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LETTERS TO THE EDITOR

Synthesis of Diaryl-Substituted 3,4-Dimethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-5-carboxamides

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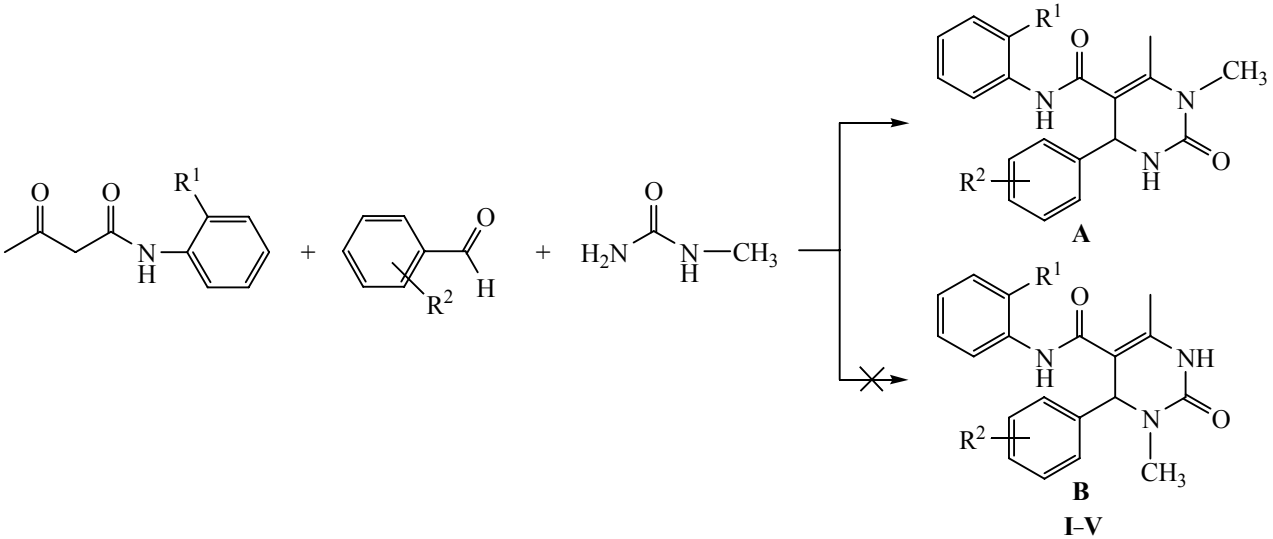
The multicomponent reactions, in particular Biginelli reaction, are commonly used to construct the heterocyclic systems as the preparation method of a broad range of compounds containing the pyrimidine ring [1, 2].

Previously we have shown that the *N*-aryl-substituted 6-aryl-4-methyl-2-oxo-1,2,3,6-tetrahydropyrimidine-5-carboxamides were formed in the reaction of acetylacetic acid *N*-arylamides with aromatic aldehyde and urea [3].

Continuing study in this area, we carried out a three-component condensation of *N*-2-methyl(chloro)-acetoacetanilides with *N*-methylurea and aromatic aldehydes to obtain the diaryl-substituted 3,4-dimethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-5-carboxamides **I**–**V**. The reaction occurs at 120–150°C in the solvent-free conditions within 10–15 min.

Compounds **I**–**V** are colorless crystalline substances, which are soluble in DMF, DMSO, chloroform, and ethanol (under heating), insoluble in water.

In the ^{1}H NMR spectra of compounds **I**–**V**, alongside the signals of aromatic protons and groups attached to the aromatic ring, there are two singlets at 3.05–3.10 and 1.91–2.27 ppm belonging to the CH_3 groups, the doublets of C^6H proton at 5.22–5.64 ppm, and of the N^1H proton at 7.60–7.96 ppm ($J_{1,6}$ 2.95–3.33 Hz), the singlet of the amide protons in the range of 9.02–9.43 ppm. The splitting of signals of the $H^{1,6}$ protons of the pyrimidine ring indicates that the



R^1 = Me, R^2 = H (**I**), R^1 = Me, R^2 = 2-Cl (**II**), R^1 = Cl, R^2 = H (**III**), R^1 = Cl, R^2 = 3-NO_2 (**IV**), R^1 = Cl, R^2 = 2-Cl (**V**).

reaction proceeds regioselectively, and the structure B is not formed.

The mass spectrum of compound **IV** contains a molecular ion peak at *m*/*z* 400 $[M]^+$ and the peaks of fragment ions at *m*/*z* 274 $[M - ClC_6H_4NH]^+$ and 153 $[M - ClC_6H_4NH - C_6H_4NO_2]^+$. In the mass spectrum of **V** there are the molecular ion peak at *m*/*z* 391 $[M]^+$ and the peaks of fragment ions at *m*/*z* 266 $[M - ClC_6H_4NHCO - C_6H_4Cl]^+$ and 77 $[Ph]^+$ (*m*/*z* 77), which confirm the assumed structure.

