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Synthesis of Substituted 3,4-Dihydropyrimidin-2(1*H*)-ones and Pyrimidin-2(1*H*)-ones by the Biginelli Reaction with 3,5-Di-*tert*-butyl-4-hydroxybenzaldehyde

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Abstract—Three-component acid-catalyzed cyclocondensation of 3,5-di-*tret*-butyl-4-hydroxybenzaldehyde with urea and ethyl acetoacetate or α-nitroacetophenone (Biginelli reaction) under homogeneous conditions gave the corresponding 5-substituted 3,4-dihydropyrimidin-2(1*H*)-ones having in position *4* of the heteroring an aryl substituent with sterically shielded hydroxy group. The condensation catalyzed by inorganic salts (Fe^{3+}, Co^{2+}, Zn^{2+}, Li^{+}) was successful only with ethyl acetoacetate as initial methylene-active component. Under analogous conditions, acetophenone and 4-fluoroacetophenone gave rise to 4,6-diarylpyrimidin-2(1*H*)-ones which are capable of undergoing phenol–quinonemethide tautomerism.

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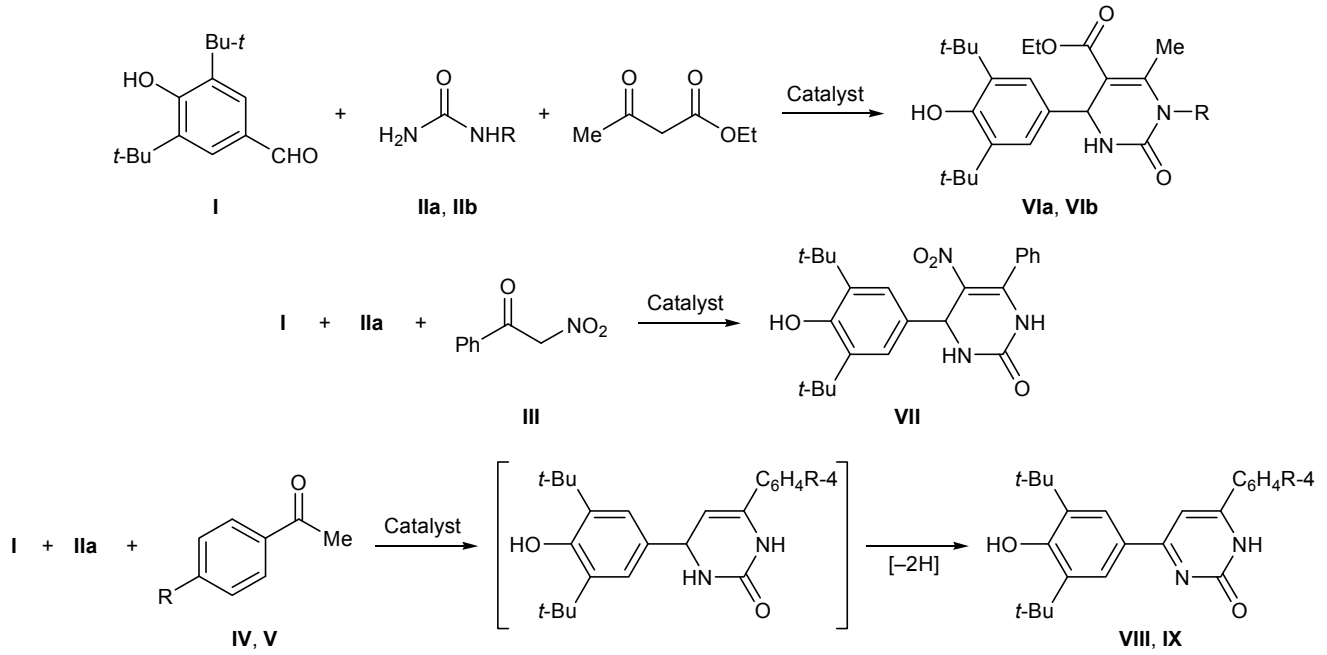
3,4-Dihydropyrimidin-2(1*H*)-ones exhibit a broad spectrum of biological activity, but the most interesting is their ability to modulate calcium channels [1–3]. We found that 4-aryl-5-nitro-6-phenyl-3,4-dihydropyrimidin-2(1*H*)-ones are low-toxic compounds and that they exert an appreciable antiarrhythmic effect even at a very low dose [4]. A usual technique in the design of biologically active compounds with a broad spectrum of biological activity is incorporation into a biologically active molecule of one or several additional pharmacophoric groups with a different activity [5]. In this connection, introduction into a 3,4-dihydropyrimidin-2-one molecule of a phenol fragment having sterically shielded hydroxy group could give rise to new properties, e.g., antiradical and antioxidant activity. Heterocyclic compounds containing a 3,5-di-*tert*-butyl-4-hydroxyphenyl group have been reported to exhibit antioxidant activity in combination with other kinds of biological activity. Examples are calcium channel antagonists of the 1,4-dihydropyridine [6] and thiazolidinone series [7], antisclerotic agents of the oxadiazole series [8], and lipoprotein oxidation inhibitors of the dihydropyrazole series [9]. Compounds possessing antioxidant properties were found among 4-aryl-3,4-dihydropyrimidin-2-one derivatives substituted at the 5-position with an alkoxycarbonyl group having both simple and bulky alkyl radicals [10].

