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SHORT COMMUNICATIONS

Bicyclic Compounds Obtained by the Biginelli Reaction

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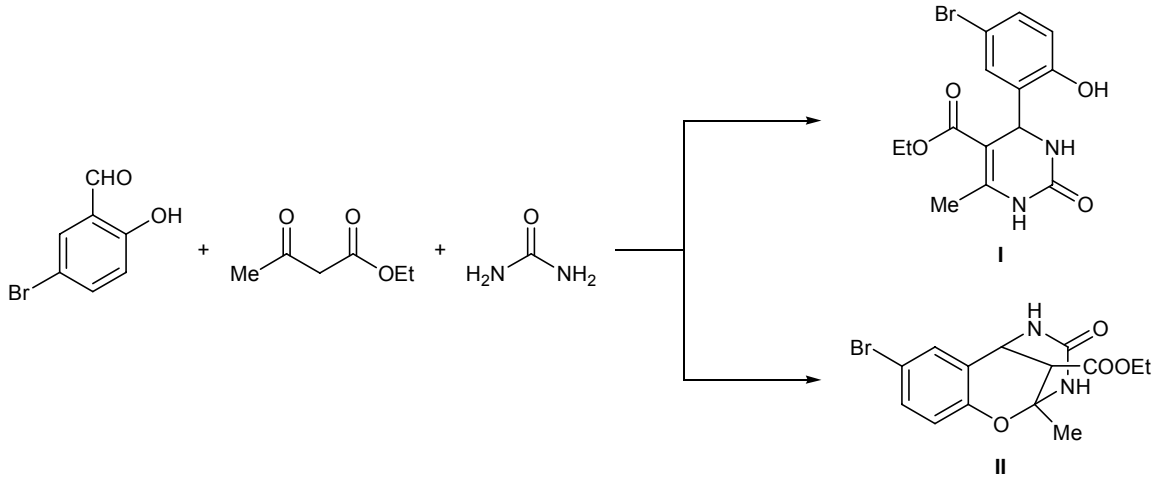
It was found for the first time that three-component condensation of 2-hydroxynaphthalene-1-carbaldehyde with ethyl acetoacetate and urea in the presence of trichloroacetic acid yields ethyl 1-methyl-15-oxo-2-oxa-14,16-diazatetracyclo[11.3.1.$0^{3.12}$.$0^{6.11}$]heptadeca-3,5,7,9,11-pentaene-17-carboxylate [1]. While continuing studies in this line, 5-bromosalicylaldehyde was selected as substrate for the above three-component condensation. The reaction of 5-bromosalicylaldehyde with ethyl acetoacetate and urea in the presence of trichloroacetic acid gave, depending on the conditions, ethyl 4-(5-bromo-2-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**I**) or ethyl 4-bromo-9-methyl-11-oxo-8-oxa-10,12-diazatricyclo-[7.3.1.$0^{2.7}$]trideca-2,4,6-triene-13-carboxylate (**II**) (Scheme 1). Ester **I** was formed when the reactants were heated for 2–4 h in boiling ethanol, whereas bicyclic compound **II** was isolated when the reaction mixture was heated for 7–9 h at 40°C. The progress of the reaction was monitored by thin-layer chromatography. The structure of compounds **I** and **II** was proved by IR and NMR spectroscopy and X-ray diffraction data (Fig. 1).

For comparison, three-component condensation of 5-bromosalicylaldehyde with acetylacetone and thiourea was examined. Under analogous conditions, the products were 1-[4-(5-bromo-2-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl]-ethanone (**III**) and 1-(4-bromo-9-methyl-11-thioxo-8-oxa-10,12-diazatricyclo[7.3.1.$0^{2.7}$]trideca-2,4,6-trien-13-yl)ethanone (**IV**) (Scheme 2). Compounds **III** and **IV** were isolated as crystalline substances whose structure was proved by IR and NMR spectroscopy and X-ray analysis (Fig. 2).

