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SHORT COMMUNICATIONS

Synthesis of Methyl 3-Acyl-6-amino-5-cyano-4-phenyl-4*H*-pyran-2-carboxylates and Their Rearrangement into 2-Hydroxy-4-[hydroxy(R)methylidene]-3-oxo-5-phenylcyclopent-1-ene-1-carbonitriles

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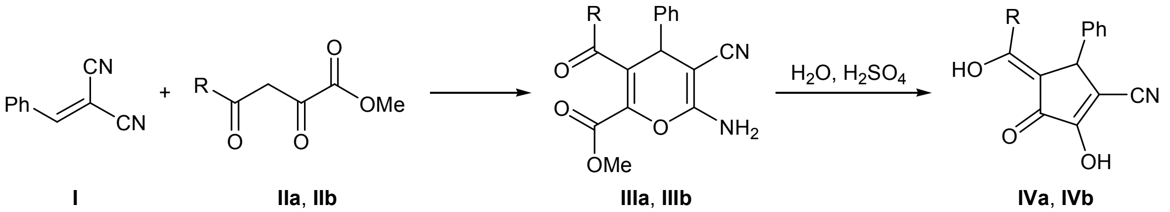
Synthesis of new 4*H*-pyrans is an important problem of organic chemistry. 4*H*-Pyran derivatives can readily be converted into organic compounds belonging to different classes. 4*H*-Pyrans, in particular 2-amino-3-cyano-4*H*-pyrans, are used as drugs, pesticides, analogs of natural compounds, dyes, and other important substances. They exhibit antimicrobial [1, 2], antiviral [3], analgesic [4], antitumor [5, 6], herbicidal [7, 8], and fungicidal [9] activity.

Methyl 2,4-dioxobutanoates are used in the synthesis of biologically active compounds [10, 11]. However, their reaction with benzylidenemalononitrile was not studied. We found that this reaction gives methyl 6-amino-3-acyl-5-cyano-4-phenyl-4*H*-pyran-2-carboxylates which can be used as intermediate products in the synthesis of carbo- and heterocycles. 2-Benzylidenemalononitrile (**I**) reacted with methyl 2,4-dioxopentanoate (**IIa**) and methyl 4-(4-methoxyphenyl)-2,4-dioxobutanoate in propan-2-ol in the presence of a catalytic amount of morpholine to produce substituted pyrans **IIIa** and **IIIb**, respectively. By heating compounds **IIIa** and **IIIb** in aqueous sulfuric acid over a period of 4–6 h we obtained cyclopentenones **IVa** and **IVb**. The structure of compounds **IIIa**, **IIIb**, **IVa**, and **IVb** was determined by IR spectroscopy, mass spectrometry, and X-ray analysis.

Development of new methods for the synthesis of cyclopentenone derivatives is important, for cyclopentenone fragment is a structural unit of many natural compounds and their analogs [12–14]. Known methods for building up 3-oxo-2-hydroxycyclopent-1-ene-1-carbonitrile fragment include three laborious steps and are characterized by poor yields (16–22%) [14]. The synthesis described in [14] required the use of organometallic compounds, chromium(III) carbonyl, titanium(IV) chloride, and iodine, as well as low temperature (–78 to –20°C). The overal reaction time in the synthesis of substituted 3-oxo-2-hydroxycyclopent-1-ene-1-carbonitrile was more than 24 h. The procedure proposed in the present work is simple and convenient, and complex multistep transformations are performed in one synthetic operation.



I **IIa**, **IIb** **IIIa**, **IIIb** **IVa**, **IVb**

R = Me (**a**), 4-MeOC$_6$H$_4$ (**b**).

Methyl 3-acetyl-6-amino-5-cyano-4-phenyl-4*H*-pyran-2-carboxylate (IIIa). Yield 82%, mp 185–186°C. IR spectrum, ν, cm^{-1}: 3399, 3317, 2198, 1734, 1691, 1647, 1602. Mass spectrum: *m*/*z* 298 $[M]^+$. Found, %: C 64.42; H 4.73; N 9.39. $C_{16}H_{14}N_2O_4$. Calculated, %: C 65.14; H 4.88; N 9.44. *M* 298.30.

