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SHORT COMMUNICATIONS

Synthesis of *N*,6-Diaryl-4-methyl-2-thioxo-1,2,3,6-tetrahydropyrimidine-5-carboxamides

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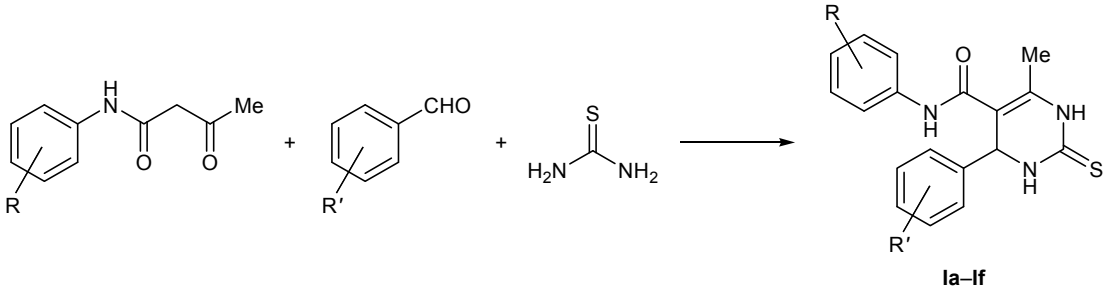
Examples of microwave-assisted Biginelli reactions have been reported. Fedorova et al. [1] developed a sonochemical method of synthesis of 2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid esters. 2-Aryl-6-hydroxy-*N*,*N*,6-trimethyl-4-oxocyclohexane-1,3-dicarboxamides were synthesized by reaction of *N*,*N*-dimethylacetoacetamide with aromatic aldehydes in the presence of piperidine [2]. Three-component condensation of *N*-arylacetoacetamides with aromatic aldehydes and thiourea was not studied previously.

With a view to obtain new heterocyclic compounds we were the first to study the reaction of acetoacetanilides [*N*-phenyl-3-oxobutanamide, *N*-(2-methylphenyl)-3-oxobutanamide, and *N*-(2,4-dimethylphenyl)-3-oxobutanamide] with a mixture of thiourea and aromatic aldehyde. The reactions were carried out by heating the reactants for 5–7 min at 120–150°C, and the products were the corresponding *N*,6-diaryl-4-methyl-2-thioxo-1,2,3,6-tetrahydropyrimidine-5-carboxamides **Ia**–**If**. The proposed procedure is characterized by shorter reaction time and higher yields than in the classical Biginelli reaction which implies prolonged (2–3 days) stirring of the reactants in ethanol in the presence of hydrochloric acid [3] or heating under reflux over a period of 3–4 h [4].

Compounds **Ia**–**If** were isolated as colorless crystalline substances that are soluble in chloroform, DMF, DMSO, and hot ethanol and insoluble in water. The IR spectra of **Ia**–**If** contained absorption bands due to stretching vibrations of the amide carbonyl group (1660–1680 cm^{-1}), N–H bonds (3150–3200 cm^{-1}), and double C=C bond (1600–1620 cm^{-1}). Compounds **Ia**–**If** displayed in the ^1H NMR spectra signals from protons in the aromatic rings, a singlet from the 4-methyl group at δ 1.85–2.05 ppm, a doublet from the 6-H proton at δ 5.32–5.36 ppm (J = 2.61–2.63 Hz), a singlet at δ 9.26–9.70 ppm and a doublet at δ 9.61–9.89 ppm (J = 1.37–1.40 Hz) from the NH protons in the pyrimidine ring, and a singlet at δ 8.96–9.44 ppm from the amide NH group. In addition, a singlet at δ 2.11 ppm was observed in the spectrum of **Ie** due to methyl protons at the aromatic ring, while compound **If** gave rise to two singlets at δ 2.09 and 2.18 ppm.

The mass spectrum of **If** contained the molecular ion peak, m/z 351 $[M]^+$, together with fragment ion peaks with m/z 231 $[M - (CH_3)_2C_6H_3NH]^+$, 121



Ia–If

I, R = H, R′ = H (**a**), 3-O_2N (**b**), 4-Cl (**c**), 2-Cl (**d**); R = 2-Me, R′ = H (**e**), R = 2,4-Me_2, R′ = H (**f**).

$[(CH_3)_2C_6H_3NH_2]^+$, and 77 $[Ph]^+$, which were consistent with the assumed structure.

4-Methyl-*N*,6-diphenyl-2-thioxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide (Ia). A mixture of 0.01 mol of acetoacetanilide, 0.01 mol of benzaldehyde, and 0.01 mol of thiourea was heated for 5–7 min at 120–150°C until gaseous products no longer evolved. The resulting material was cooled and treated with ethanol, and the precipitate was filtered off and recrystallized from alcohol. Yield 2.10 g (65%), mp 216–217°C. IR spectrum, ν, cm^{-1}: 3200 (NH), 1675 (C=O), 1600 (C=C). ^1H NMR spectrum, δ, ppm: 2.04 s (3H, CH_3), 5.32 d (1H, 6-H, J = 2.61 Hz), 7.21 m (10H, C_6H_5), 9.29 s (1H, NH), 9.59 s (1H, 3-H), 9.84 d (1H, 1-H, J = 1.37 Hz). Found, %: C 67.15, 66.65; H 5.40, 5.24; N 13.19, 12.79; S 9.71, 9.87. $C_{18}H_{17}N_3OS$. Calculated, %: C 66.85; H 5.30; N 12.99; S 9.91.

