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Five-Membered 2,3-Dioxo Heterocycles: LV.* Reaction of Methyl 1-Aryl-3-aroyl-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates with Ethyl 3-Arylaminobut-2-enoates

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Abstract—Methyl 1-aryl-3-aroyl-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates reacted with ethyl 3-arylaminobut-2-enoates to give the corresponding ethyl 1,7-diaryl-4-aroyl-3-hydroxy-8-methyl-2,6-dioxo-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylates.

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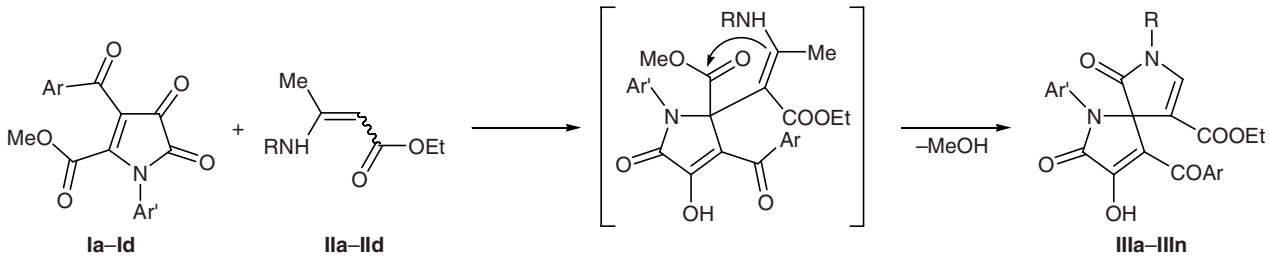
In continuation of our studies on recyclizations and heterocyclizations of acyl-substituted 1*H*-pyrrole-2,3-diones by the action of difunctional nucleophiles, the present communication reports on reactions of methyl 1-aryl-3-aroyl-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates **Ia**–**Id** with acyclic 1,3-C,N-binucleophiles, ethyl 3-arylaminobut-2-enoates **IIa**–**IId**. The reactions were carried out with equimolar amounts of the reactants by heating in boiling anhydrous benzene over a period of 0.5–2 min. As a result, we isolated the corresponding ethyl 1,7-diaryl-4-aroyl-3-hydroxy-8-methyl-2,6-dioxo-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylates **IIIa**–**IIIn** in almost quantitative yield [2] (Scheme 1). Compounds **IIIa**–**IIIn** are colorless crystalline substances which melt with decomposition at high temperature; they are readily soluble in DMF and DMSO, poorly soluble in other common organic solvents, and insoluble in saturated hydrocarbons and water. The presence of enolic hydroxy group in molecules **IIIa**–**IIIn** was confirmed by a positive color test with an alcoholic solution of iron(III) chloride.

The IR spectra of **IIIa**–**IIIn** contain absorption bands belonging to stretching vibrations of the enolic hydroxy group (one or two diffuse bands in the region 3145–3458 cm^{-1}), two lactam and one ester carbonyl groups (two or three peaks in the region 1678–1767 cm^{-1}), and ketone carbonyl group in the aroyl fragment (1626–1675 cm^{-1}). Compounds **IIIa**–**IIIn** displayed in the ^1H NMR spectra signals from protons in the aromatic rings and substituents attached thereto,

Scheme 1.



Ia–Id **IIa–IId** **IIIa–IIIn**

I, Ar = Ph (**a**–**c**), Ar′ = Ph (**a**), 4-MeC_6H_4 (**b**), 4-ClC_6H_4 (**c**); Ar = 4-$EtOC_6H_4$, Ar′ = 4-MeC_6H_4 (**d**); **II**, R = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 4-ClC_6H_4 (**d**); **III**, Ar = Ar′ = Ph; R = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 4-ClC_6H_4 (**d**); Ar = 4-MeC_6H_4, Ar′ = R = Ph (**e**); Ar = R = 4-MeC_6H_4, Ar′ = Ph (**f**); Ar = 4-MeC_6H_4, Ar′ = Ph, R = 4-$MeOC_6H_4$ (**g**), 4-ClC_6H_4 (**h**); Ar = 4-ClC_6H_4, Ar′ = Ph, R = Ph (**i**), 4-MeC_6H_4 (**j**); Ar = R = 4-ClC_6H_4, Ar′ = Ph (**k**); Ar = 4-MeC_6H_4, Ar′ = 4-$EtOC_6H_4$, R = Ph (**l**), 4-$MeOC_6H_4$ (**m**), 4-ClC_6H_4 (**n**).