In the present work we tried to synthesize new 4-aryl-3,4-dihydropyrimidin-2(1*H*)-ones with a sterically shielded hydroxy group in the aryl substituent. For this purpose, we examined three-component cyclocondensation of 3,5-di(*tert*-butyl)-4-hydroxybenzaldehyde (**I**) with urea (**IIa**) or *N*-methylurea (**IIb**) and various compounds having an activated methylene group. As the latter, we used both traditional ethyl acetoacetate and less reactive CH acids, α-nitroacetophenone (**III**), acetophenone (**IV**), and 4-fluoroacetophenone (**V**).

The reaction of ethyl acetoacetate with aldehyde **I** and urea (**IIa**) under standard Biginelli conditions (heating in boiling ethanol in the presence of a catalytic amount of hydrochloric acid) gave ethyl 4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**VIa**) in 48% yield (Scheme 1). The condensation in the presence of inorganic salts, such as $FeCl_3 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$, and $ZnCl_2$ (10 mol %) was characterized by appreciably greater yield of compound **VIa** (77–88%) and shorter reaction time. The yield of **VIa** reached 89% when the reaction was carried out in acetonitrile using LiBr as catalyst. The corresponding 1-methyl-substituted pyrimidine **VIb** was synthesized in high yield by reaction of aldehyde **I** with ethyl acetoacetate and

Scheme 1.



R = H (**a**), Me (**b**); **VIII**, R′ = H; **IX**, R′ = 4-F.

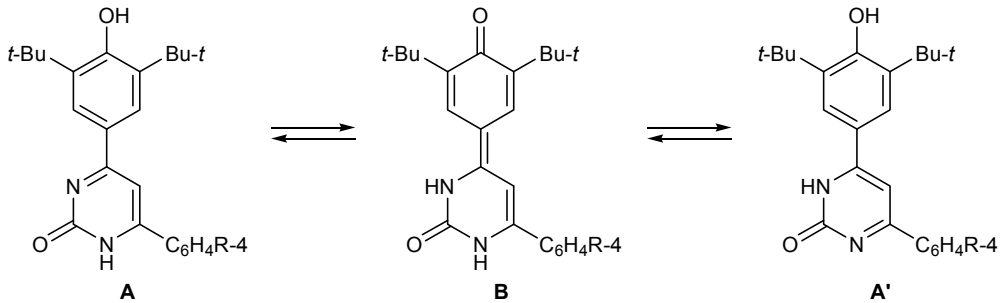
N-methylurea (**IIb**) in the presence of $CoCl_2 \cdot 6H_2O$ as catalyst.

