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Synthesis of 2-Phenyl-5,6-dihydropyrano[2,3-*c*]pyrrole-4,7-dione Derivatives

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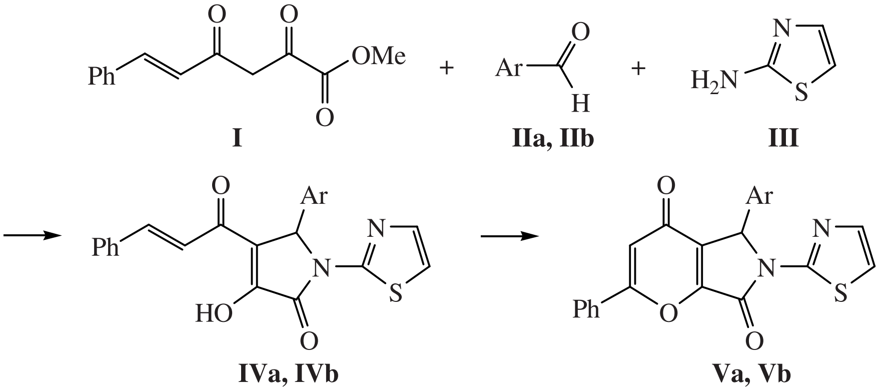
Pyrano[2,3-*c*]pyrroles constitute a poorly explored class of fused heterocyclic compounds. We have found only one publication where the synthesis of such compounds containing an alkoxycarbonyl or carboxy group in the 2-position has been described [1]. We have developed a new synthetic approach to pyrano[2,3-*c*]pyrrole-4,7-dione derivatives on the basis of methyl (*E*)-6-phenyl-2,4-dioxohex-5-enoate (**I**) [2]. By heating equimolar amounts of compound **I**, aromatic aldehyde **IIa** or **IIb**, and 2-aminothiazole (**III**) in glacial acetic acid for a short time we obtained the corresponding 5-aryl-3-hydroxy-4-(3-phenylprop-2-enoyl)-1-(1,3-thiazol-2-yl)-1,5-dihydro-2*H*-pyrrol-2-ones **IVa** and **IVb** in moderate yield. Compounds of type **IV** have been reported previously [3]. The structure of pyrroles **IVa** and **IVb** was confirmed by elemental analyses and IR and ^{1}H NMR spectra. On heating in DMSO in the presence of a catalytic amount of iodine, compounds **IVa** and **IVb** underwent intramolecular cyclization to 5-aryl-2-phenyl-6-(1,3-thiazol-2-yl)-5,6-dihydropyrano[2,3-*c*]pyrrole-4,7-diones **Va** and **Vb**, respectively. Such cyclization with formation of pyran ring is used in the chemistry of chromone [4, 5].



Ar = C_6H_5 (**a**), 4-ClC_6H_4 (**b**).

Compounds **Va** and **Vb** are colorless crystalline substances which are sparingly soluble in acetic acid, dioxane, benzene, and acetonitrile. The IR spectra (KBr) contain three strong absorption bands in the region 1600–1750 cm^{-1}: 1620–1640, 1660–1680, 1710–1740 cm^{-1}. No absorption was observed in the region 3150–3600 cm^{-1}, indicating that the cyclization involved the hydroxy group in **IV**. The ^{1}H NMR spectra of pyranopyrroles **Va** and **Vb** are consistent with the assumed structure. The 5-H proton resonates as a singlet at δ 6.30–6.50 ppm, and the 3-H signal appeared as a singlet at δ 7.15–7.25 ppm.

The described procedure makes it possible to obtain a wide series of 2-aryl-5,6-dihydropyrano[2,3-*c*]pyrrole-4,7-dione derivatives which attract interest from the viewpoint of the search for biologically active compounds and the examine their chemical properties. The scope of application of this method for building up fused pyranone derivatives will be considered elsewhere.

