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SHORT COMMUNICATIONS

Reactions of Methyl 4-Hetaryl-2,4-dioxobutanoates with a Mixture of Aminoazole and Aromatic (Heteroaromatic) Aldehyde

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We previously described methods of synthesis of methyl 6-acyl-7-aryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylates and methyl 6-acyl-7-aryl-4,7-dihydrotriazolo[1,5-*a*]pyrimidine-5-carboxylates by reactions of methyl acylpyruvates with a mixture of an aromatic aldehyde and 5-aminotetrazole [1] or 3-amino-1,2,4-triazole [2], respectively. With a view to further study how the structure of heterocyclic amine affects the direction of these reactions in the present work we examined reactions of methyl 4-(2-thienyl)- and 4-(2-furyl)-2,4-dioxobutanoates with mixtures of aromatic (heteroaromatic) aldehydes and 5-amino-1-methyltetrazole, 3,5-diamino-1,2,4-tetrazole, and ethyl 5-amino-1*H*-imidazole-4-carboxylate.

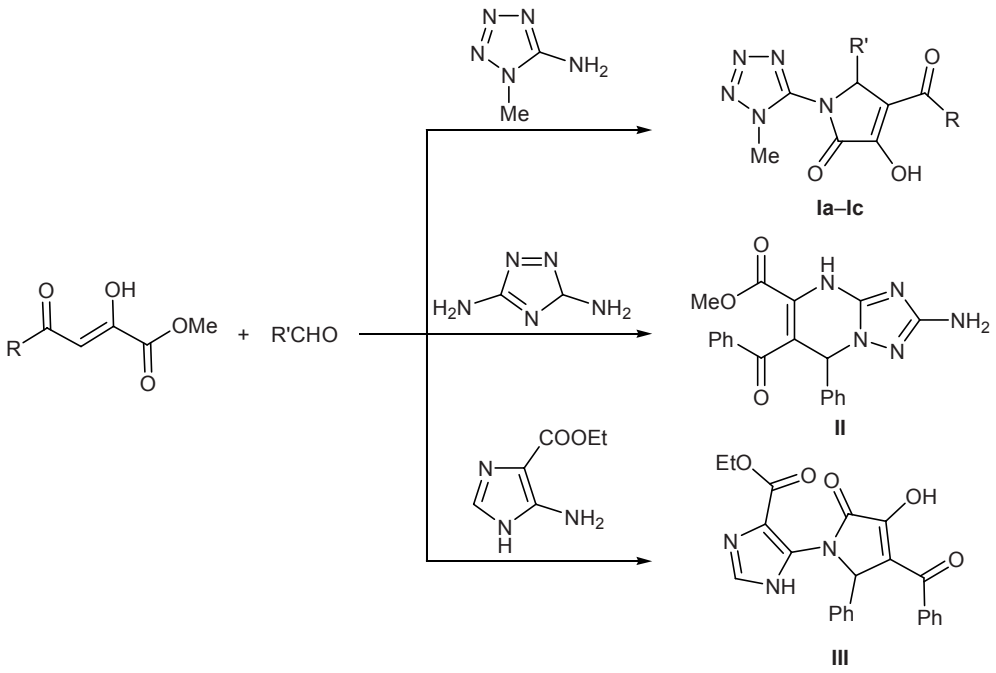
By heating for a short time a mixture of methyl 4-(2-thienyl)- or 4-(2-furyl)-2,4-dioxobutanoate, 5-amino-1-methyltetrazole, and thiophene-2-carbaldehyde, benzaldehyde, or pyridine-3-carbaldehyde in acetic acid we obtained the corresponding 5-aryl(hetaryl)-4-hetaroyl-3-hydroxy-1-(1-methyltetrazol-5-yl)-2,5-dihydro-1*H*-pyrrol-2-ones **Ia**–**Ic** (Scheme 1). Compounds **Ia**–**Ic** are colorless or slightly colored crystalline substances, which are readily soluble in DMF and DMSO, soluble in ethanol and acetic acid on heating, and insoluble in water. They give rise to a positive color test (cherry color) with an alcoholic solution of $FeCl_3$. The ^{1}H NMR spectra of **Ia**–**Ic** contain signals from aromatic protons, hydroxy proton, CH proton in the 5-position of the pyrrole ring (δ 6.13–6.48 ppm), and protons in the methyl group (δ 4.27–4.33 ppm, s). In the IR spectra of **Ia**–**Ic** we observed absorption bands due to vibrations of the ketone carbonyl group (1607–1620 cm^{-1}), lactam carbonyl group (1701–1755 cm^{-1}), and enol OH group (3250–3269 cm^{-1}).