Under standard conditions (see above), aldehyde **I** reacted with α-nitroacetophenone (**III**) and urea (**IIa**) to give the expected condensation product, 4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-5-nitro-6-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (**VII**) (Scheme 1). However, the reaction occurred at a much lower rate; even after heating for 24 h under reflux, the mixture contained traces of initial aldehyde **I**, and the yield of compound **VII** was 55%. Attempts to effect the condensation in the presence of 10 mol % of $CoCl_2 \cdot 6H_2O$ were unsuccessful: no cyclization product was detected after heating of the reaction mixture for 16 h under reflux. The use of a larger amount of the catalyst was undesirable, for it could favor side processes, including retro-Henry reaction, which was observed by us previously [11].

The structure of dihydropyrimidinones **VIa**, **VIb**, and **VII** was confirmed by the analytical and spectral data which were consistent with those reported for other 5-alkoxycarbonyl- and 5-nitro-4-aryl-3,4-dihydropyrimidin-2(1*H*)-ones. The mass spectra of **VIa** and **VIb** contained all fragment ion peaks typical of such compounds: $[M]^+$, $[M - C_2H_5]^+$, $[M - COOC_2H_5]^+$, $[M - Ar]^+$, $[M - Ar - C_2H_4]^+$, $[M - C_2H_5OH]^+$, $[M - Ar - COOC_2H_5]^+$ [12]. Analogous fragmentation pattern was observed for compound **VII**; it completely coincided with the data reported for other 5-nitrodihydropyrimidinones [4].

In the condensations of aldehyde **I** with urea and acetophenones **IV** and **V** having even less activated methylene group than that in nitroacetophenone **III**, instead of the expected diaryl-substituted 3,4-dihydropyrimidin-2(1*H*)-one derivatives we isolated the corre-

Scheme 2.



sponding dehydrogenation products, 6-phenyl- and 6-(4-fluorophenyl)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)pyrimidin-2(1*H*)-ones **VIII** and **IX**. Their formation is consistent with the behavior of other aromatic aldehydes in such reactions [13]. The condensation was difficult to occur, and unreacted aldehyde **I** was present in the reaction mixture even after 24 h. The use of a catalytic amount of $FeCl_3 \cdot 6H_2O$ or $CoCl_2 \cdot 6H_2O$ had no appreciable effect on the reaction course.

Compounds **VIII** and **IX** displayed in the IR spectra an absorption band at 1630 cm^{-1} which is typical of stretching vibrations of the carbonyl group in diarylpyrimidin-2(1*H*)-ones but is not characteristic of the corresponding dihydro derivatives [14]. The mass spectra of **VIII** and **IX** contained strong molecular ion peaks $[M]^+$ ($I_{rel} \geq 50\%$) and $[M - 15]^+$ ion peaks (I_{rel} 100%), in keeping with published data for structurally related compounds [15]; also, other fragment ion peaks with intensities below 10% were present. The ^{1}H NMR spectra of **VIII** and **IX** confirmed the assumed structure.

Electronic absorption spectra could provide additional information on the structure of the isolated compounds. In the UV spectra of 5-ethoxycarbonyl derivatives **VIa** and **VIb** we observed a strong absorption band in the region λ 280–290 nm, while the corresponding band in the spectrum of 5-nitro derivative **VII** was displaced by ~60 nm toward longer wavelengths, which is typical of 5-nitrodihydropyrimidin-2-ones [4, 14].

As shown previously [13, 14], the long-wave absorption band in the UV spectra of 4,6-diarylpyrimidin-2(1*H*)-ones is located in the region λ 340–360 nm (log ε 4.0–4.5). Analogous absorption band is observed at λ 354 nm (log ε 4.3) in the UV spectra of compounds **VIII** and **IX**. However, unlike other diarylpyrimidinones, the electronic absorption spectra of **VIII** and **IX** in ethanol contain an absorption band in the visible region (λ ~480 nm; log ε 2.52 and 2.25, respectively). This band may be attributed to structure **B** appearing as a result of phenol–quinonemethide tautomerism **A** ↔ **B** (Scheme 2).

