Three Component Condensation Reaction as an Efficient Route for the Synthesis of Furo[2,3-*d*]pyrimidines

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Abstract: The condensation reactions of alkyl isocyanides with 1,3-dimethylbarbituric acid and aryl carboxaldehydes to afford 6-(alkylamino)-5-(3-aryl)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione, in excellent yields under neutral conditions, are reported.

Keywords: Aldehydes, condensation reaction, fused heterocycles, isocyanides, 1,3-dimethylbarbituric acid, 1,3-dimethylfuro[2,3-*d*]pyrimidine.

INTRODUCTION

Some reagents such as isocyanides are useful reagents for synthesis of organic structures [1, 2]. There are many diverse cycloaddition reactions in which isocyanides play a key role for synthesis of different types of heterocycles [3-7]. A general feature of isocyanide reactions is the formation of α,α-addition reaction products: *i.e.* two new bonds are formed to the terminal isocyanide carbon atom. Typical examples are the reaction of isocyanide with protonic acids, carbon-oxygen and carbon-carbon double bond or triple bond of electron-deficient compounds [2, 3, 8]. Fused heterocyclic structures containing pyrimidine or furan rings exhibited diverse biological activities such as antimicrobial [9, 10], anti-inflammatory [11], antiviral [12], anti HIV [13] and antitumor [14].

In continuation of our investigations on development of synthesis of five and six membered rings [6, 15-20], we now describe the synthesis of furo[2,3-*d*]pyrimidine derivatives containing a cyclohexyl or *tert*-butylamine substitution on C-2 position of furan ring by means of a mild one-pot reaction between aldehydes and isocyanides in the presence of 1,3-dimethylbarbituric acid.

RESULTS AND DISCUSSION

Herein, a number of new furo[2,3-*d*]pyrimidine derivatives **4** were prepared using isocyanides **1**, aldeydes **2** and 1,3-dimethylbarbituric acid **3** at room temperature reaching completion in 6-15 hours. The structural assignments of the desired 5-aryl-6-(alkylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine derivatives **4a**-**k** were made on the basis of their ^{1}H and ^{13}C NMR spectra which are supported by their IR and mass spectrometry as well as elemental analyses (Scheme **1**).

The ^{1}H NMR spectrum of **4a** exhibited three sharp singlets δ = 1.16, 3.37 and 3.55 ppm arising from both *tert*-butyl and *N*-methyl groups, respectively. NH proton of **4a** appeared at δ = 3.34 ppm as a broad signal which was disappeared in D_2O exchange experiment. All arylic protons resonate at aromatic region (δ = 7.22-7.61 ppm).

The ^{1}H decoupled ^{13}C NMR spectrum of **4a** showed four signals readily recognized as arising from two *N*CH_3 group (δ = 27.25 and 28.38 ppm), three methyl of *tert*-butyl (δ = 29.16 ppm) and quaternary carbon of *tert*-butyl group (δ = 53.48 ppm) as well as other twelve distinct resonances in agreement with the proposed structure. The characteristic signals for the carbonyl groups of C-2 and C-4 were observed at δ 150.48 and 157.02 ppm, respectively.

The IR spectrum of compound **4a** at the carbonyl region displayed distinct absorption bands resulting from the carbonyl and NH groups respectively for each compound.

An illustrative mechanism for this reaction is shown in Scheme **2**. The first step may involve a Knovenagel condensation between the aldehyde **2a** and 1,3-dimethylbarbituric acid **3** for the formation of the stable intermediate enone **5**, which undergoes nucleophilic attack by isocyanide **1a** to generate adduct **6**. This adduct undergo intra nucleophilic addition by oxanion for cyclization process of five-member ring to afford compound **7** which then can undergo tautomerization to output the final compound **4a**.