Compounds **Ib**–**If** were synthesized in a similar way.

4-Methyl-6-(3-nitrophenyl)-*N*-phenyl-2-thioxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide (Ib). Yield 1.91 g (53%), mp 234–235°C. IR spectrum, ν, cm^{-1}: 3200 (NH), 1680 (C=O), 1612 (C=C). ^1H NMR spectrum, δ, ppm: 1.99 s (3H, CH_3), 5.36 d (1H, 6-H, J = 2.63 Hz), 7.23 m (9H, H_{arom}), 9.44 s (1H, NH), 9.70 s (1H, 3-H), 9.89 d (1H, 1-H, J = 1.38 Hz). Found, %: C 58.98, 58.38; H 4.48, 4.28; N 15.40, 15.01; S 8.90, 8.62. $C_{18}H_{16}N_4O_3S$. Calculated, %: C 58.68; H 4.38; N 15.21; S 8.70.

6-(4-Chlorophenyl)-4-methyl-*N*-phenyl-2-thioxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide (Ic). Yield 1.8 g (51%), mp 221–223°C. IR spectrum, ν, cm^{-1}: 3200 (NH), 1680 (C=O), 1612 (C=C). ^1H NMR spectrum, δ, ppm: 2.05 s (3H, CH_3), 5.32 d (1H, 6-H, J = 2.61 Hz), 7.30 m (9H, H_{arom}), 9.40 s (1H, NH), 9.59 s (1H, 3-H), 9.61 d (1H, 1-H, J = 1.40 Hz). Found, %: C 60.71, 60.21; H 4.41, 4.59; N 11.58, 11.82; S 8.72, 9.19. $C_{18}H_{16}ClN_3OS$. Calculated, %: C 60.41; H 4.51; N 11.74; S 8.96.

6-(2-Chlorophenyl)-4-methyl-*N*-phenyl-2-thioxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide (Id). Yield 1.4 g (39%), mp 218–219°C. IR spectrum, ν, cm^{-1}: 3200 (NH), 1680 (C=O), 1612 (C=C). ^1H NMR spectrum, δ, ppm: 1.99 s (3H, CH_3), 5.56 d (1H, 6-H, J = 2.63 Hz), 7.27 m (9H, H_{arom}), 9.18 s (1H, NH), 9.70 s (1H, 3-H), 9.89 d (1H, 1-H, J = 1.37 Hz). Found, %: C 60.20, 60.62; H 4.41, 4.61; N 11.54, 11.92; S 8.74, 9.21. $C_{18}H_{16}ClN_3OS$. Calculated, %: C 60.41; H 4.51; N 11.74; S 8.96.

4-Methyl-*N*-(2-methylphenyl)-6-phenyl-2-thioxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide (Ie). Yield 2.05 g (61%), mp 229–231°C. IR spectrum, ν, cm^{-1}: 3200 (NH), 1680 (C=O), 1612 (C=C). ^1H NMR spectrum, δ, ppm: 1.90 s (3H, 4-CH_3), 2.11 s (3H, C**H**$_3C_6H_4$), 5.33 d (1H, 6-H, J = 2.62 Hz), 7.16 m (9H, H_{arom}), 9.05 s (1H, NH), 9.26 s (1H, 3-H), 9.81 d (1H, 1-H, J = 1.37 Hz). Found, %: C 67.93, 67.42; H 5.78, 5.54; N 12.24, 12.65; S 9.65, 9.35. $C_{19}H_{19}N_3OS$. Calculated, %: C 67.63; H 5.68; N 12.45; S 9.50.

***N*-(2,4-Dimethylphenyl)-4-methyl-6-phenyl-2-thioxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide (If).** Yield 1.60 g (46%), mp 238–239°C. IR spectrum, ν, cm^{-1}: 3200 (NH), 1680 (C=O), 1612 (C=C). ^1H NMR spectrum, δ, ppm: 1.85 s (3H, 4-CH_3), 2.09 s and 2.18 s (3H each, 2′-CH_3, 4′-CH_3), 5.33 d (1H, 6-H, J = 2.61 Hz), 7.23 m (8H, H_{arom}), 8.96 s (1H, NH), 9.24 s (1H, 3-H), 9.77 d (1H, 1-H, J = 1.37 Hz). Found, %: C 68.05, 68.55; H 6.12, 5.90; N 11.75, 12.16; S 9.24, 8.85. m/z 351 $[M]^+$. $C_{20}H_{21}N_3OS$. Calculated, %: C 68.35; H 6.02; N 11.96; S 9.12 M 351.47.

The IR spectra were recorded in mineral oil on a Specord M-80 spectrophotometer. The ^1H NMR spectra were measured on a Bruker 500 instrument at 500.13 MHz using DMSO-d_6 as solvent and tetramethylsilane as internal reference. The mass spectrum (electron impact, 70 eV) was obtained on a Finnigan MAT INCOS-50 mass spectrometer.

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