3,4-Dimethyl-*N*-(2-methylphenyl)-6-phenyl-2-oxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide (I). A mixture of 0.01 mol of 2-methylacetoacetanilide, 0.01 mol of benzaldehyde, and 0.01 mol of *N*-methylurea was heated at 120–150°C for 10–15 min until the gas evolution completed and the reaction mixture solidified. After cooling, the residue was treated with ethanol, filtered off, and recrystallized from ethanol. Yield 2.24 g (67%), mp 210–212°C. ^{1}H NMR spectrum, δ_H, ppm: 1.94 s (3H, C^4H_3), 2.21 s (3H, $\underline{CH_3}C_6H_4$), 3.05 s (3H, C^3H_3), 5.24 d (1H, CH, $J_{1,6}$ 2.95 Hz), 7.61 m (9H, Ar), 7.64 d (1H, N^1H, $J_{1,6}$ 2.95 Hz), 9.31 s (1H, NH_{amide}). Found, %: C 71.73, 71.51; H 6.23, 6.39; N 12.43, 12.63. $C_{20}H_{21}N_3O_2$. Calculated, %: C 71.62; H 6.31; N 12.53.

3,4-Dimethyl-*N*-(2-methylphenyl)-6-(2-chlorophenyl)-2-oxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide (II) was prepared similarly. Yield 2.66 g (72%), mp 192–194°C. ^{1}H NMR spectrum, δ_H, ppm: 1.91 s (3H, C^4H_3), 2.23 s (3H, $\underline{CH_3}C_6H_4$), 3.09 s (3H, C^3H_3), 5.64 d (1H, CH, $J_{1,6}$ 2.95 Hz), 7.35 m (8H, Ar), 7.60 d (1H, N^1H, $J_{1,6}$ 2.95 Hz), 9.02 s (1H, NH_{amide}). Found, %: C 64.85, 65.06; H 5.38, 5.52; N 11.27, 11.48. $C_{20}H_{20}ClN_3O_2$. Calculated, %: C 64.95; H 5.45; N 11.36.

3,4-Dimethyl-*N*-2-chlorophenyl-6-phenyl-2-oxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide (III) was prepared similarly. Yield 2.77 g (78%), mp 195–197°C. ^{1}H NMR spectrum, δ_H, ppm: 2.26 s (3H, C^4H_3), 3.05 s (3H, C^3H_3), 5.22 d (1H, CH, $J_{1,6}$ 3.20 Hz), 7.43 m (9H, Ar), 7.62 d (1H, N^1H, $J_{1,6}$ 3.20 Hz), 9.04 s (1H, NH_{amide}). Found, %: C 63.96, 64.26; H 5.02, 5.17; N 11.70, 11.91. $C_{19}H_{18}ClN_3O_2$. Calculated, %: C 64.14; H 5.10; N 11.81.

3,4-Dimethyl-6-(3-nitrophenyl)-*N*-2-chlorophenyl-2-oxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide (IV) was prepared similarly. Yield 3.24 g (81%), mp 184–186°C. ^{1}H NMR spectrum, δ_H, ppm: 2.27 s (3H, C^4H_3), 3.10 s (3H, C^3H_3), 5.41 d (1H, CH, $J_{1,6}$ 3.33 Hz), 7.85 m (8H, Ar), 7.96 d (1H, N^1H, $J_{1,6}$ 3.33 Hz), 9.43 s (1H, NH_{amide}). Found, %: C 56.80, 57.09; H 4.22, 4.37; N 13.88, 14.07. $C_{19}H_{17}ClN_4O_4$. Calculated, %: C 56.94; H 4.28; N 13.98.

4-(2-Chlorophenyl)-1,6-dimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid *N*-(2-chlorophenyl)amide (V) was obtained similarly. Yield 2.44 g (69%), mp 203–205°C. ^{1}H NMR spectrum, δ_H, ppm: 2.26 s (3H, C^4H_3), 3.08 s (3H, C^3H_3), 5.62 d (1H, CH, $J_{1,6}$ 3.19 Hz), 7.40 m (8H, Ar), 7.65 d (1H, N^1H, $J_{1,6}$ 3.19 Hz), 9.40 s (1H, NH_{amide}). Found, %: C 58.39, 58.61; H 4.33, 4.47; N 10.68, 10.89. $C_{19}H_{17}Cl_2N_3O_2$. Calculated, %: C 58.48; H 4.39; N 10.77.

The ^{1}H NMR spectra were recorded on a Bruker 500 (500.13 MHz) spectrometer in DMSO-d_6, internal reference TMS. The mass spectra were obtained on a Finnigan MAT INCOS-50 instrument with ionization energy of 70 eV.

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