It must be mentioned that the effects of substitution (electron donating or electron with drawing groups) on aryl ring have been investigated in this reaction. Additional experiments showed that the benzaldehydes with electron donating substituents have not satisfactory results, whereas benzaldehydes containing electron with drawing substituents react with any side product formation. For example, no reaction between *p*-*N*,*N*-dimethylaminobenzaldehyde or 2,4-dimethoxy benzaldehyde and 1,3-dimethylbarbituric acid in

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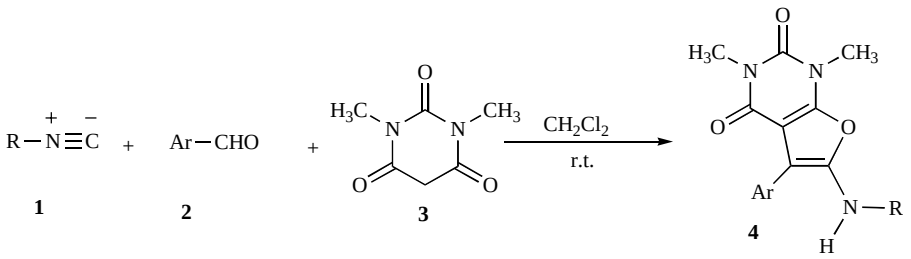
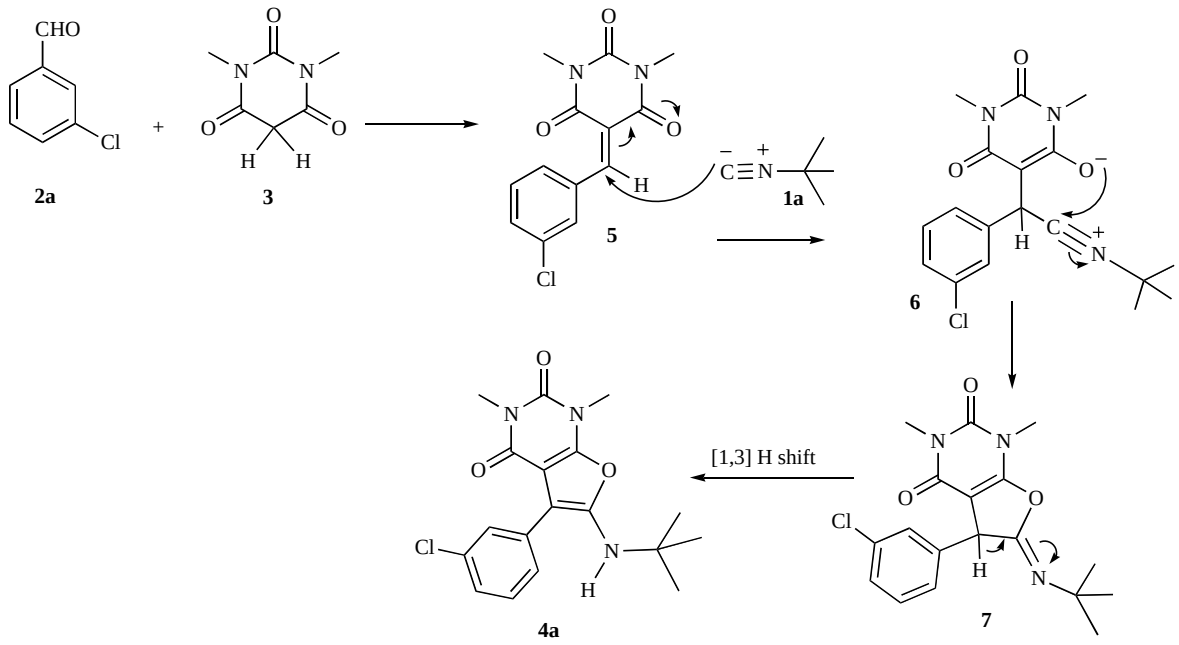


4	R	Ar	time (*h*)[a]	% yield
a	*t*-butyl	3-chlorophenyl	6	97
b	*t*-butyl	4-chlorophenyl	11	97
c	cyclohexyl	4-chlorophenyl	9	94
d	*t*-butyl	4-methylphenyl	12	96
e	cyclohexyl	4-methylphenyl	13	92
f	*t*-butyl	2-chlorophenyl	13	98
g	cyclohexyl	2-chlorophenyl	10	87
h	*t*-butyl	2-methylphenyl	15	94
i	cyclohexyl	2-methylphenyl	9	96
j	*t*-butyl	2,4-dichlorophenyl	11	86
k	cyclohexyl	2,4-dichlorophenyl	8	91

[a] All reaction times are reported base on TLC monitoring.

Scheme 1.



Scheme 2.

the presence of isocyanides for the synthesis of other analogous of compound **4** was observed.

In conclusion, we have reported the in situ synthesis of 5-aryl-6-(alkylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine

derivatives by an efficient and simple approach along with three-component condensation between aromatic aldehydes, 1,3-dimethylbarbituric acid and isocyanides.

