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Five-Membered 2,3-Dioxo Heterocycles: XCIII.* Spiro Heterocyclization of 4,5-Diaroyl-1*H*-pyrrole-2,3-diones with Acyclic Enamine. Crystalline and Molecular Structure of Substituted 1,7-Diazaspiro[4.4]nonane

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Abstract—4,5-Diaroyl-1-aryl-1*H*-pyrrole-2,3-diones reacted with ethyl 3-amino-3-phenylprop-2-enoate to give ethyl 4-aroyl-1,6-diaryl-3-hydroxy-2-oxo-8-phenyl-1,7-diazaspiro[4.4]nona-3,6,8-triene-9-carboxylates. The crystalline and molecular structures of ethyl 4-benzoyl-3-hydroxy-1-(4-methylphenyl)-2-oxo-6,8-diphenyl-1,7-diazaspiro[4.4]nona-3,6,8-triene-9-carboxylate were determined by X-ray analysis.

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We previously described recyclizations of 4,5-diaroyl-1*H*-pyrrole-2,3-diones with aromatic amines [2] and substituted hydrazines [3, 4], which involved successive nucleophilic attacks on C^5 and carbonyl carbon atom of the aroyl group on C^4 and led to the formation of 1,5-diaryl-5-hydroxy-4-(2-aryl-1-arylamino-2-oxoethylidene)pyrrolidine-2,3-diones and *N*-aryl-2-(5-aryl-3-aroyl-1*H*-pyrazol-4-yl)-2-oxoacetamides, respectively. There are no published data on reactions of 4,5-diaroyl-1*H*-pyrrole-2,3-diones with 1,3-binucleophiles. By heating equimolar amounts of 4,5-diaroyl-1aryl-1*H*-pyrrole-2,3-diones **Ia–If** [5] and ethyl 3-amino-3-phenylprop-2-enoate (**II**) in boiling anhydrous benzene for 2–3 h (TLC) we obtained in good yields the corresponding ethyl 4-aroyl-1,6-diaryl-3-hydroxy-2-oxo-8-phenyl-1,7-diazaspiro[4.4]nona-3,6,8triene-9-carboxylates **IIIa–IIIf** (Scheme 1) whose structure was confirmed by the X-ray diffraction data for compound **IIIb**.**

Compounds **IIIa–IIIf** were isolated as light yellow high-melting crystalline substances, which were read-



I, III, $Ar^2 = Ph$, $Ar^1 = Ph$ (a), 4-MeC₆H₄ (b), 4-MeOC₆H₄ (c); $Ar^2 = 4-MeC_6H_4$, $Ar^1 = Ph$ (d), 4-MeC₆H₄ (e), 4-MeOC₆H₄ (f).

** For preliminary communication, see [6].

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

ily soluble in DMF, DMSO, chloroform, acetone, and ethyl acetate, poorly soluble in alcohols and carbon tetrachloride, and insoluble in saturated hydrocarbons and water. The products showed a positive color test (cherry color) for enolic hydroxy group upon treatment with an alcoholic solution of iron(III) chloride.

The IR spectra of IIIa-IIIf contained absorption bands typical of stretching vibrations of enolic hydroxy group $(3170-3292 \text{ cm}^{-1})$ and ester $(1715-1725 \text{ cm}^{-1})$, lactam ($C^2=O$, 1667–1686 cm⁻¹), and ketone carbonyl groups (1632–1642 cm⁻¹). Compounds IIIa–IIIf displayed in the ¹H NMR spectra signals from protons in the aromatic rings and substituents attached thereto, a triplet (δ 1.13–1.15 ppm, CH₃) and a multiplet $(\delta 4.11 - 4.15 \text{ ppm}, \text{CH}_2)$ from the ester ethoxy group, and a broadened singlet from the enolic hydroxy proton at δ 12.61–12.80 ppm. In the ¹³C NMR spectrum of IIIb we observed signals from carbon atoms in aromatic and aliphatic substituent, double-bonded carbon atoms in the pyrrole rings, carbonyl carbon atoms in the aroyl and ester groups ($\delta_{\rm C}$ 187.90 and 161.96 ppm, respectively), lactam carbonyl carbon atom (δ_{C} 165.77 ppm), C⁶ (δ_{C} 161.73 ppm), and spiro carbon atom ($\delta_{\rm C}$ 81.69 ppm).

