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5-Aryl-2-furaldehydes in the synthesis of tetrahydropyrimidinones by Biginelli reaction

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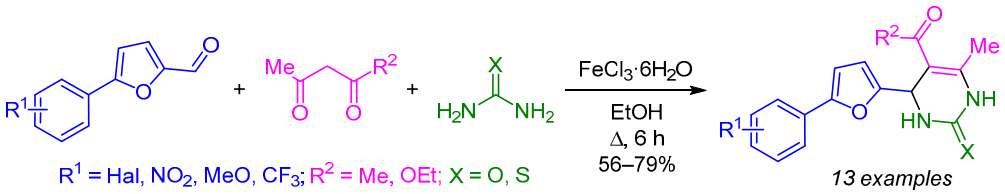

5-Aryl-2-furaldehydes, obtained by furfural arylation with arenediazonium salts, react with ethyl acetoacetate or acetylacetone and (thio)-urea in the presence of $FeCl_3 \cdot 6H_2O$ as a catalyst. A series of ethyl 4-(5-aryl-2-furyl)-6-methyl-2-oxo(thioxo)-1,2,3,4-tetrahydropyrimidine-5-carboxylates was obtained.

Keywords: 5-aryl-2-furaldehydes, pyrimidine derivatives, tetrahydropyrimidines, Biginelli reaction, crystal structure, multicomponent reactions.

Multicomponent reactions (MCRs) are extremely useful organic transformations that are taking place with the participation of three or more components, which react with each other consistently to form the desired product.[1] MCRs have been widely used in organic and medicinal chemistry for the generation of diverse compound libraries,[2] demonstrating synthetic efficiency and significant advantages, reducing time of the reaction, and increasing reaction rate along with high yields and reproducibility. Diversity, efficiency, and fast access to complex functionalized organic molecules make MCRs favorites among synthetic chemists. The current interest in the creation of combinatorial libraries and optimization of chemical processes demonstrates the universality of the MCR approach.[2h,3] These reactions can be an excellent tool for building diverse and variously oriented compound libraries of a new generation.

The Biginelli reaction is a convenient method for the synthesis of functionalized tetrahydropyrimidin-2-ones.[4] Pyrimidine fragment is an important component of a variety of biologically active compounds, including compounds with pharmaceutical application (synthetic drugs) and compounds of natural origin (nucleic acids, vitamins, alkaloids, etc.).[5] Some recently synthesized tetrahydropyrimidin-2-ones are widely used as therapeutic agents and possess pharmacological properties including antiviral, antimitotic, anticancer, antihypertensive, anxiolytic, and hypnotic.[6]

On the other hand, many compounds of the arylfuran series (in particular, 4-nitrophenylfuran derivatives) exhibit a broad spectrum of biological activity.[7] Some of them are already used in therapeutic practice (dantrolene, clodanolene, azimilide, etc.).[7a,b] Therefore, the combination of pyrimidine and arylfuran fragments is of great interest from the point of view of medicinal chemistry, as, for example, evidenced in particular study of the properties of the Biginelli reaction products obtained using 5-(3-trifluoromethylphenyl)furan-2-carbaldehyde.[8] Here we report on the series of 5-aryl-2-furaldehydes as starting compounds in a three-component Biginelli cyclization with (thio)urea and ethyl acetoacetate or acetylacetone.

One of the most convenient approaches to functionalized arylfuraldehydes, which are practical and useful reagents, is arylation of furaldehydes by aryl diazonium salts.[9] Using this methodology, we obtained 5-aryl-2-furaldehydes **3a**–**l** starting from anilines **1a**–**l** *via* diazonium salts **2a**–**l** (Scheme 1).

