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ONE-POT CHEMOSELECTIVE SYNTHESIS OF NOVEL FUSED PYRIMIDINE DERIVATIVES

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One-pot triple-component reaction of 4-hydroxycoumarin with aromatic aldehydes and 2-aminobenzimidazole, 3-amino-1H-1,2,4-triazole, or 6-aminouracil in acetonitrile in the presence of catalytic amounts of sulfamic acid led to a chemoselective synthesis of chromeno[4,3-d]pyrimidine-6-one, triazolo-[1,5-a]pyrimidin-5-one, and pyrido[2,3-d]-pyrimidine-2,4,7-trione derivatives, respectively, in good yields.

Keywords: chromeno[4,3-*d*]pyrimidinones, pyrido[2,3-*d*]pyrimidine-2,4,7-triones, pyrimidine derivatives, sulfamic acid, triazolo[1,5-*a*]pyrimidin-5-ones, multicomponent reaction.

Multicomponent reactions (MCRs) are of increasing significance in organic and medicinal chemistry. MCRs are economically and environmentally profitable because they allow compounds to be synthesized in a few steps and usually in a one-pot operation [1, 2]. Also diverse chemical libraries of "drug-like" molecules could be generated from MCRs and may appear attractive from the drug discovery perspective [3, 4]. Designing new MCRs for synthesis of heterocyclic compounds has attracted much attention in recent years [5, 6].

Pyrimidine and its derivatives have been studied for several years because of their chemical and biological significance. They have been reported as antibacterial, antiviral, and antitumor agents [7]. Numerous heterocyclic systems fused with pyrimidines are known for their important biological activities [8]. Some chromenopyrimidine derivatives show antiplatelet and antithrombotic activities [9]. Triazolopyrimidine derivatives likewise have attracted considerable attention due to their biological properties. Some of them are potent and selective serotonin 5-HT_6 receptor antagonists [10]. They also exhibit various types of biological activity, including analgesic [11], antibiotic [12], cytotoxic [13], and antitumor properties [14]. It is already known that some pyrimido[4,5-*b*]quinolin-4-one derivatives display important analgesic, anti-inflammatory, and antimicrobial activities [15].

As part of our continuing efforts on the development of new routes for the synthesis of heterocyclic compounds [16–18], herein, we wish to report an one-pot chemoselective synthesis of some new chromeno-[4,3-*d*]pyrimidinone, triazolo[1,5-*a*]pyrimidin-5-one, and pyrido[2,3-*d*]pyrimidine-2,4,7-trione derivatives *via* reaction of 4-hydroxycoumarin (**1**) with aromatic aldehydes **2** and 2-aminobenzimidazole (**3**), 3-amino-1H-1,2,4-triazole (**4**), or 6-aminouracil (**5**) in the presence of catalytic amounts of sulfamic acid (SA) as an efficient and available catalyst (Scheme 1) [19].

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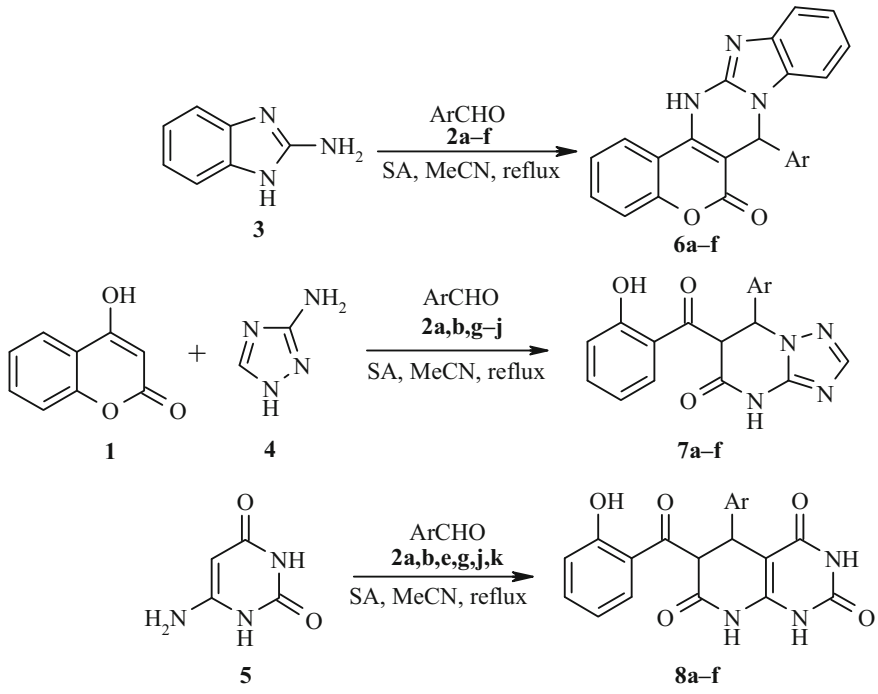
Scheme 1