The product structure indicates that replacement of hydrogen at N^1 in the 5-aminotetrazole molecule by methyl group prevents formation of fused tetrazolo-[1,5-*a*]pyrimidine system.

Fusion of methyl 4-phenyl-2,4-dioxobutanoate with 3,5-diamino-1,2,4-triazole, and benzaldehyde at 125–150°C gave methyl 2-amino-6-benzoyl-7-phenyl-4,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidine-5-carboxylate (**II**) which was isolated as a weakly colored crystalline substance soluble in organic solvents and insoluble in water. Compound **II** displayed in the ^{1}H NMR spectrum a two-proton doublet at δ 5.30 ppm from the primary amino group, a three-proton singlet at δ 3.20 ppm from the ester methyl group, a singlet at δ 6.21 ppm from the 7-H proton, a multiplet centered at δ 7.33 ppm from protons in the phenyl rings, and a singlet at δ 10.80 ppm from the NH proton in position *4*. The IR spectrum of **II** was consistent with the assumed structure. Presumably, triazolopyrimidine **II** is formed according to the mechanism proposed previously for methyl 6-acyl-7-aryl-4,7-dihydrotriazolo[1,5-*a*]pyrimidine-5-carboxylates [2].

Analogous reaction of methyl 4-phenyl-2,4-dioxobutanoate with ethyl 5-amino-1*H*-imidazole-4-carboxylate and benzaldehyde at 120–150°C led to the formation of ethyl 5-(4-benzoyl-3-hydroxy-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrol-1-yl)-1*H*-imidazole-4-carbox-

Scheme 1.



I, R = 2-thienyl (**a**), 2-furyl (**b**, **c**); R′ = 2-thienyl (**a**), Ph (**b**), 3-pyridyl (**c**).

ylate (**III**). Compound **III** is a weakly colored crystalline substance which is insoluble in water and soluble in organic solvents on heating. It gives a positive color test (cherry color) with an alcoholic solution of $FeCl_3$, which is typical of pyrrolediones. The ^{1}H NMR spectrum of **III** contained signals from protons in the ethoxy group and aromatic rings, a singlet from the 5-H proton in the pyrrole ring (δ 6.38 ppm), a singlet from 2-H in the imidazole ring (δ 8.55 ppm), and singlets from the NH and OH protons at δ 12.80 and 11.02 ppm, respectively. Presumably, the nucleophilicity and basicity of the NH nitrogen atom in ethyl 5-amino-1*H*-imidazole-4-carboxylate is considerably reduced due to enhanced aromaticity of the imidazole system and electron-withdrawing effect of the ester fragment.

3-Hydroxy-1-(1-methyltetrazol-5-yl)-4-(2-thenoyl)-5-(2-thienyl)-2,5-dihydro-1*H*-pyrrol-2-one (Ia). Thiophene-2-carbaldehyde, 0.01 mol, and an equimolar amount of 1-methyltetrazol-5-amine were dissolved on heating in 10 ml of acetic acid, 0.01 mol of methyl 4-(2-thienyl)-2,4-dioxobutanoate was added, and the mixture was heated to the boiling point and kept at room temperature until a solid separated. The precipitate was filtered off and recrystallized from acetic acid. Yield 0.63 g (16%), mp 242–244°C. IR spectrum, ν, cm^{-1}: 1620 (C=O), 1710 (C=O, lactam); 3250 (OH). ^{1}H NMR spectrum, δ, ppm: 6.48 s (1H, 5-H), 6.80 m (6H, H_{arom}), 4.33 s (3H, CH_3), 10.80 s (1H, OH). Found, %: C 47.99, 48.01; H 3.00, 2.98; N 18.80, 18.82. $C_{15}H_{11}N_5S_2O_3$. Calculated, %: C 48.25; H 2.94; N 18.76.