Scheme 1

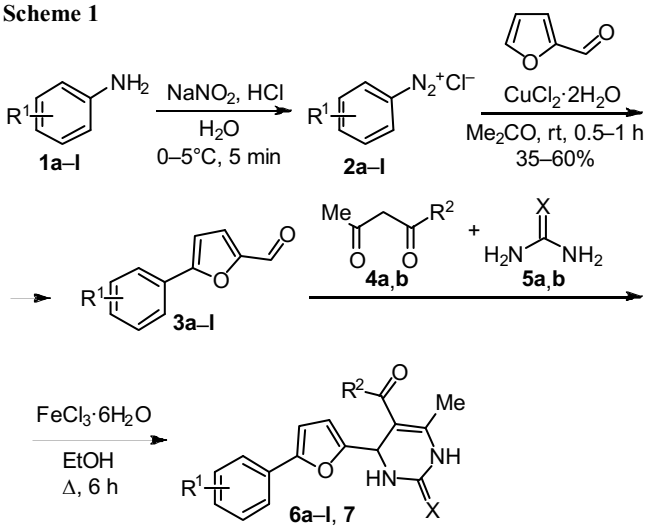

Table 1. Yields of compounds **6a**–**l**, **7**

Compound	R^1	R^2	X	Yield, %
6a	4-F	OEt	O	76
6b	4-Cl	OEt	O	59
6c	4-Br	OEt	O	79
6d	2-NO_2	OEt	O	73
6e	3-NO_2	OEt	O	69
6f	4-NO_2	OEt	O	75
6g	2,3-Cl_2	OEt	O	77
6h	2,5-Cl_2	OEt	O	68
6i	2-Cl-5-CF_3	OEt	O	70
6j	4-Cl-3-CF_3	OEt	O	65
6k	4-MeO-2-NO_2	OEt	O	68
6l	2,4-Cl_2	OEt	S	74
7	4-Br	Me	O	56

We found that aldehydes **3a**–**l** react with ethyl acetoacetate (**4a**) and urea (**5a**) or thiourea (**5b**) in the presence of $FeCl_3 \cdot 6H_2O$ as a catalyst forming ethyl 4-(5-aryl-2-furyl)-6-methyl-2-oxo(thioxo)-1,2,3,4-tetrahydropyrimidine-5-carboxylates **6a**–**l** (Scheme 1, Table 1) with the yields up to 79%.

We investigated the effect of $FeCl_3 \cdot 6H_2O$ catalyst added in 10 mol % quantity. The reactions were carried out in EtOH under reflux for 6 h. It should be noted that in the reaction of 5-aryl-2-furaldehydes **3a**–**l** with ethyl acetoacetate (**4a**) and thiourea (**5b**), resinification occurred, and only compound **6l** was obtained with sufficient yield and purity. Probably, the nature of such behavior lies in oxidizing properties of Fe^{3+} ion. On the other hand, reactions with urea (**5a**) proceeded well and without side reactions or by-products. The yield of the reactions varied in the range from 56 to 79%.

Several most frequently used Biginelli reaction catalysts were investigated for this transformation. It was found, that the hydrochloric acid as a catalyst gave poor results due to the formation of side products and resinification of the reaction mixture. $ZnCl_2$ can be utilized as a catalyst as well,

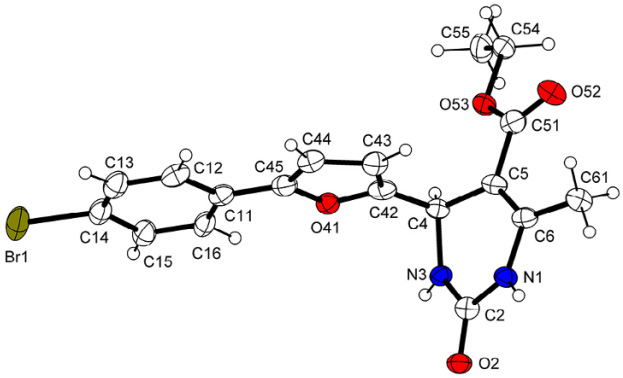

Figure 1. Molecular structure of compound **6c** with atoms represented by thermal vibration ellipsoids of 30% probability.