In going from ethanol to strongly polar solvents such as DMF and DMSO, the molar absorption coefficient at the visible absorption maximum increases approximately by an order of magnitude, indicating that the above equilibrium is displaced toward quinonemethide tautomer **B** (Figs. 1, 2). Analogous variations in the spectral pattern, produced by increase

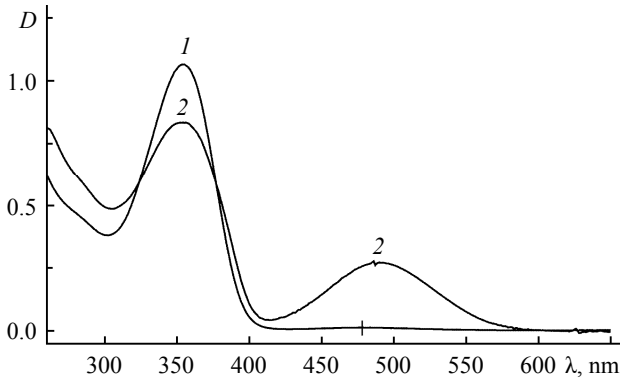


Fig. 1. Electronic absorption spectra of compound **VIII** in (*1*) ethanol, $c = 1 \times 10^{-4}$ M, l = 0.5 cm, and (*2*) dimethyl sulfoxide, $c = 0.55 \times 10^{-4}$ M, l = 1.0 cm.

in solvent polarity, were observed previously for Schiff bases having a 3,4-di-*tert*-butylphenol fragment [16]. Comparison of the intensities of the absorption bands at λ_{max} ~354 nm in the spectra of compounds **VIII** and **IX** in ethanol and DMSO shows that the fraction of tautomer **B** for compound **IX** (Fig. 2) is larger than that for **VIII** (Fig. 1). This may be due to +*M* effect of fluorine atom in the *para* position, which enhances electron-donating effect of the 6-(4-fluorophenyl) substituent (as compared to 6-phenyl) on the neighboring endocyclic nitrogen atom; increased basicity of the latter stabilizes the corresponding tautomer **B** to a greater extent.

Thus the behavior of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde in the Biginelli reaction is generally similar to the behavior of other aromatic aldehydes, and some specificity of reactions with participation of aldehyde **I** may be attributed to its reduced reactivity. First 3,4-dihydropyrimidin-2(1*H*)-one derivatives having a 3,5-di-*tert*-butyl-4-hydroxyphenyl group in posi-

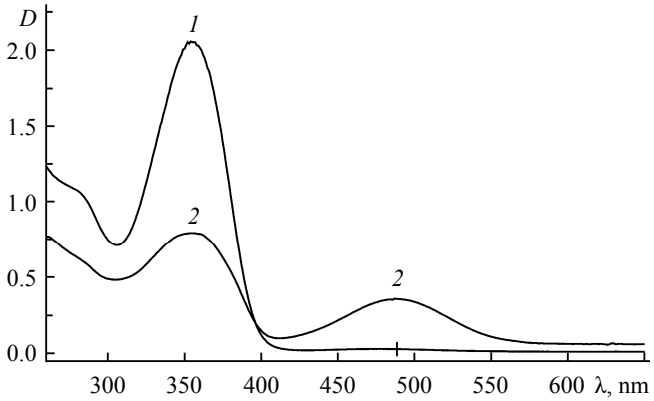


Fig. 2. Electronic absorption spectra of compound **IX** in (*1*) ethanol, $c = 1 \times 10^{-4}$ M, l = 0.5 cm, and (*2*) dimethyl sulfoxide, $c = 0.51 \times 10^{-4}$ M, l = 1.0 cm.

tion *4* of the heteroring were synthesized. The use of inorganic salts like Fe^{3+}, Co^{2+}, Zn^{2+}, Li^{+} as catalysts appreciably increases the yield of the cyclocondensation product obtained from ethyl acetoacetate rather than from α-nitroacetophenone. The condensations with acetophenone and 4-fluoroacetophenone lead to the formation of only the corresponding oxidized products, 4,6-diarylpyrimidin-2(1*H*)-ones, which give rise to phenol–quinonemethide tautomeric equilibrium.