At first, triple-component reaction of 4-hydroxycoumarin (**1**), 4-nitrobenzaldehyde (**2a**, Ar = 4-$O_2NC_6H_4$), and 2-aminobenzimidazole (**3**) in acetonitrile was carried out as a model reaction. In the absence of SA either at room temperature or under reflux conditions, no product was observed. It was found that in the presence of SA a trace amount of product **6a** (Ar = 4-$O_2NC_6H_4$) was observed after a longer reaction time (48 h) at room temperature. When the mentioned model reaction was conducted under reflux conditions, the desired product **6a** was obtained in high yield (85%) with shorter reaction time (4 h). It should be noted that when the triple-component reaction was conducted under solvent-free conditions, the desired product was obtained in low yield (55%). Varying the amount of SA, the best result was obtained using 30 mol% of catalyst. After that, the effect of different solvents was investigated to identify the most appropriate medium for the preparation of chromeno[4,3-*d*]-pyrimidinone **6a** (Table 1). The change of solvent did not give any improvement in the yield, and the best result remained with refluxing acetonitrile.

Scheme 2

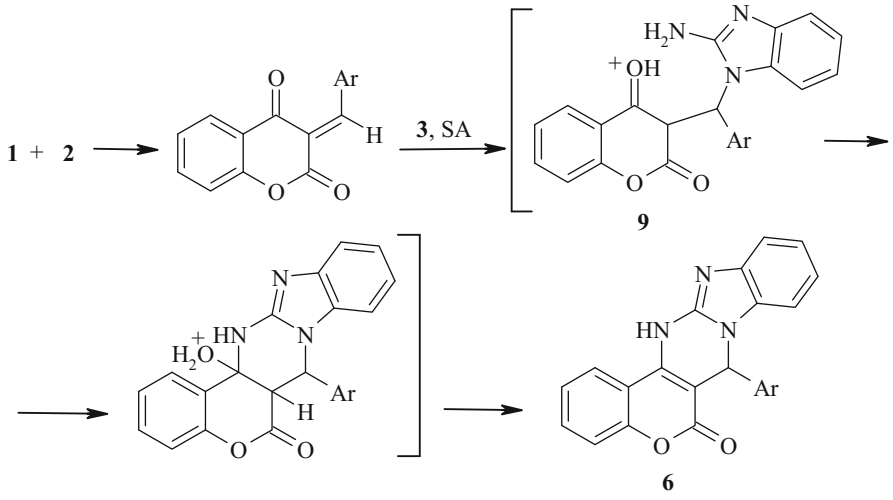


TABLE 1. Effect of Solvent on the Yield of Chromeno[4,3-*d*]pyrimidinone **6a**

Entry	Solvent	Time, h	Yield, %
1	EtOH	7	55
2	H_2O	10	5
3	CH_2Cl_2	24	5
4	C_6H_5Me	24	Trace
5	MeCN	4	85

The proposed mechanism for the synthesis of chromeno[4,3-*d*]pyrimidinone derivatives **6** is presented in Scheme 2. The first step may involve adduct formation by condensation of 4-hydroxycoumarin (**1**) and aromatic aldehyde **2**, followed by attack of 2-aminobenzimidazole (**3**) to give the intermediate **9**. In the presence of SA, ketone carbonyl is prone to attack by nucleophilic nitrogen to form product **6**.

In order to expand the scope of the present work, various aromatic aldehydes **2b**–**f** were examined, and the desired products **6b**–**f** were obtained in good yields (Table 2).

To examine the reactivity and chemoselectivity of 3-amino-1H-1,2,4-triazole (**4**) and 6-aminouracil (**5**) in the above-mentioned triple-component reaction under optimized conditions, a reaction with 4-hydroxycoumarin (**1**) and 4-nitrobenzaldehyde (**2a**) was performed (Scheme 1).