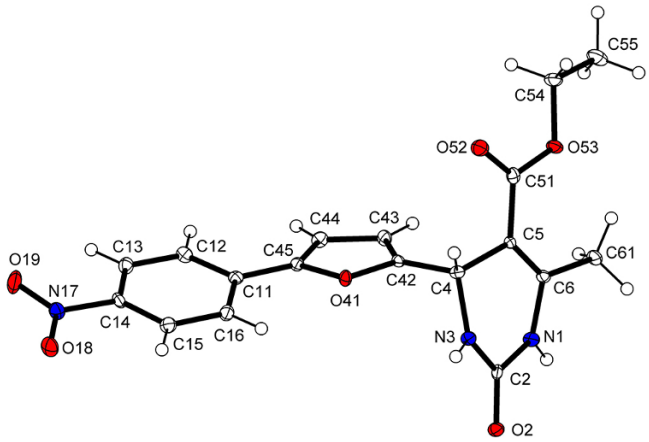

Figure 2. Molecular structure of compound **6f** with atoms represented by thermal vibration ellipsoids of 30% probability.

but in this case, yields of compounds **6a**–**l** were lower. For instance, application of $FeCl_3 \cdot 6H_2O$ as catalyst gave tetrahydropyrimidine **6a** in 76% yield, whereas in the case of $ZnCl_2$ yield of compound **6a** is only 52%.

Acetylacetone (**4b**) can be also successively exploited in this transformation under found reaction conditions. Thus, by the reaction of 5-(4-bromophenyl)-2-furaldehyde **3c** with urea (**5a**) and acetylacetone (**4b**), compound **7** was formed in 56% yield. However, in the reactions of aldehydes **3a**–**l** with urea (**5a**) and dimedone, the desired Biginelli products were not isolated. Carrying out the reactions in highly boiling solvent (acetic acid) did not give positive results too, proving that 5-aryl-2-furaldehydes are less active reagents in Biginelli reaction comparing to benzaldehydes.[4c]

The structure of compounds **6a**–**l**, **7** was confirmed by ^1H and ^{13}C NMR spectroscopy and by X-ray structural analysis (compounds **6c**,**f**, Fig. 1, 2). The geometrical parameters of compounds **6c**,**f** are comparable with the reported in the literature unsubstituted furan derivatives of methyl and ethyl tetrahydropyrimidine-5-carboxylates.[10]

Thus, a method for the synthesis of ethyl 4-(5-aryl-2-furyl)-6-methyl-2-oxo(thioxo)-1,2,3,4-tetrahydropyrimidine-5-carboxylates *via* the Biginelli reaction has been developed utilizing 5-aryl-2-furaldehydes as starting compounds.

Experimental

^{1}H and ^{13}C NMR spectra were acquired on a Bruker WH-400 spectrometer (400 and 100 MHz, respectively) in DMSO-d_6, using TMS as internal standard. Elemental analysis was performed on a Carlo Erba 1106 instrument. Melting points were determined on a Boetius apparatus.

Synthesis of 5-aryl-2-furaldehydes 3a–l (General method).[9] A solution of $NaNO_2$ (15.2 g, 0.22 mol) in H_2O (30 ml) was added dropwise to a stirred and ice-cooled (0–5°C) mixture of the substituted aniline **1a**–**l** (0.2 mol), concd HCl (40 ml), and water (30 ml). Then cold diazonium salt **2a**–**l** solution was slowly added to the vigorously stirred solution of $CuCl_2·2H_2O$ (2.0 g, 11.0 mmol) and furaldehyde (19.2 g, 0.2 mol) in Me_2CO (80 ml) at 20–25°C. The dropping rate was adjusted in a way that nitrogen was evolved at 2-3 bubbles/s (0.5–1 h). When bubbling stopped (all nitrogen was removed), the product was filtered off, washed 3 times with water, and re-crystallized from EtOH or EtOH–DMF mixture. Characteristics of compounds **3a**–**l** were in good agreement with literature data.[8,11]

Synthesis of compounds 6a–l, 7 (General method). A mixture of 5-aryl-2-furaldehyde **3a**–**l** (2.0 mmol), ethyl acetoacetate (**4a**) or acetylacetone (**4b**) (2.0 mmol), urea (**5a**) or thiourea (**5b**) (2.0 mmol), and $FeCl_3·6H_2O$ (0.054 g, 0.2 mmol) in EtOH (10 ml) was heated under reflux for 6 h. After cooling to room temperature, the reaction mixture was poured into distilled water (50 ml). The precipitate was filtered off and washed several times with distilled water. The crude product was recrystallized from EtOH–DMF (1:2) mixture.