* For communication LIV, see [1].

a singlet from the methyl group on C^8 (δ 2.06–2.13 ppm), a triplet and a quartet from the ester ethyl group (δ 1.20–1.23 and 4.07–4.12 ppm, respectively), and a broadened singlet from the enolic hydroxy proton (δ 12.38–12.72 ppm). The spectral parameters of spirodipyrroles **IIIa**–**IIIn** are fairly similar to those reported for structurally related spiro-fused heterocycles including a pyrrole [2], indole [3, 4], and isoquinoline fragments [5], whose structure was proved by X-ray analysis [4, 5].

Presumably, the first stage of the process is addition of the activated β-CH group of enamine **II** at the C^2 atom of pyrroledione **I**. The subsequent closure of the second pyrrole ring occurs via intramolecular attack by the amino group in the enamine fragment on the ester carbonyl carbon atom, which is accompanied by elimination of methanol. The described reaction is a rare example of regioselective synthesis of a difficultly accessible spiroheterocyclic system having various functional substituents in both heterocyclic fragments.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrophotometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were measured on a Bruker WP-400 instrument at 400 MHz using DMSO-d_6 as solvent and TMS as internal reference. The mass spectra (electron impact, 70 eV) were obtained on an MKh-1320 mass spectrometer. The purity of the isolated compounds was checked by TLC on Silufol plates using ethyl acetate or ethyl acetate–benzene (1:5) as eluent; spots were visualized by treatment with iodine vapor.

Ethyl 4-benzoyl-3-hydroxy-8-methyl-2,6-dioxo-1,7-diphenyl-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIa). A solution of 1.0 mmol of pyrroledione **Ia** and 1.0 mmol of enamine **IIa** in 10 ml of anhydrous benzene was heated for 1 min under reflux. The mixture was cooled, and the precipitate was filtered off. Yield 0.45 g (88%), mp 234–236°C (decomp., from ethyl acetate). IR spectrum, ν, cm^{-1}: 3350 br (OH); 1740, 1710, 1680 (9-C=O, C^2=O, C^6=O); 1628 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.22 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.0 Hz), 2.09 s (3H, Me), 4.11 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.0 Hz), 7.15–7.77 m (15H, H_{arom}), 12.64 br.s (1H, OH). Found, %: C 70.85; H 4.74; N 5.53. $C_{30}H_{24}N_2O_6$. Calculated, %: C 70.86; H 4.76; N 5.51.

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

Ethyl 4-benzoyl-3-hydroxy-8-methyl-7-(4-methylphenyl)-2,6-dioxo-1-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIb). Yield 82%, mp 237–238°C (decomp., from ethyl acetate). IR spectrum, ν, cm^{-1}: 3450 br, 3180 br (OH); 1754, 1698, 1682 (9-C=O, C^2=O, C^6=O); 1633 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.22 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.0 Hz), 2.07 s (3H, Me), 2.39 s (3H, $\mathbf{Me}C_6H_4$), 4.11 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.0 Hz), 7.14–7.76 m (14H, H_{arom}), 12.66 br.s (1H, OH). Found, %: C 71.26; H 5.04; N 5.32. $C_{31}H_{26}N_2O_6$. Calculated, %: C 71.25; H 5.02; N 5.36.

Ethyl 4-benzoyl-3-hydroxy-7-(4-methoxyphenyl)-8-methyl-2,6-dioxo-1-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIc). Yield 87%, mp 183–185°C (decomp., from ethyl acetate). IR spectrum, ν, cm^{-1}: 3425 br (OH); 1758, 1705, 1688 (9-C=O, C^2=O, C^6=O); 1637 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.22 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.0 Hz), 2.07 s (3H, Me), 3.82 s (3H, OMe), 4.11 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.0 Hz), 7.11–7.76 m (14H, H_{arom}), 12.58 br.s (1H, OH). Found, %: C 69.16; H 4.85; N 5.25. $C_{31}H_{26}N_2O_7$. Calculated, %: C 69.14; H 4.87; N 5.20.

