1642 (4-C=O). ¹H NMR spectrum, δ , ppm: 2.12 s (3H, Me), 2.15 s (3H, COMe), 2.33 s (3H, C₆H₄Me), 6.98–7.81 m (13H, H_{arom}), 7.64 d (1H, COCH=CHPh, J = 15.7 Hz), 7.72 d (1H, COCH=CHPh, J = 15.7 Hz), 7.72 d (1H, COCH=CHPh, J = 15.7 Hz), 12.88 br.s (1H, OH). Found, %: C 64.25; H 4.20; N 4.65. C₃₂H₂₅BrN₂O₅. Calculated, %: C 64.33; H 4.22; N 4.69.

9-Acetyl-7-benzyl-4-cinnamoyl-3-hydroxy-1-(4-methoxyphenyl)-8-methyl-1,7-diazaspiro[4.4]nona-3,8-diene-2,6-dione (IIIe). Yield 74%, mp 216– 217°C (from ethyl acetate). IR spectrum, v, cm⁻¹: 3304 (OH), 1748 (C⁶=O), 1707 (C²=O), 1669 (9-C=O), 1647 (4-C=O). ¹H NMR spectrum, δ , ppm: 2.15 s (3H, COMe), 2.28 s (3H, Me), 4.74 d and 4.93 d (1H each, CH₂Ph, J = 16.7 Hz), 6.84–7.69 m (14H, H_{arom}) 7.60 d (1H, COCH=CHPh, J = 15.8 Hz), 7.72 d (1H, COCH=CHPh, J = 15.8 Hz), 13.13 br.s (1H, OH). Found, %: C 72.19; H 5.10; N 5.13. C₃₃H₂₈N₂O₆. Calculated, %: C 72.25; H 5.14; N 5.11.

9-Acetyl-4-cinnamoyl-3-hydroxy-1-(4-methoxyphenyl)-8-methyl-7-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-2,6-dione (IIIf). Yield 84%, mp 222–223°C (from ethyl acetate). IR spectrum, v, cm⁻¹: 3313 (OH), 1746 (C⁶=O), 1713 (C²=O), 1671 (9-C=O), 1642 (4-C=O). ¹H NMR spectrum, δ , ppm: 2.13 s (3H, Me), 2.14 s (3H, COMe), 3.79 s (3H, OMe), 7.01–7.71 m (14H, H_{arom}), 7.65 d (1H, COCH=CHPh, *J* = 15.8 Hz), 7.73 d (1H, COCH=CHPh, *J* = 15.8 Hz), 12.81 br.s (1H, OH). Found, %: C 71.81; H 4.93; N 5.22. C₃₂H₂₆N₂O₆. Calculated, %: C 71.90; H 4.90; N 5.24.

The X-ray diffraction data for compound **IIIf** were acquired on an Xcalibur-3 automatic four-circle diffractometer with a CCD detector [λ (Mo K_{α}) 0.71073 Å, 295(2) K, graphite monochromator, ω -scanning through a step of 1°] from a 0.25 × 0.20 × 0.15-mm fragment of a light-yellow prismatic crystal. No correction for absorption was introduced because of its smallness ($\mu = 0.092 \text{ mm}^{-1}$). Total of 16326 reflection

intensities were measured in the range $2.70 < \theta <$ 28.29°; 6549 reflections were independent ($R_{int} =$ 0.0357), and 2608 reflections were characterized by $I > 2\sigma(I)$. Completeness 98% for $\theta < 28.29^{\circ}$. Monoclinic crystal system, space group $P2_1/n$; unit cell parameters: a = 9.8107(10), b = 12.6792(11), c =21.876(2) Å; $\beta = 98.400(9)^{\circ}$. The structure was solved and refined using SHELXTL 5.1 software package [5]. The positions and temperature parameters of nonhydrogen atoms were refined first in isotropic and then in anisotropic approximation by the full-matrix leastsquares procedure against F^2 . Hydrogen atoms (except for the OH hydrogen atom) were localized by the electron density maxima, and their positions were refined according to the riding model. The position of the OH hydrogen atom was refined independently in isotropic approximation. The final divergence factors were $wR_2 = 0.0587$, $R_1 = 0.0383$ for reflections with $I > 2\sigma(I)$ and $R_1 = 0.1144$, $wR_2 = 0.0621$ for all reflections; goodness of fit S = 1.004. The complete set of crystallographic data for compound IIIf was deposited to the Cambridge Crystallographic Data Centre (entry no. CCDC 900794) and is available at www.ccdc.cam.ac.uk/data request/cif.

9-Acetyl-4-cinnamoyl-3-hydroxy-1-(4-methoxyphenyl)-8-methyl-7-(4-methylphenyl)-1,7-diazaspiro[4.4]nona-3,8-diene-2,6-dione (IIIg). Yield 79%, mp 252–253°C (from toluene). IR spectrum, v, cm^{-1} : 3196 (OH), 1755 (C⁶=O), 1713 (C²=O), 1673 (9-C=O), 1642 (4-C=O). ¹H NMR spectrum, δ , ppm: 2.12 s (3H, Me), 2.13 s (3H, COMe), 2.38 s (3H, C₆H₄**Me**), 3.79 s (3H, OMe), 7.01–7.71 m (13H, H_{arom}) 7.65 d (1H, COC**H**=CHPh, *J* = 15.9 Hz), 7.73 d (1H, COCH=C**H**Ph, *J* = 15.9 Hz), 13.05 br.s (1H, OH). Found, %: C 72.28; H 5.11; N 5.08. C₃₅H₂₈N₂O₆. Calculated, %: C 72.25; H 5.14; N 5.11.

This study was performed under financial support by the Ministry of Education and Science of the Russian Federation (project no. 2.19.10) and by the Russian Foundation for Basic Research (project no.12-03-00696-a).

REFERENCES

- Maslivets, V.A. and Maslivets, A.N., *Russ. J. Org. Chem.*, 2012, vol. 48, p. 1233.
- Silaichev, P.S., Filimonov, V.O., Slepukhin, P.A., and Maslivets, A.N., *Russ. J. Org. Chem.*, 2012, vol. 48, p. 561.
- Bannikova, Yu.N., Khalturina, V.V., Sedegova, E.A., and Maslivets, A.N., *Russ. J. Org. Chem.*, 2007, vol. 43, p. 154.
- Kazitsyna, L.A. and Kupletskaya, N.B., Primenenie UF, IK, YaMR i mass spektroskopii v organicheskoi khimii (Applications of UV, IR, and NMR Spectroscopy and Mass Spectrometry in Organic Chemistry), Moscow: Mosk. Gos. Univ., 1979.
- Sheldrick, G.M., Acta Crystallogr., Sect. A, 2008, vol. 64, p. 112.