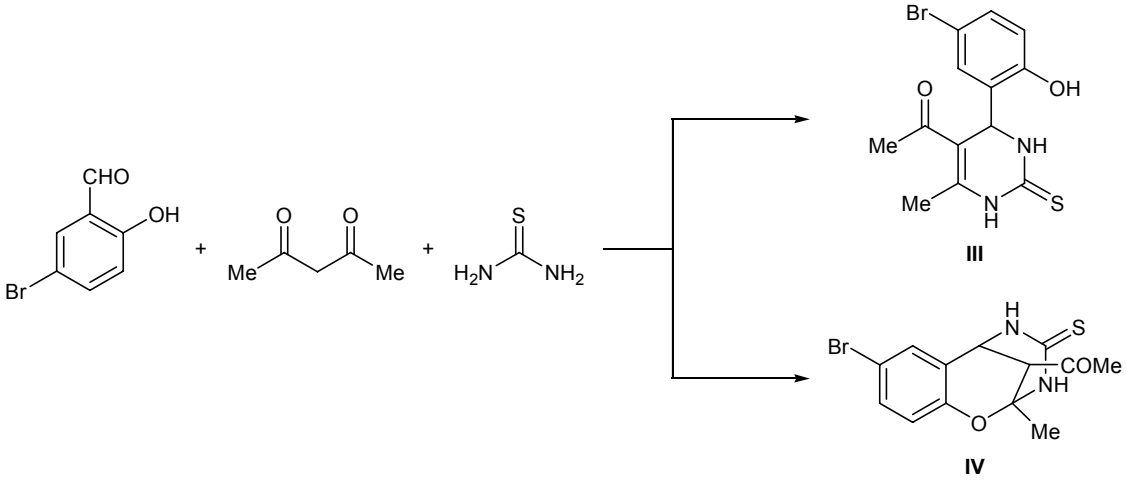
A probable mechanism of formation of bicyclic products **II** and **IV** is shown in Scheme 3.

Ethyl 4-(5-bromo-2-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (I). A mixture of 5.025 g (0.025 mol) of 5-bromosalicylaldehyde, 4.8 ml (0.038 mol) of ethyl acetoacetate, 1.5 g (0.025 mol) of urea, and 25 mg of trichloroacetic

Scheme 1.



Scheme 2.



acid in 10 ml of ethanol was stirred for 2–4 h on heating under reflux. The progress of the reaction was monitored by TLC. When the reaction was complete, the mixture was cooled to room temperature, and the precipitate was filtered off, washed with ethanol, dried, and recrystallized from aqueous ethanol. Yield 75%, mp 190–191°C. IR spectrum, ν, cm^{-1}: 3325, 1745, 1660. ^1H NMR spectrum, δ, ppm: 1.30 t (3H, $CH_2C\mathbf{H}_3$), 2.57 s (3H, CH_3), 4.25 q (2H, CH_2O), 5.70 s (1H, CH), 7.70–7.00 m (4H, H_{arom}), 8.00 s (1H, NH), 9.41 s (1H, NH), 10.11 s (1H, OH). Found %: C 47.36; H 4.25; Br 22.60; N 7.91. $C_{14}H_{15}BrN_2O_4$. Calculated, %: C 47.32; H 4.22; Br 22.53; N 7.88.