Figure shows the structure of compound IIIb determined by X-ray analysis. Compound IIIb crystallizes as a 1:1 solvate with benzene in centrosymmetric space group belonging to monoclinic crystal system. Molecule IIIb consists of two spiro-fused pyrrole rings, one of which is a 3*H*-pyrrole, and the other, 2,5-dihydro-1*H*-pyrrole. The bond lengths and bond angles in molecule IIIb do not differ from the corresponding standard values to an appreciable extent. The bond angles at the C⁶ spiro carbon atom range from 100 to 115°, which may be due to distortions intrinsic to five-membered rings. Molecule IIIb may be regarded as sterically overcrowded; therefore, the planes of all aryl groups are more or less turned relative to the pyrrole ring planes. In addition, a serious disordering of substituents on the 3H-pyrrole ring is observed. In particular, atoms in both benzene rings are disordered by two positions with equal populations. The benzene ring on C^2 (see figure) is disordered via rotation about the $C^2 \cdots C^{28}$ axis through an angle of ~66°, and dis-ordering of the phenyl group on C^{10} may be described as libration with respect to the $C^{20}-C^{32}$ bond (this disordering is not shown for the sake of simplicity). Insofar as the coordinates of a number of atoms in the disordered fragments were fairly similar, some constraints were applied to their anisotropic thermal parameters (ISOR 0.01 C16 C36 O5 C34 C34a, EADP

C16 C16a, EADP C36 C36a, EADP O5 O5a commands were introduced into the instruction file of the XL refinement program).

The hydrogen atom in the 3*H*-pyrrole ring was expectedly localized on O³ [C²³–O³ 1.3396(13) Å] rather than on O² [O²–C³ 1.2203(13) Å; see figure]; it is involved in intermolecular hydrogen bond with O⁴ (–*x* + 1/2, –*y* + 1/2, –*z*) in the ethoxycarbonyl group [O³–H³ 0.87(2), O⁴…H³ 1.90(2), O⁴…O³ 2.720(2) Å].

The benzene solvate molecule occupies a partial position and is also disordered by two positions. Presumably, the positions of its disordered components in the crystal packing are consistent with the disordering of substituents, otherwise extremely short intermolecular contacts $C \cdots H$, $H \cdots H$, and $C \cdots C$ could appear.

Compounds **IIIa–IIIf** are likely to be formed via addition of the enamine CH group to C^5 of pyrrole-2,3dione **I** and subsequent intramolecular cyclization as a result of nucleophilic attack by the primary amino group on the carbonyl carbon atom in the aroyl substituent on C^5 and elimination of water. The described reaction is the first example of direct spiro heterocyclization of 4,5-diaroyl-1*H*-pyrrole-2,3-diones with enamines, which follows a previously unknown scheme and yields difficultly accessible spiroheterocyclic 1,7-diazaspiro[4.4]nona-3,6,8-triene system.

EXPERIMENTAL

The IR spectra were recorded on a Perkin Elmer Spectrum Two spectrometer from samples dispersed in



Ball-and-rod structure of the molecule of ethyl 4-benzoyl-3hydroxy-1-(4-methylphenyl)-2-oxo-6,8-diphenyl-1,7-diazaspiro[4.4]nona-3,6,8-triene-9-carboxylate (**IIIb**) according to the X-ray diffraction data. Hydrogen atoms, except for the OH hydrogen atom, are not shown for the sake of simplicity.

mineral oil. The ¹H and ¹³C NMR spectra were measured on a Bruker AM-400 spectrometer at 400 and 100 MHz, respectively, using DMSO-*d*₆ as solvent and tetramethylsilane as internal reference. The purity of the isolated compounds was checked by TLC using benzene–ethyl acetate (5:1) as eluent.