EXPERIMENTAL

Melting points and IR spectra of all compounds were measured on an Electrothermal 9100 apparatus and a Shimadzu Prestige 21 FT-IR spectrometer, respectively. Also, the ^{1}H and ^{13}C NMR spectra were obtained with a BRUKER DRX-400 AVANCE instruments using $CDCl_3$ as a solvent and TMS as internal standard at (400.1, 100.1) MHz, respectively. Elemental analyses for C, H and N were performed using a Heraeus CHN-O-Rapid analyzer. In addition, the mass spectra were recorded on a Shimadzu GCMS-QP5050A mass spectrometer operating at an ionization potential of 70 eV. Isocyanides, 1,3-dimethylbarbituric acid and aromatic carbaldehyde derivatives were purchased from Fluka, Merck and Acros companies and used without further purification.

General Procedure for Preparation of furo[2,3-*d*]pyrimidine Derivatives (Exemplified by 4a)

To a magnetically stirred solution of 3-chlorocarbaldehyde **2** (1 mmol) and 1,3-dimethylbarbituric acid **3** (1 mmol) in CH_2Cl_2 (10 mL) was added, dropwise, a mixture of *tert*-butylisocyanide (1.1 mmol) in CH_2Cl_2 (3 mL) over 10 min at room temperature. After 6 hours stirring at room temperature, the solvent was removed and the crude product washed by diethyl ether (2×3 mL), then the residual was recrystalized in a mixture of ethyl acetate/n-hexane (3:1) to afford final product **4a**.

6-(tert-butylamino)-5-(3-chlorophenyl)-1,3-dimethylfuro [2,3-d]pyrimidine-2,4(1H,3H)-dione (4a)

White powder, yield: 0.35 g (97%), mp 149-152 °C, IR (KBr) (ν_{max}, cm^{-1}): 3297 (NH), 1705 and 1689 (C=O). MS (*m/z, %*): 363 (M^++2, 15), 362 (M^++1, 11), 361 (M^+, 45), 346 (4), 305 (100), 293 (5), 250 (21), 248 (62), 75 (4), 57 (31). Anal. Calcd. for $C_{18}H_{20}ClN_3O_3$ (361.82): C, 59.75; H, 5.57; N, 11.61%. Found: C, 59.70; H, 5.68; N, 11.49%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 1.16 (9H, s, NC*Me*$_3$), 3.34 (1H, br s, N*H*), 3.37 and 3.55 (6H, 2s, 2 NC*H*$_3$), 7.22-7.28 (1H, m, CH_{arom}), 7.32 (1H, t, J = 8.0 Hz, CH_{arom}), 7.50 (1H, dt, J_1 = 7.7, J_2 = 1.2 Hz, CH_{arom}), 7.61 (1H, t, J = 1.9 Hz, CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 27.25 and 28.38 (2s, 2 NCH_3), 29.16 (s, NC*Me*$_3$), 53.48 (s, N*C*Me$_3$), 94.32 (s, C-4a), 109.01 (s, C-5), 126.28, 126.84, 128.23 and 128.30 (4s, 4 CH_{arom}), 131.27 and 132.73 (2s, 2 C_{arom}), 147.20 (s, C-6), 149.38 (s, C-7a), 150.48 (s, C-2), 157.02 (s, C-4).

6-(tert-butylamino)-5-(4-chlorophenyl)-1,3-dimethylfuro [2,3-d]pyrimidine-2,4(1H,3H)-dione (4b)

White powder, yield: 0.35 g (97%), mp 165-168 °C (decomposed), IR (KBr) (ν_{max}, cm^{-1}): 3305 (NH), 1706 and 1698 (C=O). MS (*m/z, %*): 363 (M^++2, 1), 361 (M^+, 3), 341 (96), 326 (2), 285 (100), 257 (62), 156 (34), 57 (32), 41 (26). Anal. Calcd. for $C_{18}H_{20}ClN_3O_3$ (361.82): C, 59.75; H, 5.57; N, 11.61%. Found: C, 59.67; H, 5.64; N, 11.53%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 1.15 (9H, s, NC*Me*$_3$), 3.31 (1H, br s, N*H*), 3.37 and 3.55 (6H, 2s, 2 NC*H*$_3$), 7.35 (2H, d, J = 8.4 Hz, 2 CH_{arom}), 7.55 (2H, d, J = 8.4 Hz, 2 CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 27.21 and 28.70 (2s, 2 NCH_3), 29.16 (s, NC*Me*$_3$), 53.51 (s, N*C*Me$_3$), 94.41 (s, C-4a), 109.70 (s, C-5), 127.24 (s, 2 CH_{arom}), 127.96 (s, C_{arom}), 129.89 (s, 2 CH_{arom}), 132.15 (s, C_{arom}), 146.97 (s, C-6), 149.45 (s, C-7a), 150.60 (s, C-2), 157.14 (s, C-4).