Ethyl 4-benzoyl-7-(4-chlorophenyl)-3-hydroxy-8-methyl-2,6-dioxo-1-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIId). Yield 80%, mp 223–225°C (decomp., from ethyl acetate). IR spectrum, ν, cm^{-1}: 3448 br (OH); 1745, 1699, 1680 (9-C=O, C^2=O, C^6=O); 1654 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.22 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.0 Hz), 2.11 s (3H, Me), 4.12 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.0 Hz), 7.14–7.76 m (14H, H_{arom}), 12.59 br.s (1H, OH). Mass spectrum, m/z (I_{rel}, %): 542 (10) $[M]^+$, 437 (5) $[M - PhCO]^+$, 152 (18), 318 (13), 105 (100) $[PhCO]^+$, 77 (28) $[Ph]^+$. Found, %: C 66.37; H 4.28; Cl 6.52; N 5.15. $C_{30}H_{23}ClN_2O_6$. Calculated, %: C 66.36; H 4.27; Cl 6.53; N 5.16. M 542.98.

Ethyl 4-benzoyl-3-hydroxy-8-methyl-1-(4-methylphenyl)-2,6-dioxo-7-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIe). Yield 80%, mp 218–220°C (decomp., from methanol). IR spectrum, ν, cm^{-1}: 3455 br (OH); 1742, 1700, 1685 (9-C=O, C^2=O, C^6=O); 1635 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.23 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.0 Hz), 2.09 s (3H, Me), 2.35 s (3H, $\mathbf{Me}C_6H_4$), 4.11 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.0 Hz), 7.03–7.76 m (14H, H_{arom}), 12.65 br.s (1H, OH). Found, %: C 71.26; H 5.01; N 5.35. $C_{31}H_{26}N_2O_6$. Calculated, %: C 71.25; H 5.02; N 5.36.

Ethyl 4-benzoyl-3-hydroxy-8-methyl-1,7-bis(4-methylphenyl)-2,6-dioxo-1,7-diazaspiro[4.4]nona-

3,8-diene-9-carboxylate (IIIf). Yield 82%, mp 233–234°C (decomp., from ethyl acetate). IR spectrum, ν, cm^{-1}: 3420 br (OH); 1752, 1710 (9-C=O, C^2=O, C^6=O); 1645 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.22 t (3H, $OCH_2C\mathbf{H}_3$, *J* = 7.0 Hz), 2.07 s (3H, Me), 2.34 s (3H, $\mathbf{Me}C_6H_4$), 2.39 s (3H, $\mathbf{Me}C_6H_4$), 4.09 q (2H, $OC\mathbf{H}_2CH_3$, *J* = 7.0 Hz), 7.00–7.75 m (13H, H_{arom}), 12.60 br.s (1H, OH). Found, %: C 71.65; H 5.28; N 5.20. $C_{32}H_{28}N_2O_6$. Calculated, %: C 71.63; H 5.26; N 5.22.

Ethyl 4-benzoyl-3-hydroxy-7-(4-methoxyphenyl)-8-methyl-1-(4-methylphenyl)-2,6-dioxo-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIg). Yield 86%, mp 214–215°C (decomp., from methanol). IR spectrum, ν, cm^{-1}: 3456 br (OH); 1767, 1705, 1695 (9-C=O, C^2=O, C^6=O); 1643 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.22 t (3H, $OCH_2C\mathbf{H}_3$, *J* = 7.0 Hz), 2.07 s (3H, Me), 2.35 s (3H, $\mathbf{Me}C_6H_4$), 3.83 s (3H, MeO), 4.10 q (2H, $OC\mathbf{H}_2CH_3$, *J* = 7.0 Hz), 7.01–7.77 m (13H, H_{arom}), 12.59 br.s (1H, OH). Found, %: C 69.57; H 5.12; N 5.05. $C_{32}H_{28}N_2O_7$. Calculated, %: C 69.56; H 5.11; N 5.07.

