ISSN 1070-3632, Russian Journal of General Chemistry, 2011, Vol. 81, No. 3, pp. 617–619. © Pleiades Publishing, Ltd., 2011. Original Russian Text © R.N. Vydzhak, S.Ya. Panchishin, 2011, published in Zhurnal Obshchei Khimii, 2011, Vol. 81, No. 3, pp. 522–524.

LETTERS TO THE EDITOR

Synthesis of 1,2-Dihydrochromeno[2,3-*c*]pyrrole-3,9-diones Spiro Derivatives

R. N. Vydzhak and S. Ya. Panchishin

Institute of Bioorganic and Petroleum Chemistry, National Academy of Sciences of Ukraine, ul. Murmanskaya 1, Kiev, 02094 Ukraine e-mail: vydzhak@mail.ru

Received August 23, 2010

DOI: 10.1134/S1070363211030340

Previously it was found that methyl *o*-hydroxybenzoylpyruvate was easily converted into 1,2-diaryl-[1], 1-aryl-2-heteryl- [2], or 2-alkyl-1-aryl-1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-diones [3]. Isatin and its *N*-alkyl derivatives are known to behave in many transformations like aromatic aldehydes. We found that the short-time heating of equimolar amounts of methyl *o*hydroxybenzoylpyruvate **I**, *N*-methylisatin **II**, and aliphatic amines **IIIa**, **IIIb** in methanol afford spiro derivatives of 3-hydroxy-3-pyrrolin-2-one **IVa**, **IVb** in high yield. This three-component cyclocondensation has been well studied [4], but isatin and its derivatives have not been used as carbonyl components. Pyrrole derivatives **IV** possess acidic properties and form adducts with aliphatic amines. Compound **IVb** exists as an internal salt. Similar adducts with monoethanolamine were described [5].

Compounds IVa, IVb are yellow crystalline substances. Their composition was confirmed by the



elemental analysis, and structure, by the IR and ¹H NMR spectroscopy. Heating of hydroxypyrrolones **IVa**, **IVb** in acetic acid leads to their dehydration to give 1,2-spiro derivatives of dihydrochromeno[2,3-*c*]-pyrrole-3,9-diones **Va**, **Vb**. The structure of the latter was confirmed by the IR and ¹H NMR spectroscopy, and their composition, by the elemental analysis data.

The IR spectra of 1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-diones recorded from KBr pellets in the range of 1590–1730 cm⁻¹ contain the following absorption bands: 1605–1615 (moderate intensity), 1650–1680 (strong band) and 1700–1740 cm⁻¹ (two strong bands). In the range of 3200–3600 cm⁻¹ no absorption bands were observed, which confirmed the participation of OH-groups in the cyclocondensation. In the ¹H NMR spectra of compounds **Va**, **Vb** there are all the signals of hydrogen atoms. The hydrogen atoms of methylene groups in position 2 of the heterocycle are diastereotopic and appear as two multiplets.

Thus, the spiro derivatives of 1,2-dihydrochromeno-[2,3-c]pyrrole-3,9-diones, which are interesting as potential biologically active substances, were first obtained. The scope of this approach to the synthesis of condensed derivatives of chromone will be considered in the future.

The IR spectra of the compounds were recorded on a VERTEX 70 spectrometer (Bruker) from KBr pellets. The ¹H NMR spectra were obtained on a spectrometer Varian VXR-300 in DMSO- d_6 with internal reference HMDS.

3-Hydroxy-4-(2-hydroxybenzoyl)-1-(2-phenylethyl)-1,5-dihydro-2H-pyrrole-5-spiro[3'(1'-methyl-1',3'dihydro-2'H-indole)]-2,2'-dione adduct with 2-phenvlethylamine (IVa). To a suspension of 0.01 mol of Nmethylisatin II in 15 ml of anhydrous methanol was added 0.01 mol of 2-phenylethylamine IIIa. The mixture was heated to 50°C and kept for 5 min. Then the second portion of 0.01 mol of 2-phenylethylamine and 0.01 mol of methyl o-hydroxybenzoylpyruvate I was added. The reaction mixture was heated to boiling and then allowed to stand for 30 min at 35-40°C and cooled. The precipitate was filtered off, washed with methanol and ethyl acetate. The formed compound IVa was used without further purification. Yield 71%, vellow crystals. For the analysis a sample of the compound IVa was purified by crystallization from ethanol and dried at 85°C for 7 days. mp 153–155°C. IR spectrum, v, cm⁻¹: 1614 (C=O, ketone), 1696 (C=O), 1710 (C=O), 3410 (OH). ¹H NMR spectrum, δ,

ppm: 2.39–2.62 m (2H, CH₂), 2.84–3.09 m (6H, 3CH₂), 3.26 s (3H, NCH₃), 6.65–7.36 m (17H, Ph), 7.88 br.s (3H, NH₂, OH), 8.80 d (1H, Ph), 13.48 s (1H, OH). Found, %: C 73.24; H 5.70; N 7.57. $C_{27}H_{22}N_2O_5$ · $C_8H_{11}N$. Calculated, %: C 73.03; H 5.78; N 7.30.