EXPERIMENTAL

The IR spectra were recorded in KBr on a Bruker Vector 22 spectrometer. The electronic absorption spectra in the UV and visible regions were measured on a Specord M-40 spectrophotometer. The ^1H and ^{13}C NMR spectra were obtained on Bruker AV-300 and Bruker AM-400 instruments using DMSO-d_6 as solvent and reference (δ 2.50, δ_C 39.50 ppm). The mass spectra (electron impact, 70 eV) were recorded on a Finnigan MAT 8200 mass spectrometer with direct sample admission into the ion source. The purity of the isolated compounds was checked by TLC on Silufol UV-254 plates using chloroform–ethanol (15 : 1) as eluent.

Ethyl 4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (VIa). *a*. A mixture of 1.56 g (12 mmol) of ethyl acetoacetate, 2.34 g (10 mmol) of aldehyde **I**, 1.20 g (20 mmol) of urea, 20 ml of ethanol, and 1.5 ml of concentrated hydrochloric acid was heated for 8.5 h under reflux. Additional portions of urea, 0.50 g (8 mmol), and concentrated hydrochloric acid, 0.3 ml, were added, and the mixture was heated for 8.5 h more under reflux. After cooling, the precipitate was filtered off and washed in succession with ethanol, a saturated solution of $NaHCO_3$, water, and ethanol again. Yield 1.67 g (48%), mp 247–248°C (from EtOH). UV spectrum (EtOH), λ_{max}, nm (logε): 206 (4.41), 283 (4.04). IR spectrum, ν, cm^{-1}: 3612 (OH); 3238, 3110 (NH); 2955 (C–H in *t*-Bu); 1711, 1696 (C=O); 1227 (C–O). ^1H NMR spectrum (400 MHz), δ, ppm: 1.13 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 1.35 s (18H, *t*-Bu), 2.21 s (3H, 6-Me), 4.01 q (2H, CH_2O, ^3J = 7.2 Hz), 5.05 d (1H, 4-H, ^3J = 3.2 Hz), 6.82 s (1H, OH), 7.04 s (2H, H_{arom}), 7.55 br.s (1H, 3-H), 9.06 s (1H, 1-H). ^{13}C NMR spectrum (100 MHz), δ_C, ppm: 14.18 (**C**H$_3$CH$_2$), 17.67 (6-CH$_3$), 30.29 [(**C**H$_3$)$_3$C], 34.43 [(CH$_3$)$_3$**C**)], 53.92 (C^4), 59.14 (CH_2O), 100.14 (C^5), 122.31 (C^9, C^{11}), 136.18 (C^7), 138.89 (C^8, C^{12}), 147.59 (C^6), 152.52 and 152.94 (C^2, C^{10}), 165.53 (5-CO). Mass spectrum, *m*/*z* (I_{rel}, %): 388 (38.3) $[M]^+$, 373 (14.4) $[M - Me]^+$, 359 (100) $[M - Et]^+$, 331 (75.8) $[M - t\text{-Bu}]^+$, 315 (57.2) $[M - COOEt]^+$, 183 (90.7) $[M - C_6H_2(Bu\text{-}t)_2OH]^+$, 155 (30.6), 137 (21.7) $[M - Ar - EtOH]^+$, 110 (6.4) $[M - Ar - COOEt]^+$. Found, %: C 68.30; H 8.38; N 6.92. $[M]^+$ 388.2363 (HRMS). $C_{22}H_{32}N_2O_4$. Calculated, %: C 68.01; H 8.30; N 7.21. *M* 388.2362.