Ethyl 4-[5-(4-fluorophenyl)furan-2-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6a). Yield 0.52 g (76%), white powder, mp 225–226°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.16 (3H, t, *J* = 7.1, C$\underline{H_3}$CH$_2$); 2.26 (3H, s, CH$_3$); 4.06 (2H, q, *J* = 7.1, CH$_3$C$\underline{H_2}$); 5.25 (1H, d, *J* = 3.2, CH); 6.20 (1H, d, *J* = 3.3, H Fur); 6.81 (1H, d, *J* = 3.3, H Fur); 7.27 (2H, dd, J_{HH} = 8.8, J_{HF} = 8.8, H Ar); 7.66 (2H, dd, J_{HH} = 8.8, J_{HF} = 5.5, H Ar), 7.84 (1H, br. s, NH); 9.31 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 14.7; 18.2; 48.3; 59.8; 97.1; 106.7; 107.9; 116.4 (2C, d, *J* = 22.0); 125.7 (2C, d, *J* = 8.2); 127.5; 150.1; 151.6; 153.0; 156.4; 161.9 (d, *J* = 244.6); 165.5. Found, %: C 62.54; H 4.77; N 7.92. $C_{18}H_{17}FN_2O_4$. Calculated, %: C 62.79; H 4.98; N 8.14.

Ethyl 4-[5-(4-chlorophenyl)furan-2-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6b). Yield 0.43 g (59%), light-brown powder, mp 254–255°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (3H, t, *J* = 7.0, C$\underline{H_3}$CH$_2$); 2.26 (3H, s, CH$_3$); 4.06 (2H, q, *J* = 7.0, CH$_3$C$\underline{H_2}$); 5.26 (1H, d, *J* = 2.8, CH); 6.22 (1H, d, *J* = 3.1, H Fur); 6.89 (1H, d, *J* = 3.1, H Fur); 7.49 (2H, d, *J* = 8.0, H Ar); 7.64 (2H, d, *J* =8.0, H Ar); 7.84 (1H, br. s, NH); 9.32 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.7; 18.2; 48.4; 59.8; 97.0; 107.7; 108.1; 125.2 (2C); 129.4 (2C); 129.6; 132.2; 150.1; 151.3; 153.0; 156.8; 165.5. Found, %: C 59.74; H 4.51; N 7.92. $C_{18}H_{17}ClN_2O_4$. Calculated, %: C 59.92; H 4.75; N 7.76.

Ethyl 4-[5-(4-bromophenyl)furan-2-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6c). Yield 0.64 g (79%), light-yellow needles, mp 204–205°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (3H, t, *J* = 7.1, C$\underline{H_3}$CH$_2$); 2.26 (3H, s, CH$_3$); 4.06 (2H, q, *J* = 7.1, CH$_3$C$\underline{H_2}$); 5.26 (1H, d, *J* = 3.3, CH); 6.22 (1H, d, *J* = 3.3, H Fur); 6.90 (1H, d, *J* = 3.3, H Fur); 7.57 (2H, d, *J* = 8.6, H Ar); 7.62 (2H, d, *J* = 8.6, H Ar); 7.86 (1H, br. s, NH); 9.32 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.7; 18.2; 48.4; 59.8; 97.0; 107.8; 108.1; 120.7; 125.5 (2C); 129.9; 132.3 (2C); 150.1; 151.4; 153.0; 156.8; 165.5. Found, %: C 53.11; H 3.92; N 6.63. $C_{18}H_{17}BrN_2O_4$. Calculated, %: C 53.35; H 4.23; N 6.91.