3-Hydroxy-5-phenyl-4-(3-phenylprop-2-enoyl)-1-(1,3-thiazol-2-yl)-1,5-dihydro-2*H*-pyrrol-2-one (IVa). A mixture of 0.01 mol of compound **I**, 0.01 mol of benzaldehyde, and 0.01 mol of 2-aminothiazole in 15 ml of glacial acetic acid was heated for 20 min under reflux. The mixture was cooled, and the precipitate was filtered off, washed with 5 ml of acetic acid and 10 ml of ethanol, and recrystallized from DMF–ethanol. Yield 42%, mp 246–247°C. IR spectrum, ν, cm^{-1}: 1600 (C=C), 1650 (C=O, ketone), 1690 (C=O, lactam), 3250 (OH). ^1H NMR spectrum, δ, ppm: 6.12 s (1H, 5-H), 7.18–7.71 m (14H, H_{arom}). Found, %: C 68.26; H 4.22; N 7.09; S 8.23. $C_{22}H_{16}N_2O_3S$. Calculated, %: C 68.03; H 4.15; N 7.21; S 8.25.

5-(4-Chlorophenyl)-3-hydroxy-4-(3-phenylprop-2-enoyl)-1-(1,3-thiazol-2-yl)-1,5-dihydro-2*H*-pyrrol-2-one (IVb) was synthesized in a similar way. Yield 45%, mp 242–243°C (from DMF–ethanol, 4:1). IR spectrum, ν, cm^{-1}: 1600 (C=C), 1650 (C=O, ketone), 1690 (C=O, lactam), 3200 (OH). ^1H NMR spectrum, δ, ppm: 6.07 s (1H, 5-H), 7.23–7.71 m (13H, Harom). Found, %: C 62.77; H 3.61; Cl 8.30; N 6.49; S 7.66. $C_{22}H_{15}ClN_2O_3S$. Calculated, %: C 62.49; H 3.58; Cl 8.38; N 6.62; S 7.58.

2,5-Diphenyl-6-(1,3-thiazol-2-il)-5,6-dihydropyrano[2,3-*c*]pyrrole-4,7-dione (Va). A catalytic amount of iodine was added to a solution of 0.003 mol of compound **IVa** in 15 ml of DMSO, and the mixture was heated for 30 min under reflux. It was then diluted with 50 ml of water, and the precipitate was filtered off, washed with a 5% solution of sodium thiosulfate (to remove traces of iodine) and water, and recrystallized from DMF–ethanol (3:1). Yield 42%, mp 288–289°C. IR spectrum, ν, cm^{-1}: 1630 (C=C), 1680 (C^4=O), 1720 (C^7=O). ^1H NMR spectrum, δ, ppm: 6.37 s (1H, 5-H), 7.19 s (1H, 3-H), 7.25–7.65 m (10H, H_{arom}), 7.97–8.05 m (2H, H_{arom}). Found, %: C 68.07; H 3.81; N 7.24; S 8.55. $C_{22}H_{14}N_2O_3S$. Calculated, %: C 68.38; H 3.65; N 7.25; S 8.30.

5-(4-Chlorophenyl)-2-phenyl-6-(1,3-thiazol-2-yl)-5,6-dihydropyrano[2,3-*c*]pyrrole-4,7-dione (Vb) was obtained in a similar way. Yield 47%, mp 259–260°C (from DMF–ethanol, 4:1). IR spectrum, ν, cm^{-1}: 1630 (C=C), 1680 (C^4=O), 1720 (C^7=O). ^1H NMR spectrum, δ, ppm: 6.39 s (1H, 5-H), 7.21 s (1H, 3-H), 7.35–7.65 m (9H, H_{arom}), 7.97–8.05 m (2H, H_{arom}). Found, %: C 63.02; H 3.35; Cl 8.69; N 6.81; S 7.87. $C_{22}H_{13}ClN_2O_3S$. Calculated, %: C 62.78; H 3.11; Cl 8.42; N 6.66; S 7.62.

The IR spectra were recorded in KBr on a UR-20 spectrometer. The ^1H NMR spectra were measured on a Varian VXR-300 instrument from solutions in DMSO-d_6 using hexamethyldisiloxane as internal reference.

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