6-(Cyclohexylamino)-5-(4-chlorophenyl)-1,3-dimethylfuro [2,3-d]pyrimidine-2,4(1H,3H)-dione (4c)

White powder, yield: 0.36 g (94%), mp 151-154 °C, IR (KBr) (ν_{max}, cm^{-1}): 3311 (NH), 1701 and 1693 (C=O). MS (*m/z, %*): 389 (M^++2, 5), 388 (M^++1, 3), 387 (M^+, 13), 305 (10), 293 (100), 279 (3),139 (38), 126 (6), 111 (27), 99 (5), 75 (17), 58 (25), 41 (16).Anal. Calcd. for $C_{20}H_{22}ClN_3O_3$ (387.86): C, 61.93; H, 5.72; N, 10.83%. Found: C, 61.99; H, 5.67; N, 10.72%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 1.11-1.92 (10H, m, 5 C*H*$_2$ of cyclohexyl), 3.11-3.18 (1H, m, NC*H*), 3.37 (3H, s, NC*H*$_3$), 3.48 (1H, d, $^{3}J_{HH}$ = 6.7 Hz, N*H*), 3.57 (3H, s, NC*H*$_3$), 7.36 (2H, d, $^{3}J_{HH}$ = 8.5 Hz, 2 CH_{arom}), 7.52 (2H, d, $^{3}J_{HH}$ = 8.5 Hz, 2 CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 23.70 and 24.50 (2s, 3 *C*H$_2$ of cyclohexyl), 27.25 and 28.72 (2s, 2 NC*H*$_3$), 32.91 (s, *C*H$_2$ of cyclohexyl), 54.51 (s, N*C*H), 94.80 (s, C-4a), 103.19 (s, C-5), 127.40 and 129.54 (2s, 4 CH_{arom}), 131.80 and 135.10 (2s, 2 C_{arom}), 147.75 (s, C-6), 149.35 (s, C-7a), 149.86 (s, C-2), 157.14 (s, C-4).

6-(tert-butylamino)-5-(4-methylphenyl)-1,3-dimethylfuro [2,3-d]pyrimidine-2,4(1H,3H)-dione (4d)

Pale white powder, yield: 0.33 g (96%), mp 162-165 °C, IR (KBr) (ν_{max}, cm^{-1}): 3284 (NH), 1705 and 1670 (C=O). MS (*m/z, %*): 342 (M^++1, 4), 341 (M^+, 17), 326 (1), 285 (60), 293 (5), 259 (20), 156 (13), 57 (100), 41 (65). Anal. Calcd. for $C_{19}H_{23}N_3O_3$ (341.40): C, 66.84; H, 6.79; N, 12.31%. Found: C, 66.91; H, 6.87; N, 12.26%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 1.16 (9H, s, NC*Me*$_3$), 2.36 (3H, s, ArC*H*$_3$), 3.38 (3H, s, NC*H*$_3$), 3.43 (1H, br s, N*H*), 3.55 (3H, s, NC*H*$_3$), 7.21 (2H, d, J = 8.0 Hz, 2 CH_{arom}), 7.44 (2H, d, J = 8.0 Hz, CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 20.27 (s, Ar*C*H$_3$), 27.18 and 28.33 (2s, 2 NCH_3), 29.18 (s, NC*Me*$_3$), 53.31 (s, N*C*Me$_3$), 94.24 (s, C-4a), 110.06 (s, C-5), 126.39 (s, C_{arom}), 127.43 and 128.35 (2s, 4 CH_{arom}), 136.07 (s, C_{arom}), 146.94 (s, C-6), 150.35 (s, C-7a), 149.88 (s, C-2), 157.14 (s, C-4).