b. A mixture of 1.56 g (12 mmol) of ethyl acetoacetate, 2.34 g (10 mmol) of aldehyde **I**, 1.20 g (20 mmol) of urea, 30 ml of ethanol, and 0.28 g (1 mmol) of iron(III) chloride hexahydrate was heated for 4 h under reflux. After cooling, the precipitate was filtered off and washed with ethanol. Yield 3.0 g (77%), mp 247–248°C.

c. A mixture of 1.56 g (12 mmol) of ethyl acetoacetate, 2.34 g (10 mmol) of aldehyde **I**, 1.20 g (20 mmol) of urea, 30 ml of ethanol, and 0.24 g (1 mmol) of cobalt(II) chloride hexahydrate was heated for 5.5 h under reflux. Yield 3.1 g (80%), mp 246.5–247.5°C.

d. A mixture of 0.78 g (6 mmol) of ethyl acetoacetate, 1.17 g (5 mmol) of aldehyde **I**, 0.60 g (10 mmol) of urea, 15 ml of ethanol, and 0.10 g (1 mmol) of zinc(II) chloride was heated for 20 h under reflux. After cooling, the precipitate was filtered off and washed with ethanol and water. Yield 1.70 g (88%), mp 243–244°C (from EtOH).

e. Lithium bromide, 50 mg (0.57 mmol), was added to a mixture of reactants prepared as described above in *d* in 5 ml of acetonitrile, and the mixture was heated for 10 h under reflux. The mixture was cooled, and the precipitate was filtered off and washed with ethanol and water. Yield 1.73 g (88%).

Ethyl 4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,6-dimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (VIb). A mixture of 0.78 g (6 mmol) of ethyl acetoacetate, 1.17 g (5 mmol) of aldehyde **I**, 0.74 g (10 mmol) of *N*-methylurea (**IIb**), 15 ml of ethanol, and 0.12 g (0.5 mmol) of cobalt(II) chloride hexahydrate was heated for 6 h under reflux. After cooling, the precipitate was filtered off and washed with ethanol and water. Yield 1.55 g (77%), mp 190–191°C (from EtOH). UV spectrum (EtOH), λ_{max}, nm (logε): 204 (4.52), 285 (3.99). IR spectrum, ν, cm^{-1}: 3605 (OH), 3381 (NH), 2965 (C–H in *t*-Bu), 1705 and 1680 (C=O), 1611, 1240 (C–O). ^1H NMR spectrum (400 MHz), δ, ppm: 1.16 t (3H, C**H**$_3$CH$_2$, ^3J = 7.0 Hz), 1.34 s (18H, *t*-Bu), 2.43 s (3H, 6-CH$_3$), 3.11 s (3H, 1-CH$_3$), 4.05 q (2H, CH_2O, ^3J = 7.0 Hz), 5.05 d (1H,

4-H, ^3J = 3.6 Hz), 6.86 s (1H, OH), 6.99 s (2H, H_{arom}), 7.78 d (1H, 3-H). ^{13}C NMR spectrum (100 MHz), δ_C, ppm: 14.19 (**C**H_3), 16.01 (6-CH_3), 29.63 (1-CH_3), 30.32 [(**C**H_3)$_3$C], 34.54 [(CH_3)$_3$**C**], 52.46 (C^4), 59.58 (CH_2O), 103.95 (C^5), 122.06 (C^9, C^{11}), 135.42 (C^7), 139.07 (C^8, C^{12}), 149.60 (C^6), 153.05 and 153.70 (C^2, C^{10}), 165.82 (5-CO). Mass spectrum, *m*/*z* (I_{rel}, %): 402 (31.5) $[M]^+$, 387 (15.9) $[M - Me]^+$, 373 (85.1) $[M - Et]^+$, 345 (23.3) $[M - Bu]^+$, 329 (51.4) $[M - COOEt]^+$, 197 (100) $[M - Ar]^+$, 169 (26.8), 151 (28.5) $[M - Ar - EtOH]^+$, 124 (9.4) $[M - Ar - COOEt]^+$. Found, %: C 68.96; H 8.66; N 6.83. $[M]^+$ 402.2524 (HRMS). $C_{23}H_{34}N_2O_4$. Calculated, %: C 68.63; H 8.51; N 6.96. *M* 402.2518.