Ethyl 4-benzoyl-7-(4-chlorophenyl)-3-hydroxy-8-methyl-1-(4-methylphenyl)-2,6-dioxo-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIh). Yield 79%, mp 240–242°C (decomp., from ethyl acetate). IR spectrum, ν, cm^{-1}: 3452 br (OH); 1752, 1715, 1680 (9-C=O, C^2=O, C^6=O); 1648 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.22 t (3H, $OCH_2C\mathbf{H}_3$, *J* = 7.0 Hz), 2.12 s (3H, Me), 2.34 s (3H, $\mathbf{Me}C_6H_4$), 4.11 q (2H, $OC\mathbf{H}_2CH_3$, *J* = 7.0 Hz), 7.00–7.75 m (13H, H_{arom}), 12.72 br.s (1H, OH). Found, %: C 66.88; H 4.51; Cl 6.39; N 5.02. $C_{31}H_{25}ClN_2O_6$. Calculated, %: C 66.85; H 4.52; Cl 6.36; N 5.03.

Ethyl 4-benzoyl-1-(4-chlorophenyl)-3-hydroxy-8-methyl-2,6-dioxo-7-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIi). Yield 89%, mp 243–245°C (decomp., from ethyl acetate). IR spectrum, ν, cm^{-1}: 3455 br (OH); 1745, 1705, 1690 (9-C=O, C^2=O, C^6=O); 1638 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.21 t (3H, $OCH_2C\mathbf{H}_3$, *J* = 7.0 Hz), 2.13 s (3H, Me), 4.10 q (2H, $OC\mathbf{H}_2CH_3$, *J* = 7.0 Hz), 7.16–7.76 m (14H, H_{arom}), 12.69 br.s (1H, OH). Found, %: C 66.37; H 4.26; Cl 6.54; N 5.14. $C_{30}H_{23}ClN_2O_6$. Calculated, %: C 66.36; H 4.27; Cl 6.53; N 5.16.

Ethyl 4-benzoyl-1-(4-chlorophenyl)-3-hydroxy-8-methyl-7-(4-methylphenyl)-2,6-dioxo-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIj). Yield 85%, mp 239–241°C (decomp., from ethyl acetate). IR spectrum, ν, cm^{-1}: 3450 br (OH); 1746, 1698, 1680 (9-C=O, C^2=O, C^6=O); 1635 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.21 t (3H, $OCH_2C\mathbf{H}_3$, *J* = 7.0 Hz), 2.11 s (3H, Me), 2.39 s (3H, $\mathbf{Me}C_6H_4$), 4.09 q (2H, $OC\mathbf{H}_2CH_3$, *J* = 7.0 Hz), 7.16–7.75 m (13H, H_{arom}), 12.68 br.s (1H, OH). Found, %: C 66.86; H 4.53; Cl 6.38; N 5.04. $C_{31}H_{25}ClN_2O_6$. Calculated, %: C 66.85; H 4.52; Cl 6.36; N 5.03.

Ethyl 4-benzoyl-1,7-bis(4-chlorophenyl)-3-hydroxy-8-methyl-2,6-dioxo-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIk). Yield 78%, mp 223–225°C (decomp., from ethyl acetate–dichloroethane). IR spectrum, ν, cm^{-1}: 3458 br (OH); 1745, 1697, 1678 (9-C=O, C^2=O, C^6=O); 1636 (PhC=O). ^{1}H NMR spectrum, δ, ppm: 1.21 t (3H, $OCH_2C\mathbf{H}_3$, *J* = 7.0 Hz), 2.15 s (3H, Me), 4.10 q (2H, $OC\mathbf{H}_2CH_3$, *J* = 7.0 Hz), 7.15–7.75 m (13H, H_{arom}), 12.86 br.s (1H, OH). Found, %: C 62.43; H 3.81; Cl 12.29; N 4.82. $C_{30}H_{22}Cl_2N_2O_6$. Calculated, %: C 62.40; H 3.84; Cl 12.28; N 4.85.