Ethyl 6-methyl-4-[5-(2-nitrophenyl)furan-2-yl]-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6d). Yield 0.54 g (73%), yellow-brown powder, mp 230–231°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (3H, t, *J* = 7.1, C$\underline{H_3}$CH$_2$); 2.26 (3H, s, CH$_3$); 4.05 (2H, q, *J* = 7.1, CH$_3$C$\underline{H_2}$); 5.22 (1H, d, *J* = 3.2, CH); 6.29 (1H, d, *J* = 3.3, H Fur); 6.79 (1H, d, *J* = 3.3, H Fur); 7.53 (1H, t, *J* = 7.8, H Ar); 7.70 (1H, t, *J* = 7.8, H Ar); 7.75 (1H, br. s, NH); 7.78 (1H, d, *J* = 7.8, H Ar); 7.83 (1H, d, *J* = 7.8, H Ar); 9.27 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.6; 18.2; 48.3; 59.7; 96.7; 108.1; 111.0; 123.1; 124.4; 128.7; 129.4; 132.8; 147.2 (2C); 150.3; 152.8; 158.3; 165.3. Found, %: C 58.01; H 4.79; N 11.00. $C_{18}H_{17}N_3O_6$. Calculated, %: C 58.22; H 4.61; N 11.32.

Ethyl 6-methyl-4-[5-(3-nitrophenyl)furan-2-yl]-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6e). Yield 0.51 g (69%), light-yellow powder, mp 249–250°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.19 (3H, t, *J* = 7.1, C$\underline{H_3}$CH$_2$); 2.30 (3H, s, CH$_3$); 4.11 (2H, q, *J* = 7.1, CH$_3$C$\underline{H_2}$); 5.37 (1H, d, *J* = 3.1, CH); 6.30 (1H, d, *J* = 3.3, H Fur); 7.12 (1H, d, *J* = 3.3, H Fur); 7.72 (1H, t, *J* = 8.0, H Ar); 7.88 (1H, br. s, NH); 8.08–8.12 (2H, m, H Ar); 8.44 (1H, s, H Ar); 9.33 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.3; 17.9; 48.4; 59.6; 96.9; 108.1; 109.2; 117.6; 121.9; 129.5; 130.8; 132.3; 148.9; 150.3 (2C); 153.0; 157.7; 165.4. Found, %: C 58.44; H 4.37; N 11.04. $C_{18}H_{17}N_3O_6$. Calculated, %: C 58.22; H 4.61; N 11.32.

Ethyl 6-methyl-4-[5-(4-nitrophenyl)furan-2-yl]-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6f). Yield 0.56 g (75%), light-yellow crystals, mp 231–232°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (3H, t, *J* = 7.0, C$\underline{H_3}$CH$_2$); 2.27 (3H, s, CH$_3$); 4.07 (2H, q, *J* = 7.0, CH$_3$C$\underline{H_2}$); 5.31 (1H, d, *J* = 3.0, CH); 6.34 (1H, d, *J* = 3.3, H Fur); 7.20 (1H, d, *J* = 3.3, H Fur); 7.86 (2H, d, *J* = 8.8, H Ar); 7.92 (1H, br. s, NH); 8.28 (2H, d, *J* = 8.8, H Ar); 9.36 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.7; 18.2; 48.4; 59.9; 96.7; 108.8; 111.6; 124.1 (2C); 125.0 (2C); 136.5; 146.3; 150.4; 150.5; 152.9; 158.8; 165.4. Found, %: C 57.98; H 4.79; N 11.57. $C_{18}H_{17}N_3O_6$. Calculated, %: C 58.22; H 4.61; N 11.32.

Ethyl 4-[5-(2,3-dichlorophenyl)furan-2-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6g). Yield 0.61 g (77%), white powder, mp 233–234°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.16 (3H, t, *J* = 7.1, C$\underline{H_3}$CH$_2$); 2.26 (3H, s, CH$_3$); 4.07 (2H, q, *J* = 7.1, CH$_3$C$\underline{H_2}$); 5.29 (1H, d, *J* = 2.8, CH); 6.31 (1H, d, *J* = 3.3,

H Fur); 7.11 (1H, d, *J* = 3.3, H Fur); 7.45 (1H, t, *J* = 7.8, H Ar); 7.59 (1H, d, *J* = 7.8, H Ar); 7.72 (1H, d, *J* = 7.8, H Ar); 7.88 (1H, br. s, NH); 9.35 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.7; 18.2; 48.3; 59.8; 96.9; 108.0; 113.4; 126.6; 127.4; 128.9; 129.6; 131.1; 133.7; 148.1; 150.3; 153.0; 157.2; 165.5. Found, %: C 54.52; H 3.92; N 6.88. $C_{18}H_{16}Cl_2N_2O_4$. Calculated, %: C 54.70; H 4.08; N 7.09.