Compound **IVb** was prepared similarly without adding the second portion of amine.

3-Hydroxy-4-(2-hydroxybenzoyl)-1-[3-(dimethylamino)propyl]-1,5-dihydro-2*H***-pyrrole-5-spiro-[3'(1'-methyl-1',3'-dihydro-2'***H***-indole)]-2,2'-dione (IVb).** Yield 67%, yellow crystals, mp 241–243°C (ethyl acetate). IR spectrum, v, cm⁻¹: 1612 (C=O, ketone), 1697 (C=O), 1727 (C=O), 3432 (OH). ¹H NMR spectrum, δ, ppm: 1.51–1.67 m (2H, CH₂), 2.59– 2.76 m [7H, H_B NCH₂, N(CH₃)₂], 2.81–2.92 m (2H, CH₂NMe₂), 3.15 m (1H, H_A NCH₂), 3.25 s (3H, NCH₃), 6.56–6.75 m (2H, Ph), 6.87–7.08 m (3H, Ph), 7.14–7.32 m (2H, Ph), 8.75 d (1H, Ph), 9.68 s (1H, OH), 13.22 s (1H, OH). Found, %: C 66.35; H 5.83; N 9.57. C₂₄H₂₅N₃O₅. Calculated, %: C 66.19; H 5.79; N 9.65.

2-(2-Phenylethyl)-1,2-dihydrochromeno[2,3-c]pyrrole-1-spiro[3'(1'-methyl-1',3'-dihydro-2'*H*indole)]-3,9,2'-trione (Va). A solution of adduct IVa in 10 ml of glacial acetic acid was refluxed for 1 h, cooled, and concentrated. The residue was ground with 15 ml of 2-propanol. The precipitate was filtered off, washed with 2-propanol and crystallized from DMF– ethanol mixture, 1:3. Yield 67%, colorless crystals, mp 237–238°C. IR spectrum, v, cm⁻¹: 1610 (C=C), 1669 (C=O), 1715 (C=O), 1726 (C=O). ¹H NMR spectrum, δ , ppm: 2.59–2.73 m (2H, CH₂Ph), 3.24–3.31 m (2H, NCH₂), 3.34 s (3H, NCH₃), 6.96–7.29 m (8H, Ph), 7.45–7.59 m (2H, Ph), 7.85–7.92 m (2H, Ph), 7.99 d (1H, Ph). Found, %: C 73.99; H 4.45; N 6.57. C₂₇H₂₀N₂O₄. Calculated, %: C 74.30; H 4.62; N 6.42.

2-[3-(Dimethylamino)propyl]-1,2-dihydrochromeno[2,3-c]pyrrole-1-spiro[3'(1'-methyl-1',3'dihydro-2'*H***-indol)]-3,9,2'-trione (Vb). A solution of 0.005 mol of dione IVb in 10 ml of glacial acetic acid was refluxed for 1 h, cooled, and concentrated. The residue was dissolved in 50 ml of a ice-water mixture, neutralized with saturated sodium hydrogen carbonate solution, and alkalinized with 5% NaOH solution to pH 8.5–9. The precipitate was filtered off, washed with ice water to the neutral reaction, dried, and crystallized from ethanol. Yield 67%, colorless crystals, mp 195– 197°C. IR spectrum, v, cm⁻¹: 1610 (C=C), 1672 (C=O), 1718 (C=O), 1731(C=O). ¹H NMR spectrum,** δ, ppm: 1.34–1.54 m (2H, CH₂), 1.97 s [6H, N(CH₃)₂], 2.03–2.13 m (2H, CH₂NMe₂), 3.06 m (1H, H_B NCH₂), 3.21 m (1H, H_A NCH₂), 3.32 s (3H, NCH₃), 7.03 d.d (1H, Ph), 7.21–7.28 m (2H, Ph), 7.43–7.58 m (2H, Ph), 7.84–7.92 m (2H, Ph), 8.02 d (1H, Ph). Found, %: C 69.57; H 5.44; N 10.23. C₂₄H₂₃N₃O₄. Calculated, %: C 69.05; H 5.55; N 10.07.

REFERENCES

1. Vydzhak, R.N. and Panchishin, S.Ya., *Zh. Obshch. Khim.*, 2006, vol. 76, no. 10. p. 1753.

- Vydzhak, R.N. and Panchishin, S.Ya., Bezuglaya, E.M., and Chernega, A.N., *Zh. Org. Farm. Khim.*, 2005, vol. 3, no. 3(11), p. 58.
- 3. Vydzhak, R.N. and Panchishin, S.Ya., *Zh. Obshch. Khim.*, 2008, vol. 78, no. 12, p. 2045.
- Perevalov, S.G., Burgart, Ya.V., Saloutin, V.I., and Chupakhin, O.N., *Usp. Khim.*, 2001, vol. 70, no. 11, p. 1039.
- Gein, V.L., Shumilovskikh, E.V., Voronina, E.V., Saraeva, R.F., Gein, L.F., Ugrak, B.I., and Andreichikov, Yu.S., *Zh. Obshch. Khim.*, 1994, vol. 64, no. 7, p. 1203.