Ethyl 4-bromo-9-methyl-11-oxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene-13-carboxylate (II). A mixture of 5.025 g (0.025 mol) of 5-bromosalicylaldehyde, 4.8 ml (0.038 mol) of ethyl acetoacetate, 1.5 g (0.025 mol) of urea, and 25 mg of trichloroacetic acid in 10 ml of ethanol was heated for 7–9 h at 40°C. After cooling, the precipitate was filtered off and dried. Yield 55%, mp 197°C. IR spectrum, ν, cm^{-1}: 3350, 1740, 1680. ^1H NMR spectrum, δ, ppm: 1.27 t (3H, $CH_2C\mathbf{H}_3$), 2.35 s (3H, CH_3), 3.27 d (1H, CH), 4.16 q (2H, CH_2O), 4.46 d (1H, CH), 6.77–7.21 m (3H, H_{arom}), 8.36 s (1H, NH), 8.41 s (1H, NH). Found, %: C 47.39; H 4.27; Br 22.59; N 7.95. $C_{14}H_{15}BrN_2O_4$. Calculated, %: C 47.32; H 4.22; Br 22.53; N 7.88.

1-[4-(5-Bromo-2-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl]ethanone (III) was synthesized as described above for compound **I** from 1.9 g (0.025 mol) of thiourea. Yield

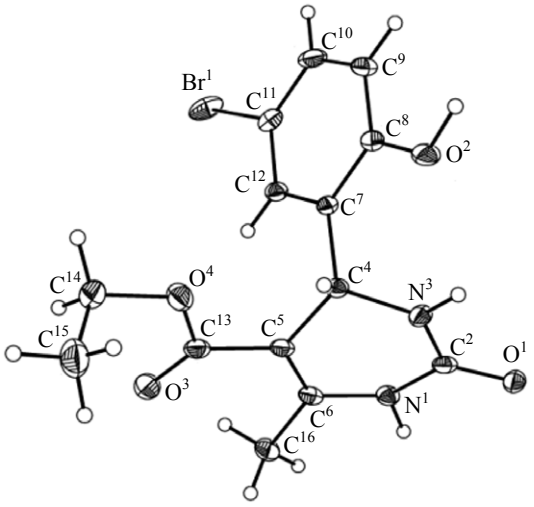


Fig. 1. Structure of the molecule of ethyl 4-(5-bromo-2-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**I**) according to the X-ray diffraction data.

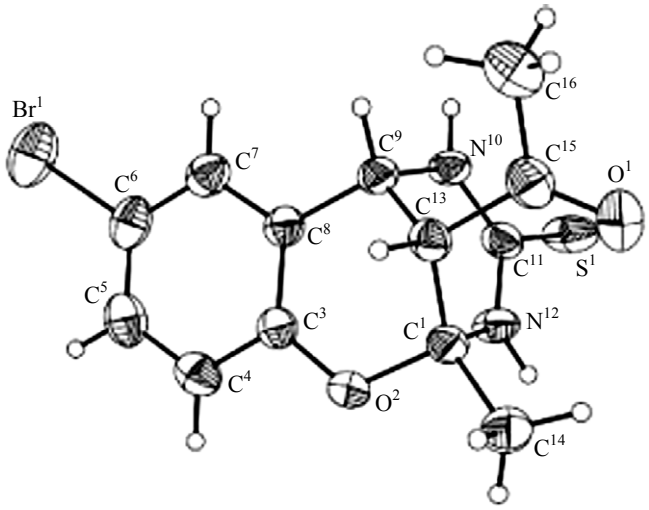
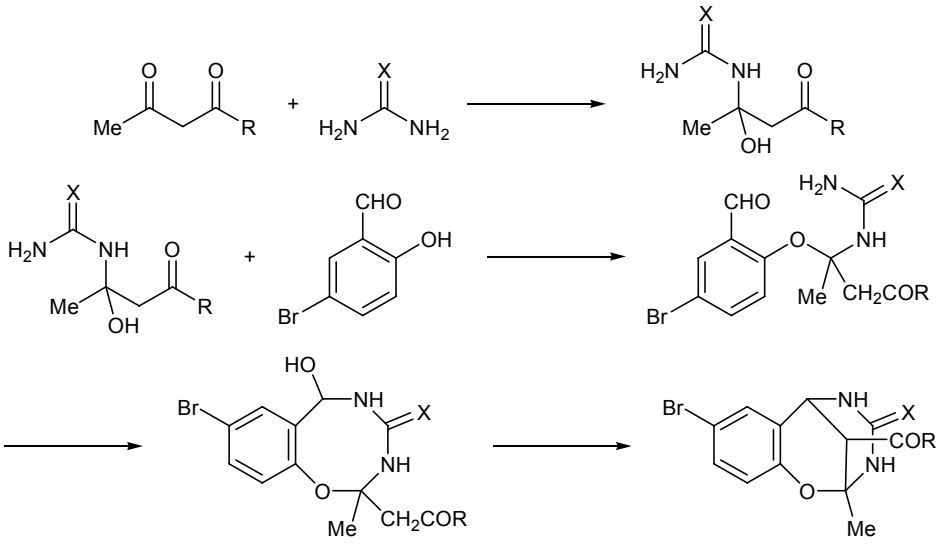