Ethyl 4-benzoyl-3-hydroxy-2-oxo-1,6,8-triphenyl-1,7-diazaspiro[4.4]nona-3,6,8-triene-9-carboxylate (IIIa). A solution of 1.0 mmol of compound Ia and 1.0 mmol of enamine II in 20 ml of anhydrous benzene was heated for 2 h under reflux. The mixture was evaporated by half, an equal volume of petroleum ether (bp 40–70°C) was added to the residue, the mixture was cooled, and the precipitate was filtered off and recrystallized from benzene. Yield 71%, mp 195– 196°C. IR spectrum, v, cm⁻¹: 3170 (OH), 1715 (C=O, ester), 1686 (C²=O), 1640 (4-C=O). ¹H NMR spectrum, δ , ppm: 1.14 t (3H, CH₂CH₃), 4.13 m (2H, OCH₂), 7.03–8.02 m (20H, Ph), 12.80 brs (1H, OH). Found, %: C 75.77; H 4.70; N 5.02. C₃₅H₂₆N₂O₅. Calculated, %: C 75.80; H 4.73; N 5.05.

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

Ethyl 4-benzoyl-3-hydroxy-1-(4-methylphenyl)-2-oxo-6,8-diphenyl-1,7-diazaspiro[4.4]nona-3,6,8triene-9-carboxylate (IIIb). Yield 71%, mp 196– 197°C (from benzene–ethyl acetate, 1:1). IR spectrum, v, cm⁻¹: 3265 (OH), 1719 (C=O, ester), 1669 (C²=O), 1640 (4-C=O). ¹H NMR spectrum, δ, ppm: 1.14 t (3H, CH₂CH₃), 2.21 s (3H, Me), 4.14 m (2H, OCH₂), 6.89– 8.00 m (19H, H_{arom}), 12.73 br.s (1H, OH). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 13.67 (CH₂CH₃), 20.44 (Me), 60.11 (OCH₂), 81.69 (C⁵), 124.83–137.65, 161.73 (C⁶), 161.96 (C=O, ester), 165.77 (C²), 177.72 (C³), 187.90 (4-C=O). Found, %: C 75.99; H 4.91; N 4.89. C₃₆H₂₈N₂O₅. Calculated, %: C 76.04; H 4.96; N 4.93.

The X-ray diffraction data for compound **IIIb** were acquired at 150(2) K on an Xcalibur S automatic X-ray diffractometer according to standard procedure $[\lambda MoK_a 0.71073 \text{ Å}, \omega$ -scanning with a step of 1°, crystal–detector distance 50 mm] from a $0.25 \times 0.20 \times$ 0.15-mm light yellow single crystal. Total of 11776 reflection intensities were measured in the θ range from 2.89 to 28.28°; 7396 reflections were independent ($R_{\text{int}} = 0.022$), and 4357 reflections were characterized by $I > 2\sigma(I)$. No correction for absorption was applied. Monoclinic crystal system, space group C2/c; unit cell parameters: a = 33.5487(13), b = 9.1118(6), c = 20.6818(14) Å; $\beta = 93.674(4)^{\circ}$. The structure was solved and refined by the full-matrix least-squares procedure (with respect to F^2) in anisotropic approximation for non-hydrogen atoms using SHELXTL software package [7]. Hydrogen atoms attached to carbons were placed into geometrically calculated positions and were refined according to the riding model; the OH hydrogen atom was refined independently in isotropic approximation. The final divergence factors were $R_1 = 0.0369$, $wR_2 = 0.0701$ for reflections with $I > 2\sigma(I)$ and $R_1 = 0.0781$, $wR_2 = 0.0754$ for all reflections; goodness of fit S = 1.004; completeness 96.9% $(\theta < 26.0^{\circ})$; maximum and minimum residual electron densities 0.204 and $-0.207 \ \bar{e} \text{\AA}^{-3}$. The complete set of crystallographic data for compound IIb was deposited to the Cambridge Crystallographic Data Centre (entry no. CCDC 939281) and is available at www.ccdc.cam.ac.uk/conts/retrieving.html.