Ethyl 4-[5-(2,5-dichlorophenyl)furan-2-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6h). Yield 0.54 g (68%), yellow-brown powder, mp 232–233°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.17 (3H, t, *J* = 7.1, C<u>H</u>$_3$CH$_2$); 2.26 (3H, s, CH$_3$); 4.08 (2H, q, *J* = 7.1, CH$_3$C<u>H</u>$_2$); 5.30 (1H, d, *J* = 3.4, CH); 6.30 (1H, d, *J* = 3.6, H Fur); 7.14 (1H, d, *J* = 3.6, H Fur); 7.37 (1H, dd, *J* = 8.6, *J* = 2.6, H Ar); 7.56 (1H, d, *J* = 8.6, H Ar); 7.80 (1H, d, *J* = 2.6, H Ar); 7.94 (1H, br. s, NH); 9.37 (1H, d, *J* = 1.4, NH). ^{13}C NMR spectrum, δ, ppm: 14.7; 18.2; 48.3; 59.9; 96.7; 108.1; 113.4; 126.9; 127.7; 128.7; 130.2; 132.7; 133.0; 147.3; 150.4; 153.0; 157.2; 165.5. Found, %: C 54.87; H 4.26; N 7.23. $C_{18}H_{16}Cl_2N_2O_4$. Calculated, %: C 54.70; H 4.08; N 7.09.

Ethyl 4-{5-[2-chloro-5-(trifluoromethyl)phenyl]furan-2-yl}-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6i). Yield 0.60 g (70%), white powder, mp 219–220°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.16 (3H, t, *J* = 7.1, C<u>H</u>$_3$CH$_2$); 2.26 (3H, s, CH$_3$); 4.07 (2H, q, *J* = 7.1, CH$_3$C<u>H</u>$_2$); 5.33 (1H, d, *J* = 3.4, CH); 6.33 (1H, d, *J* = 3.5, H Fur); 7.21 (1H, d, *J* = 3.5, H Fur); 7.66 (1H, dd, *J* = 8.4, *J* = 2.0, H Ar); 7.79 (1H, d, *J* = 8.4, H Ar); 7.97 (1H, br. s, NH); 8.07 (1H, d, *J* = 2.0, H Ar); 9.37 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.6; 18.2; 48.3; 59.8; 96.7; 108.2; 113.9; 124.0 (q, *J* = 3.7); 124.1 (q, *J* = 270.0); 125.3 (q, *J* = 3.9); 128.9 (q, *J* = 32.5); 129.5; 132.6; 133.1 (q, *J* = 0.8); 147.2; 150.4; 153.0; 157.6; 165.5. Found, %: C 52.95; H 3.58; N 6.76. $C_{19}H_{16}ClF_3N_2O_4$. Calculated, %: C 53.22; H 3.76; N 6.53.

Ethyl 4-{5-[4-chloro-3-(trifluoromethyl)phenyl]furan-2-yl}-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6j). Yield 0.56 g (65%), yellow-brown powder, mp 226–227°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.16 (3H, t, *J* = 7.1, C<u>H</u>$_3$CH$_2$); 2.26 (3H, s, CH$_3$); 4.07 (2H, q, *J* = 7.1, CH$_3$C<u>H</u>$_2$); 5.29 (1H, d, *J* = 3.3, CH); 6.27 (1H, d, *J* = 3.4, H Fur); 7.12 (1H, d, *J* = 3.4, H Fur); 7.78 (1H, d, *J* = 8.5, H Ar); 7.88–7.93 (2H, m, H Ar, NH); 8.01 (1H, d, *J* = 1.7, H Ar); 9.35 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.6; 18.2; 48.3; 59.8; 96.8; 108.3; 109.6; 122.3 (q, *J* = 5.3); 123.2 (q, *J* = 271.3); 127.8 (q, *J* = 30.7); 128.6; 129.3 (q, *J* = 1.5); 130.2; 132.8; 149.9; 150.3; 153.0; 157.6; 165.5. Found, %: C 53.47; H 3.82; N 6.86. $C_{19}H_{16}ClF_3N_2O_4$. Calculated, %: C 53.22; H 3.76; N 6.53.