4-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-5-nitro-6-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (VII). A mixture of 1.98 g (12 mmol) of nitroacetophenone (**III**), 2.34 g (10 mmol) of aldehyde **I**, 1.20 g (20 mmol) of urea, and 26 ml of ethanol was stirred, 1.5 ml of concentrated hydrochloric acid was added, and the mixture was heated for 5 h under reflux. A 0.6-g (10-mmol) portion of urea was added, the mixture was heated for 5 h under reflux, 0.3 g (5 mmol) of urea and 0.5 ml of concentrated hydrochloric acid in 8 ml of ethanol were added, the mixture was heated under reflux, and the last portion of urea (0.3 g) and 6 ml of ethanol were added in 19 h after the mixture began to boil. The progress of the reaction was monitored by TLC. When the initial aldehyde disappeared (overall reaction time 24 h), the yellow–orange transparent mixture was cooled to room temperature and was left to stand for several hours. The precipitate was filtered off, washed with a small amount of 90% ethanol, water, and ethanol again, and dried on a filter. Yield 2.2 g. The filtrate was kept in a refrigerator to isolate an additional portion (0.15 g) of compound **VII**. Overall yield 2.35 g (55%), mp 243–244°C (from EtOH). UV spectrum (EtOH), λ_{max}, nm (logε): 206 (4.64), 236 (4.15), 348 (3.74). IR spectrum, ν, cm^{-1}: 3630 (OH), 3370, 3215 (NH), 2959 (C–H in *t*-Bu), 1701 (C=O), 1628, 1499 and 1321 (NO_2), 1246. ^{1}H NMR spectrum (400 MHz), δ, ppm: 1.07 t (1.5H, C**H**$_3$CH$_2$OH, ^3J = 7.0 Hz), 1.42 s (18H, *t*-Bu), 3.45 q (1H, CH$_3$C**H**$_2$OH, ^3J = 7.0 Hz), 5.55 d (1H, 4-H, ^3J = 3.7 Hz), 6.99 s (1H, OH), 7.21 s (2H, H_{arom}), 7.38 m (2H, H_{arom}), 7.50 m (3H, H_{arom}), 8.22 br.s (1H, 3-H), 10.0 s (1H, 1-H). ^{13}C NMR spectrum (100 MHz), δ_C, ppm: 18.41 (**C**H$_3$CH$_2$OH); 30.23 [(**C**H$_3$)$_3$C]; 34.46 [(CH$_3$)$_3$**C**]; 54.24 (C^4); 56.00 (CH$_3$**C**H$_2$OH); 122.30 (C^5); 122.43 (C^9, C^{11}); 127.46, 128.45, 129.77, 132.61 (C^{13}, C^{14}, C^{15}, C^{16}, C^{17}, C^{18}); 133.12 (C^7); 139.36 (C^8, C^{12}); 149.14 (C^6); 150.48 (C^{10}); 153.64 (C^2). Mass spectrum, *m*/*z* (I_{rel}, %): 423 (22.4) $[M]^+$, 406 (100) $[M - OH]^+$, 378 (17.0) $[M - OH - CO]^+$, 377 (62.6) $[M - NO_2]^+$, 376 (7.2) $[M - HNO_2]^+$, 361 (31.6), 334 (24.9), 292 (17.3), 218 (39.6) $[M - Ar]^+$, 171 (22.6) $[M - Ar - HNO_2]^+$, 104 (12.9) $[PhC{=}NH]^+$, 77 (6.1) $[Ph]^+$. Found, %: C 67.29; H 6.90; N 9.38. $[M]^+$ 423.2148 (HRMS). $C_{24}H_{29}N_3O_4 \cdot 0.5C_2H_5OH$. Calculated, %: C 67.24; H 7.22; N 9.41. *M* 423.2158.