6-(Cyclohexylamino)-5-(4-methylphenyl)-1,3-dimethylfuro [2,3-d]pyrimidine-2,4(1H,3H)-dione (4e)

White powder, yield: 0.34 g (92%), mp 241-244 °C (decomposed), IR (KBr) (ν_{max}, cm^{-1}): 3255 (NH), 1698 and 1691 (C=O). MS (*m/z, %*): 367 (M^+, 1), 285 (2), 273 (100), 178 (9), 119 (65), 91 (63), 56 (93), 43 (53). Anal. Calcd. for $C_{21}H_{25}N_3O_3$ (367.44): C, 68.64; H, 6.86; N, 11.44%. Found: C, 68.72; H, 6.90; N, 11.53%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 0.88-2.17 (10H, m, 5 C*H*$_2$ of cyclohexyl), 2.39 (3H, s, ArC*H*$_3$), 3.25 and 3.36 (6H, 2s, 2 NC*H*$_3$), 3.85-3.93 (1H, m, NC*H*), 5.20 (1H, d, $^{3}J_{HH}$ = 8.1 Hz, N*H*), 7.22 (2H, d, $^{3}J_{HH}$ = 8.0 Hz, 2 CH_{arom}), 7.35 (2H, d, $^{3}J_{HH}$ = 8.0 Hz, 2 CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 20.64 (s, Ar*C*H$_3$), 23.78 and 24.45 (2s, 4 *C*H$_2$ of cyclohexyl), 27.74 and 27.80 (2s, 2 N*C*H$_3$), 31.67 (s, *C*H$_2$ of cyclohexyl), 47.78 (s, N*C*H), 94.77 (s, C-4a), 107.41 (s, C-5), 127.11 and 127.93 (2s, 4 CH_{arom}), 130.39 and 131.79 (2s, 2 C_{arom}), 140.44 (s, C-6), 150.11 (s, C-7a), 150.75 (s, C-2), 160.03 (s, C-4).

6-(tert-butylamino)-5-(2-chlorophenyl)-1,3-dimethylfuro [2,3-d]pyrimidine-2,4(1H,3H)-dione (4f)

Pale white powder, yield: 0.35 g (98%), mp 156-159 °C, IR (KBr) (ν_{max}, cm^{-1}): 3264 (NH), 1701 and 1670 (C=O). MS (*m/z, %*): 363 (M^++2, 14), 361 (M^+, 40), 326 (1), 305 (100), 293 (7), 248 (65), 176 (76), 57 (49), 41 (29). Anal. Calcd. for $C_{18}H_{20}ClN_3O_3$ (361.82): C, 59.75; H, 5.57; N, 11.61%. Found: C, 59.63; H, 5.62; N, 11.58%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 1.17 (9H, s, NC*Me*$_3$), 3.35 (1H, s, N*H*), 3.37 and 3.55 (6H, 2s, 2 NC*H*$_3$), 7.25-7.28 (1H, m, CH_{arom}), 7.32 (1H, t, *J* = 7.9 Hz, CH_{arom}), 7.51 (1H, dt, J_1 = 7.6, J_2 = 1.4 Hz, CH_{arom}), 7.62 (1H, t, *J* = 1.8 Hz, CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 27.26 and 28.38 (2s, 2 N*C*H$_3$), 29.20 (s, NC*Me*$_3$), 53.50 (s, N*C*Me$_3$), 94.38 (s, C-4a), 109.14 (s, C-5), 126.34, 126.89, 128.26 and 128.37 (4s, 4 CH_{arom}), 131.44 and 132.81 (2s, 2 C_{arom}), 147.24 (s, C-6), 149.45 (s, C-7a), 150.54 (s, C-2), 157.05 (s, C-4).