Fig. 2. Structure of the molecule of 1-(4-bromo-9-methyl-11-thioxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-trien-13-yl)ethanone (**IV**) according to the X-ray diffraction data.

Scheme 3.



X = O, S; R = Me, OEt.

75%, mp 175°C. IR spectrum, ν, cm^{-1}: 3345, 1665. ^1H NMR spectrum, δ, ppm: 1.90 s (3H, CH_3), 2.47 s (3H, CH_3), 5.57 s (1H, CH), 7.10 s (1H, NH), 7.36–7.45 m (4H, H_{arom}), 8.14 s (1H, NH), 9.50 s (1H, OH). Found, %: C 45.80; H 3.77; Br 23.40; N 8.30; S 9.45. $C_{13}H_{13}BrN_2O_2S$. Calculated, %: C 45.74; H 3.81; Br 23.46; N 8.21; S 9.38.

1-(4-Bromo-9-methyl-11-thioxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-trien-13-yl)ethanone (IV) was synthesized as described above for compound **II** from 1.9 g (0.025 mol) of thiorea. Yield 55%, mp 187–188°C. IR spectrum, ν, cm^{-1}: 3350, 1670. ^1H NMR spectrum, δ, ppm: 1.79 s (3H, CH_3), 2.31 s (3H, CH_3), 3.33 d (1H, CH), 4.59 d (1H, CH), 6.84–7.20 m (3H, H_{arom}), 8.97 s (1H, NH), 9.12 s (1H, NH). Found, %: C 45.78; H 3.79; Br 23.42; N 8.27; S 9.44. $C_{13}H_{13}BrN_2O_2S$. Calculated, %: C 45.74; H 3.81; Br 23.46; N 8.21; S 9.38.

X-Ray diffraction study. Single crystals of compounds **I** and **IV** suitable for X-ray analysis were obtained by double recrystallization from ethanol. The X-ray diffraction data were acquired on a Bruker APEX II CCD diffractometer (100 K, λMo$K_α$ irradiation, graphite monochromator, φ- and ω-scanning, $2θ_{max}$ = 56°). The structures were solved by the direct method and were refined by the least-squares procedure in anisotropic approximation for non-hydrogen atoms. Hydrogen atoms in the hydroxy and amino groups were localized by the Fourier difference syntheses, and their positions were refined in isotropic approximation with fixed positional and thermal parameters. The positions of the other hydrogen atoms were calculated on the basis of geometry considerations and were refined in isotropic approximation with fixed positional and thermal parameters. All calculations were performed using SHELXTL PLUS and SADABS software packages [2, 3]. The complete sets of crystallographic data for compounds **I** and **IV** were deposited to the Cambridge Crystallographic Data Centre (entry nos. CCDC 694407 and CCDC 707349).

The ^1H NMR spectra were recorded at 25°C from solutions in DMSO-d_6 on a Bruker-300 spectrometer operating at 300 MHz. The IR spectra were obtained on a Specord 75IR instrument from samples dispersed in mineral oil. The progress of reactions and the purity of products were monitored by TLC.

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