4-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-6-phenylpyrimidin-2(1*H*)-one (VIII). A mixture of 0.72 g (6 mmol) of acetophenone, 1.2 g (5 mmol) of aldehyde **I**, 0.6 g (10 mmol) of urea, 10 ml of ethanol, and 0.8 ml of concentrated hydrochloric acid was heated for 13 h under reflux. Additional portions of urea, 0.2 g (3.3 mmol), and concentrated hydrochloric acid, 0.2 ml, were added, and the mixture was heated for 10 h more under reflux. The mixture was cooled to room temperature, and the precipitate was filtered off and washed in succession with ethanol, a saturated aqueous solution of sodium hydrogen carbonate, water, and ethanol again. Yield 0.6 g (32%), mp 355–356°C (from EtOH). Electronic absorption spectrum, λ_{max}, nm (logε): in EtOH: 203 (4.63), 251 (4.13), 354 (4.32), 483 (2.52); in DMSO: 354 (4.08), 490 (3.58). IR spectrum, ν, cm^{-1}: 3628 (OH), 3282, 3186 (NH), 2951 (C–H in *t*-Bu), 1628 (C=O), 1231 (C–O). ^{1}H NMR spectrum (400 MHz), δ, ppm: 1.45 s (18H, *t*-Bu), 7.24 s (1H, 5-H), 7.51–7.64 m (4H, H_{arom}, OH), 7.74 s (2H, H_{arom}), 8.11 d (2H, H_{arom}, ^3J = 6.8 Hz), 11.59 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 376 (50.5) $[M]^+$, 361 (100) $[M - Me]^+$, 345 (5.6) $[M - 31]^+$, 104 (5.8) $[PhC{=}NH]^+$, 77 (4.2) $[Ph]^+$. Found, %: C 76.32; H 7.40; N 7.28. $[M]^+$ 376.2148 (HRMS). $C_{24}H_{28}N_2O_2$. Calculated, %: C 76.56; H 7.50; N 7.44. *M* 376.2151.

4-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-6-(4-fluorophenyl)pyrimidin-2(1*H*)-one (IX) was synthesized in a similar way. Yield 0.63 g (32%), mp 355–356.5°C (from EtOH). Electronic absorption spectrum, λ_{max}, nm (logε): in EtOH: 203 (4.63), 252 (4.01), 354 (4.31), 479 (2.20); in DMSO: 356 (4.19), 488 (3.67). IR spectrum, ν, cm^{-1}: 3629 (OH), 3402, 3279 (NH), 2955 (C–H in *t*-Bu), 1630 (C=O), 1231 (C–O). ^{1}H NMR spectrum (300 MHz), δ, ppm: 1.47 s (18H, *t*-Bu), 7.27 s (1H, 5-H), 7.36 d.d (2H, H_{arom}, $^3J_{HF}$ = 8.6, $^3J_{HH}$ = 8.4 Hz), 7.55 s (OH), 7.71 s (2H, H_{arom}), 8.23 d.d (2H, H_{arom}, $^3J_{HH}$ = 8.0, $^4J_{HF}$ = 5.6 Hz), 12.0 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 394 (47.4) $[M]^+$, 379 (100) $[M - Me]^+$, 363 (5.8) $[M - 31]^+$, 122 (8.9) $[FC_6H_4C{=}NH]^+$, 95 (3.3) $[FC_6H_4]^+$. Found, %:

C 72.87; H 6.81; F 5.00; N 7.11. $[M]^+$ 394.2052 (HRMS). $C_{24}H_{27}FN_2O_2$. Calculated, %: C 73.07; H 6.90; F 4.82; N 7.10. *M* 394.2056.

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