Ethyl 4-(4-ethoxybenzoyl)-3-hydroxy-8-methyl-1-(4-methylphenyl)-2,6-dioxo-7-phenyl-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIl). Yield 79%, mp 259–261°C (decomp., from methanol). IR spectrum, ν, cm^{-1}: 3435 br (OH); 1745, 1698 (9-C=O, C^2=O, C^6=O); 1630 (ArC=O). ^{1}H NMR spectrum, δ, ppm: 1.21 t (3H, $OCH_2C\mathbf{H}_3$, *J* = 7.0 Hz), 1.37 t (3H, $C_6H_4OCH_2C\mathbf{H}_3$, *J* = 7.1 Hz), 2.08 s (3H, Me), 2.34 s (3H, $\mathbf{Me}C_6H_4$), 4.09 q (2H, $OC\mathbf{H}_2CH_3$, *J* = 7.0 Hz), 4.13 q (2H, $C_6H_4OC\mathbf{H}_2CH_3$, *J* = 7.1 Hz), 7.01–7.77 (13H, H_{arom}), 12.42 br.s (1H, OH). Found, %: C 69.96; H 5.35; N 4.96. $C_{33}H_{30}N_2O_7$. Calculated, %: C 69.95; H 5.34; N 4.94.

Ethyl 4-(4-ethoxybenzoyl)-3-hydroxy-7-(4-methoxyphenyl)-8-methyl-1-(4-methylphenyl)-2,6-dioxo-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIm). Yield 74%, mp 245–246°C (decomp., from ethyl acetate). IR spectrum, ν, cm^{-1}: 3440 br, 3145 br (OH); 1750, 1694, 1682 (9-C=O, C^2=O, C^6=O); 1626 (ArC=O). ^{1}H NMR spectrum, δ, ppm: 1.20 t (3H, $OCH_2C\mathbf{H}_3$, *J* = 7.0 Hz), 1.36 t (3H, $C_6H_4OCH_2C\mathbf{H}_3$, *J* = 7.1 Hz), 2.06 s (3H, Me), 2.34 s (3H, $\mathbf{Me}C_6H_4$), 3.83 s (3H, OMe), 4.07 q (2H, $OC\mathbf{H}_2CH_3$, *J* = 7.0 Hz), 4.14 q (2H, $C_6H_4OC\mathbf{H}_2CH_3$, *J* = 7.1 Hz), 7.00–7.77 m (12H, H_{arom}), 12.38 br.s (1H, OH). Found, %: C 68.46; H 5.44; N 4.72. $C_{34}H_{32}N_2O_8$. Calculated, %: C 68.45; H 5.41; N 4.70.

Ethyl 7-(4-chlorophenyl)-4-(4-ethoxybenzoyl)-3-hydroxy-8-methyl-1-(4-methylphenyl)-2,6-dioxo-1,7-diazaspiro[4.4]nona-3,8-diene-9-carboxylate (IIIn). Yield 80%, mp 255–257°C (decomp., from ethyl acetate). IR spectrum, ν, cm^{-1}: 3410 br, 3300 br

(OH); 1758, 1722 (9-C=O, C^2=O, C^6=O); 1675 (ArC=O). ^{1}H NMR spectrum, δ, ppm: 1.21 t (3H, $OCH_2C\mathbf{H}_3$, *J* = 7.0 Hz), 1.36 t (3H, $C_6H_4OCH_2C\mathbf{H}_3$, *J* = 7.1 Hz), 2.11 s (3H, Me), 2.34 s (3H, $\mathbf{Me}C_6H_4$), 4.08 q (2H, $OC\mathbf{H}_2CH_3$, *J* = 7.0 Hz), 4.14 q (2H, $C_6H_4OC\mathbf{H}_2CH_3$, *J* = 7.1 Hz), 6.99–7.78 m (12H, H_{arom}), 12.47 br.s (1H, OH). Found, %: C 65.96; H 4.88; Cl 5.92; N 4.65. $C_{33}H_{29}ClN_2O_7$. Calculated, %: C 65.94; H 4.86; Cl 5.90; N 4.66.

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