6-(Cyclohexylamino)-5-(2-chlorophenyl)-1,3-dimethylfuro [2,3-d]pyrimidine-2,4(1H,3H)-dione (4g)

White powder, yield: 0.34 g (87%), mp 170-173 °C (decomposed), IR (KBr) (ν_{max}, cm^{-1}): 3267 (NH), 1701 and 1694 (C=O). MS (*m/z, %*): 389 (M^++2, 39), 388 (M^++1, 34), 387 (M^+, 100), 352 (2), 305 (54), 277 (96), 248 (31), 101 (10), 83 (33), 67 (85), 41 (42). Anal. Calcd. for $C_{20}H_{22}ClN_3O_3$ (387.86): C, 61.93; H, 5.72; N, 10.83%. Found: C, 62.01; H, 5.68; N, 10.89%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 1.11-2.02 (10H, m, 5 C*H*$_2$ of cyclohexyl), 3.39 and 3.56 (6H, 2s, 2 NC*H*$_3$), 3.62-3.68 (1H, m, NC*H*), 6.21 (1H, d, $^3J_{HH}$ = 8.6 Hz, N*H*), 7.28-7.35 (2H, m, 2 CH_{arom}), 7.47 (1H, dt, J_1 = 7.8, J_2 = 1.3 Hz, CH_{arom}), 7.58 (1H, t, *J* = 1.6 Hz, CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 23.73 (s, C*H*$_2$ of cyclohexyl), 27.31 and 28.44 (2s, 2 N*C*H$_3$), 31.58 and 32.95 (2s, 4 C*H*$_2$ of cyclohexyl), 54.46 (s, N*C*H), 93.81 (s, C-4a), 106.32 (s, C-5), 125.84, 126.53, 128.02 and 129.08 (4s, 4 CH_{arom}), 131.37 and 133.10 (2s, 2 C_{arom}), 148.04 (s, C-6), 149.13 (s, C-7a), 150.07 (s, C-2), 157.43 (s, C-4).

6-(tert-butylamino)-5-(2-methylphenyl)-1,3-dimethylfuro [2,3-d]pyrimidine-2,4(1H,3H)-dione (4h)

Pale White powder, yield: 0.32 g (94%), mp 257-260 °C (decomposed), IR (KBr) (ν_{max}, cm^{-1}): 3284 (NH), 1700 and 1678 (C=O). MS (*m/z, %*): 342 (M^++1, 9), 341 (M^+, 38), 326 (2), 285 (100), 293 (5), 250 (21), 228 (43), 91 (22), 57 (71), 41 (37). Anal. Calcd. for $C_{19}H_{23}N_3O_3$ (341.40): C, 66.84; H, 6.79; N, 12.31%. Found: C, 66.78; H, 6.75; N, 12.26%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 1.37 (9H, s, NC*Me*$_3$), 2.31 (3H, s, ArC*H*$_3$), 3.22 and 3.38 (6H, 2s, 2 NC*H*$_3$), 5.16 (1H, br s, N*H*), 7.12 (1H, d, *J* = 7.4 Hz, CH_{arom}), 7.19-7.32 (3H, m, 3 CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 27.67 and 27.81 (2s, 2 N*C*H$_3$), 29.04 (s, NC*Me*$_3$), 52.55 (s, N*C*Me$_3$), 94.27 (s, C-4a), 108.65 (s, C-5), 123.47, 124.88, 128.23 and 129.25 (4s, 4 CH_{arom}), 133.29 and 134.94 (2s, 2 C_{arom}), 147.16 (s, C-6), 149.73 (s, C-7a), 150.01 (s, C-2), 156.96 (s, C-4).

6-(Cyclohexylamino)-5-(2-methylphenyl)-1,3-dimethylfuro [2,3-d]pyrimidine-2,4(1H,3H)-dione (4i)

Pale white powder, yield: 0.35 g (96%), mp 227-230 °C (decomposed), IR (KBr) (ν_{max}, cm^{-1}): 3284 (NH), 1698 and 1694 (C=O). MS (*m/z, %*): 367 (M^+, 6), 352 (1), 284 (100), 259 (57), 119 (60), 91 (38), 55 (47), 41 (35). Anal. Calcd. for $C_{21}H_{25}N_3O_3$ (367.44): C, 68.84; H, 6.86; N, 11.44%. Found: C, 68.90; H, 6.81; N, 11.37%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 1.10-2.01 (10H, m, 5 C*H*$_2$ of cyclohexyl), 2.33 (3H, s, ArC*H*$_3$), 3.22 and 3.38 (6H, 2s, 2 NC*H*$_3$), 3.79-3.89 (1H, m, NC*H*), 5.23 (1H, d, $^3J_{HH}$ = 8.1 Hz, N*H*), 7.13 (H, d, *J* = 7.5 Hz, CH_{arom}), 7.16-7.31 (3H, m, 3 CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 18.97 (s, Ar*C*H$_3$), 23.71 and 24.45 (2s, 3 *C*H$_2$ of cyclohexyl), 27.67 and 27.81 (2s, 2 N*C*H$_3$), 31.60 and 31.62 (2s, 2 *C*H$_2$ of cyclohexyl), 47.65 (s, N*C*H), 94.18 (s, C-4a), 117.03 (s, C-5), 123.59, 124.92, 127.91 and 129.24 (4s, 4 CH_{arom}), 133.27 and 134.76 (2s, 2 C_{arom}), 142.13 (s, C-6), 149.73 (s, C-7a), 158.63 (s, C-2), 159.21 (s, C-4).