Methyl 6-amino-5-cyano-3-(4-methoxybenzoyl)-4-phenyl-4*H*-pyran-2-carboxylate (IIIb). Yield 85%, mp 170–171°C. IR spectrum, ν, cm^{-1}: 3440, 3325, 2194, 1736, 1674, 1642, 1600. Mass spectrum: *m*/*z* 390 $[M]^+$. Found, %: C 67.75; H 4.84; N 7.02. $C_{22}H_{18}N_2O_5$. Calculated, %: C 67.69; H 4.65; N 7.18. *M* 390.39.

(*Z*)-2-Hydroxy-4-(1-hydroxyethylidene)-3-oxo-5-phenylcyclopent-1-ene-1-carbonitrile (IVa). Yield 28%, mp 179–180°C. IR spectrum, ν, cm^{-1}: 3435, 3205, 2222, 1650, 1638, 1603. Mass spectrum: *m*/*z* 241 $[M]^+$. Found, %: C 69.42; H 4.67; N 5.96. $C_{14}H_{11}NO_3$. Calculated, %: C 69.70; H 4.60; N 5.81. *M* 241.24.

(*Z*)-2-Hydroxy-4-[1-hydroxy-1-(4-methoxyphenyl)methylidene]-3-oxo-5-phenylcyclopent-1-ene-1-carbonitrile (IVb). Yield 43%, mp 169–170°C. IR spectrum, ν, cm^{-1}: 3440, 3250, 2209, 1670, 1640, 1610. Mass spectrum: *m*/*z* 333 $[M]^+$. Found, %: C 72.36; H 4.42; N 4.07. $C_{20}H_{15}NO_4$. Calculated, %: C 72.06; H 4.54; N 4.20. *M* 333.34.

The progress of reactions and the purity of the isolated compounds were monitored by TLC on Silufol UV-254 plates. The IR spectra were recorded on an FSM 1201 spectrometer from samples dispersed in mineral oil. The ^1H NMR spectra were recorded on a Bruker AM-500 instrument at 500.13 MHz using DMSO-d_6 as solvent and TMS as internal reference. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT INCOS-50 instrument.

Single crystals of compounds **IIIa** and **IVb** were examined on an Enraf–Nonius CAD-4 four-circle diffractometer (MoK_α irradiation, graphite monochromator, ω-scanning).. The unit cell parameters were determined and refined using 25 reflections in the Θ range from 11 to 20°. Compounds **IIIa** and **IVb** crystallized in triclinic crystal system, space group *P*-1, $Z = 2$. Unit cell parameters: **IIIa**: $a = 7.194(2)$, $b = 10.090(1)$, $c = 11.074(2)$ Å; $\alpha = 105.74(2)$, $\beta = 94.63(1)$, $\gamma = 75.05(2)°$; $V = 747.5(3)$ Å^3; **IVb**: $a = 9.5147(12)$, $b = 10.0778(13)$, $c = 9.5877(12)$ Å; $\alpha = 91.01(1)$, $\beta = 81.52(1)$, $\gamma = 113.13(2)°$; $V = 835.36(18)$ Å^3. The structures were solved, and the positions and thermal parameters of atoms were refined, using SHELX software package [15]. Hydrogen atoms were localized by Fourier difference syntheses, and their positions were refined in isotropic approximation. The positions and thermal vibration tensors of non-hydrogen atoms were refined in full-matrix anisotropic approximation. All non-zero reflections were involved in the refinement procedure. The unreliability coefficient was calculated from reflections with $|F^2| > 2\sigma$; number of reflections 2140 (**IIIa**) and 2850 (**IVb**). No correction for absorption was introduced taking into account insignificant linear absorption coefficient. The final *R* factor was 0.045 (**IIIa**) and 0.044 (**IVb**). The coordinates of atoms, bond lengths, angles, and thermal vibration parameters for structures **IIIa** and **IVb** were deposited to the Cambridge Crystallographic Data Centre [entry nos. CCDC 764770 (**IIIa**), CCDC 764769 (**IVb**)].

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