4-(2-Furoyl)-3-hydroxy-1-(1-methyltetrazol-5-yl)-5-phenyl-2,5-dihydro-1*H*-pyrrol-2-one (Ib) was synthesized in a similar way. Yield 0.96 g (27%), mp 266–268°C. IR spectrum, ν, cm^{-1}: 1614 (C=O), 1701 (C=O, lactam), 3266 (OH). ^{1}H NMR spectrum, δ, ppm: 6.13 s (1H, 5-H), 6.53 m (8H, H_{arom}), 4.27 s (3H, CH_3), 10.95 s (1H, OH). Found, %: C 59.79, 5976; H 3.90, 3.88; N 17.62, 17.57. $C_{17}H_{13}N_5O_4$. Calculated, %: C 59.82; H 3.81; N 17.59.

4-(2-Furoyl)-3-hydroxy-1-(1-methyltetrazol-5-yl)-5-(pyridin-3-yl)-2,5-dihydro-1*H*-pyrrol-2-one (Ic) was synthesized in a similar way. Yield 0.62 g (15%), mp 223–225°C. IR spectrum, ν, cm^{-1}: 1614 (C=O), 1701 (C=O, lactam), 3266 (OH). ^{1}H NMR spectrum, δ, ppm: 6.20 s (1H, 5-H), 6.55 m (7H, H_{arom}), 4.30 s (3H, CH_3), 10.78 s (1H, OH). Found, %: C 54.48, 54.50; H 3.38, 3.41; N 23.76, 23.80. $C_{16}H_{12}N_6O_4$. Calculated, %: C 54.54; H 3.40; N 23.86.

Methyl 2-amino-6-benzoyl-7-phenyl-4,7-dihydro-[1,2,4]triazolo[1,5-*a*]pyrimidine-5-carboxylate (II). A mixture of 0.01 mol of methyl 4-phenyl-2,4-dioxobutanoate, 0.01 mol of benzaldehyde, and 0.01 mol of

3*H*-1,2,4-triazole-3,5-diamine was heated on a metal bath at 125–150°C until gaseous products no longer evolved. The melt was cooled and treated with ethanol, and the precipitate was filtered off and recrystallized from ethanol and acetic acid. Yield 1.19 g (34%), mp 223–224°C. IR spectrum, ν, cm^{-1}: 1680 (C=O), 1715 (C=O, ester), 3210 (NH, NH_2). ^1H NMR spectrum, δ, ppm: 3.20 s (3H, OCH_3), 5.30 d (2H, NH_2), 6.21 s (1H, 7-H), 7.33 m (10H, H), 10.80 s (1H, NH). Found, %: C 61.69, 61.75; H 4.60, 4.63; N 20.15, 20.10. $C_{18}H_{16}N_5O_3$. Calculated, %: C 61.71; H 4.57; N 20.05.

5-(4-Benzoyl-3-hydroxy-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrol-1-yl)-1*H*-imidazole-4-carboxylate (III) was synthesized in a similar way. Yield 1.29 g (31%), mp 210–212°C. IR spectrum, ν, cm^{-1}: 1610 (C=O), 1705 (C=O, lactam), 1715 (C=O, ester), 3250 (OH), 3200 (NH). ^1H NMR spectrum, δ, ppm: 1.35 t (3H, CH_3), 4.37 q (2H, OCH_2), 6.38 s (1H, 5′-H), 8.55 s (1H, 2-H), 7.64 m (10H, H_{arom}), 11.02 s (1H, OH), 12.80 s (1H, NH). Found, %: C 66.20, 66.22; H 4.60, 4.62; N 10.17, 10.12. $C_{23}H_{19}N_3O_5$. Calculated, %: C 66.18; H 4.55; N 10.07.

The IR spectra were recorded on a UR-20 spectrometer from samples dispersed in mineral oil. The ^1H NMR spectra were measured on a Bruker DRX-500 instrument at 500.13 MHz in DMSO-d_6.

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