6-(tert-butylamino)-5-(2,4-dichlorophenyl)-1,3-dimethylfuro [2,3-d]pyrimidine-2,4(1H,3H)-dione (4j)

Pale white powder, yield: 0.34 g (86%), mp 174-177 °C (decomposed), IR (KBr) (ν_{max}, cm^{-1}): 3286 (NH), 1703 and 1685 (C=O). MS (*m/z, %*): 400 (M^++4, 1), 398 (M^++2, 4), 396 (M^+, 7), 339 (5), 305 (3), 293 (100), 277 (11), 173 (13), 57 (43), 41 (17). Anal. Calcd. for $C_{18}H_{19}Cl_2N_3O_3$ (396.27): C, 54.56; H, 4.83; N, 10.60%. Found: C, 54.59; H, 4.80; N, 10.67%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 1.37 (9H, s, NC*Me*$_3$), 3.24 and 3.38 (6H, 2s, 2 NC*H*$_3$), 3.45 (1H, br s, N*H*), 7.29-7.34 (2H, m, CH_{arom}), 7.46 (1H, d, *J* = 1.8 Hz, CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 27.62 and 28.65 (2s, 2 N*C*H$_3$), 27.87 (s, NC*Me*$_3$), 56.53 (s, N*C*Me$_3$), 94.52 (s, C-4a), 107.58 (s, C-5), 126.54, 126.89 and 128.21 (3s, 3 CH_{arom}), 129.77, 131.35 and 134.11 (3s, 3 C_{arom}), 147.36 (s, C-6), 148.67 (s, C-7a), 151.02 (s, C-2), 156.94 (s, C-4).

6-(Cyclohexylamino)-5-(2,4-dichlorophenyl)-1,3-dimethyl-furo[2,3-d]pyrimidine-2,4(1H,3H)-dione (4k)

Pale White powder, yield: 0.38 g (91%), mp 178-181 °C, IR (KBr) (ν_{max}, cm^{-1}): 3271 (NH), 1708 and 1693 (C=O). MS (*m/z, %*): 426 (M^++4, 1), 424 (M^++2, 3), 423 (M^++1, 9), 422 (M^+, 4), 388 (2), 339 (6), 324 (3), 293 (100), 277 (42), 173 (38), 83 (58), 41 (32). Anal. Calcd. for $C_{20}H_{21}Cl_2N_3O_3$ (422.30): C, 56.88; H, 5.01; N, 9.95%. Found: C, 56.92; H, 5.07; N, 9.87%. ^{1}H NMR (400.1 MHz, $CDCl_3$): 1.06-2.00 (10H, m, 5 C*H*$_2$ of cyclohexyl), 3.11-3.14 (1H, m, NC*H*), 3.38 (1H, d, $^3J_{HH}$ = 5.2 Hz, N*H*), 3.41 and 3.56 (6H, 2s, 2 NC*H*$_3$), 7.29-7.32 (2H, m, 2 CH_{arom}), 7.47 (1H, d, $^3J_{HH}$ = 1.8 Hz, CH_{arom}). ^{13}C NMR (100.1 MHz, $CDCl_3$): 23.63 and 24.47 (2s, 3 *C*H$_2$ of cyclohexyl), 27.12 and 28.42 (2s, 2 N*C*H$_3$), 32.85 (s, 2 *C*H$_2$ of cyclohexyl), 54.06 (s, N*C*H), 95.72 (s, C-4a), 108.71 (s, C-5), 125.97 (s, CH_{arom}), 126.91 (s, CH_{arom}), 128.42 and 132.29 (2s, 2 C_{arom}), 133.29 and 133.70 (2s, 2 C_{arom}), 147.97 (s, C-6), 149.40 (s, C-7a), 149.94 (s, C-2), 156.80 (s, C-4).

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