Ethyl 4-benzoyl-3-hydroxy-1-(4-methoxyphenyl)-2-oxo-6,8-diphenyl-1,7-diazaspiro[4.4]nona-3,6,8-triene-9-carboxylate (IIIc). Yield 71%, mp 190–191°C (from benzene). IR spectrum, v, cm⁻¹: 3292 (OH), 1721 (C=O, ester), 1669 (C²=O), 1632 (4-C=O). ¹H NMR spectrum, δ , ppm: 1.15 t (3H, CH₂CH₃), 3.67 s (3H, OMe), 4.15 m (2H, OCH₂), 6.87–8.02 m (19H, H_{arom}), 12.77 br.s (1H, OH). Found, %: C 73.99; H 4.85; N 4.76. C₃₆H₂₈N₂O₆. Calculated, %: C 73.96; H 4.83; N 4.79.

Ethyl 3-hydroxy-4-(4-methylbenzoyl)-6-(4-methylphenyl)-2-oxo-1,8-diphenyl-1,7-diazaspiro[4.4]nona-3,6,8-triene-9-carboxylate (IIId). Yield 76%, mp 199–200°C (benzene). IR spectrum, v, cm⁻¹: 3287 (OH), 1721 (C=O, ester), 1678 (C²=O), 1638 (4-C=O). ¹H NMR spectrum, δ , ppm: 1.13 t (3H, CH₂CH₃), 2.35 s (3H, CH₃), 2.37 s (3H, CH₃), 4.11 m (2H, OCH₂), 7.03–7.92 m (18H, H_{arom}), 12.62 br.s (1H, OH). Found, %: C 76.25; H 5.21; N 4.78. C₃₇H₃₀N₂O₅. Calculated, %: C 76.27; H 5.19; N 4.81.

Ethyl 3-hydroxy-4-(4-methylbenzoyl)-1,6-bis(4methylphenyl)-2-oxo-8-phenyl-1,7-diazaspiro[4.4]nona-3,6,8-triene-9-carboxylate (IIIe). Yield 76%, mp 215–216°C (from benzene–ethyl acetate, 1:1). IR spectrum, v, cm⁻¹: 3269 (OH), 1725 (C=O, ester), 1667 (C²=O), 1642 (4-C=O). ¹H NMR spectrum, δ, ppm: 1.14 t (3H, CH₂CH₃); 2.21 s, 2.35 s, and 2.37 s (3H each, CH₃); 4.11 m (2H, OCH₂), 6.89–7.90 m (17H, H_{arom}), 12.61 br.s (1H, OH). Found, %: C 76.42; H 5.39; N 4.67. C₃₈H₃₂N₂O₅. Calculated, %: C 76.49; H 5.41; N 4.69. Ethyl 3-hydroxy-1-(4-methoxyphenyl)-4-(4methylbenzoyl)-6-(4-methylphenyl)-2-oxo-8-phenyl-1,7-diazaspiro[4.4]nona-3,6,8-triene-9-carboxylate (IIIf). Yield 76%, mp 215–216°C (from benzene–ethyl acetate, 1:1). IR spectrum, v, cm⁻¹: 3192 (OH), 1719 (C=O, ester), 1682 (C²=O), 1636 (4-C=O). ¹H NMR spectrum, δ, ppm: 1.14 t (3H, CH₂CH₃), 2.35 s and 2.37 s (3H each, CH₃), 3.66 s (3H, OMe), 4.13 m (2H, OCH₂), 6.88–7.92 m (17H, H_{arom}), 12.62 br.s (1H, OH). Found, %: C 74.41; H 5.24; N 4.59. C₃₈H₃₂N₂O₆. Calculated, %: C 74.49; H 5.26; N 4.57.

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