Ethyl 4-[5-(4-methoxy-2-nitrophenyl)furan-2-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6k). Yield 0.55 g (68%), yellow-brown powder, mp 206–207°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (3H, t, *J* = 7.1, C<u>H</u>$_3$CH$_2$); 2.25 (3H, s, CH$_3$); 3.86 (3H, s, OCH$_3$); 4.05 (2H, q, *J* = 7.1, CH$_3$C<u>H</u>$_2$); 5.20 (1H, d, *J* = 3.2, CH); 6.23 (1H, d, *J* = 3.3, H Fur); 6.61 (1H, d, *J* = 3.3, H Fur); 7.29 (1H, dd, *J* = 8.8, *J* = 2.4, H Ar); 7.45 (1H, d, *J* = 2.4, H Ar); 7.67 (1H, d, *J* = 8.8, H Ar); 7.73 (1H, br. s, NH); 9.25 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.6; 18.2; 48.2; 56.6; 59.7; 96.8; 107.9; 109.4 (2C); 115.7; 118.9; 130.0; 147.3; 148.1; 150.2; 152.8; 157.5; 159.5; 165.4. Found, %: C 56.61; H 4.94; N 10.12. $C_{19}H_{19}N_3O_7$. Calculated, %: C 56.86; H 4.77; N 10.47.

Ethyl 4-[5-(2,4-dichlorophenyl)furan-2-yl]-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6l). Yield 0.61 g (74%), light-yellow powder, mp 231–232°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (3H, t, *J* = 7.1, C<u>H</u>$_3$CH$_2$); 2.30 (3H, s, CH$_3$); 4.08 (2H, q, *J* = 7.1, CH$_3$C<u>H</u>$_2$); 5.31 (1H, d, *J* = 3.7, CH); 6.34 (1H, d, *J* = 3.4, H Fur); 7.08 (1H, d, *J* = 3.4, H Fur); 7.54 (1H, dd, *J* = 8.6, *J* = 2.1, H Ar); 7.71 (1H, d, *J* = 2.1, H Ar); 7.74 (1H, d, *J* = 8.6, H Ar); 9.74 (1H, br. s, NH); 10.51 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.6; 17.6; 48.3; 60.2; 98.4; 108.9; 112.8; 127.7; 128.3; 129.0; 130.2; 130.7; 132.9; 146.8; 148.2; 155.6; 165.2; 175.7. Found, %: C 52.32; H 4.15; N 6.64. $C_{18}H_{16}Cl_2N_2O_3S$. Calculated, %: C 52.56; H 3.92; N 6.81.

5-Acetyl-4-[5-(4-bromophenyl)furan-2-yl]-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (7). Yield 0.40 g (56%), light-brown powder, mp 265–266°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.19 (3H, s, CH$_3$); 2.24 (3H, s, CH$_3$); 5.33 (1H, s, CH); 6.20 (1H, d, *J* = 3.3, H Fur); 6.86 (1H, d, *J* = 3.3, H Fur); 7.55–7.70 (4H, m, H Ar); 7.92 (1H, s, NH); 9.28 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 19.5; 30.6; 48.4; 107.9; 108.4; 120.8; 125.6 (2C); 126.7; 129.8; 132.4 (2C); 149.6; 151.6; 153.0; 156.6; 194.2. Found, %: C 54.23; H 3.89; N 7.25. $C_{17}H_{15}BrN_2O_3$. Calculated, %: C 54.42; H 4.03; N 7.47.

X-ray structural study of compounds 6c,f was performed on a four-circle Oxford Diffraction Xcalibur diffractometer. Crystal structures were solved by direct methods using the SHELXT program.[12] Full-matrix least-square refinement of atomic coordinates and anisotropic thermal parameters (for non-hydrogen atoms) was done on F^2 using the SHELXL program.[13] The positions of hydrogen atoms were found on difference Fourier maps, but in final refinement cycles were restrained geometrically to the idealized positions. Complete bond lengths and angles, coordinates, and displacement parameters have been deposited at the Cambridge Crystallographic Data Center (deposits CCDC 1534517 for compound **6c**, CCDC 1534516 for compound **6f**).

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