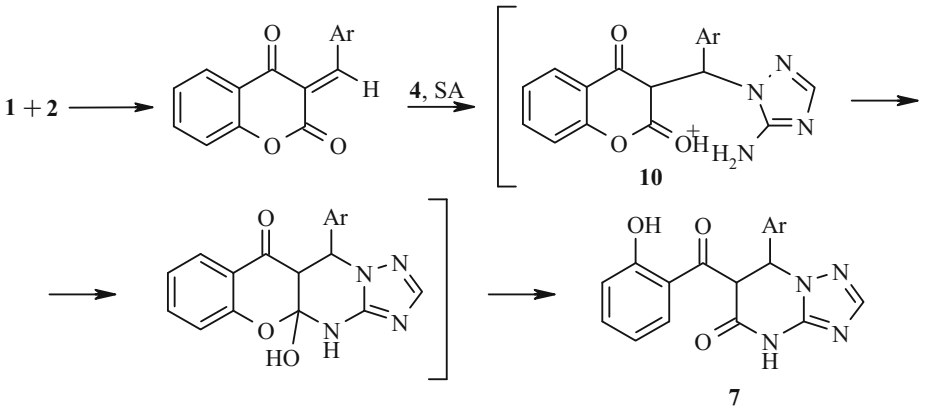
Surprisingly, the corresponding triazolo[1,5-*a*]pyrimidin-5-one and pyrido[2,3-*d*]pyrimidine-2,4,7-trione derivatives **7a** and **8a** respectively were formed. As can be seen in Scheme 3, after the formation of intermediate **10**, the lactone carbonyl group is prone to attack by the nucleophilic nitrogen of 3-amino-1H-1,2,4-triazole (**3**). A similar mechanism can be proposed when 6-aminouracil (**4**) is used in the triple-component reaction.

Finally, this protocol was also extended to the synthesis of a series of triazolo[1,5-*a*]pyrimidin-5-one and pyrido[2,3-*d*]pyrimidine-2,4,7-trione derivatives **7b**–**f** and **8b**–**f** respectively (Table 2).

TABLE 2. One-pot Reaction of Coumarin **1**, Aldehydes **2a–k,** and Heteroaromatic Amine **3, 4**, or **5**

Aldehyde	Ar	Nucleophile	Time, h	Product	Yield, %
2b	$3\text{-}O_2NC_6H_4$	**3**	4.5	**6b**	85
2c	1-Naphthyl	**3**	4.5	**6c**	87
2d	$4\text{-}FC_6H_4$	**3**	5.0	**6d**	82
2e	$4\text{-}MeC_6H_4$	**3**	5.5	**6e**	80
2f	$4\text{-}MeOC_6H_4$	**3**	5.0	**6f**	75
2a	$4\text{-}O_2NC_6H_4$	**4**	4.0	**7a**	80
2b	$3\text{-}O_2NC_6H_4$	**4**	5.5	**7b**	70
2g	$4\text{-}HOC_6H_4$	**4**	4.0	**7c**	65
2h	C_6H_5	**4**	5.5	**7d**	75
2i	$4\text{-}ClC_6H_4$	**4**	4.5	**7e**	75
2j	2-Furyl	**4**	5.5	**7f**	70
2a	$4\text{-}O_2NC_6H_4$	**5**	4.0	**8a**	85
2b	$3\text{-}O_2NC_6H_4$	**5**	5.5	**8b**	85
2e	$4\text{-}MeC_6H_4$	**5**	6.0	**8c**	75
2g	$4\text{-}HOC_6H_4$	**5**	5.5	**8d**	80
2j	2-Furyl	**5**	6.0	**8e**	72
2k	$3\text{-}BrC_6H_4$	**5**	5.0	**8f**	75

Scheme 3



Benzaldehydes bearing electron-donating or electron-withdrawing group gave good yields, although in the case of an electron-withdrawing substituent better results were achieved. It should be noted that there was no significant differrence between 2-aminobenzimidazole, 3-amino-1H-1,2,4-triazole, and 6-aminouracil reactivity, and the expected chemoselectivity was observed.

In summary, the described one-pot triple-component reaction of 4-hydroxycoumarin with aromatic aldehydes and 2-aminobenzimidazole, 3-amino-1H-1,2,4-triazole, or 6-aminouracil in acetonitrile in the presence of catalytic amounts of sulfamic acid is an extremely efficient and chemoselective method for the synthesis of chromeno[4,3-*d*]pyrimidinone, triazolo[1,5-*a*]pyrimidin-5-one, and pyrido[2,3-*d*]pyrimidine-2,4,7-trione derivatives. The products were obtained in good yield without further purification.

EXPERIMENTAL

Melting points were measured using a capillary tube method with a Bamstead Electrothermal 9200 apparatus. IR spectra were recorded on a Bruker Tensor 27 Series FT-IR instrument in KBr disks. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AQS-AVANCE spectrometer at 500 and 125 MHz, respectively, in DMSO using TMS as an internal standard. Mass spectra were recorded on an Agilent Technology (HP) mass spectrometer operating at an ionization potential of 70 eV. The elemental analysis was performed with an Elemetar Analysensysteme GmbH Vario EL CHNS.

All chemicals were obtained from Merck and used without further purification.

Synthesis of Compounds 6, 7, 8 (General Method). A mixture of 4-hydroxycoumarin (**1**) (1 mmol), an corresponding aromatic aldehyde **2** (1 mmol), 2-aminobenzimidazole (**3**), and 3-amino-1H-1,2,4-triazole (**4**), or 6-aminouracil **5** (1 mmol) and sulfamic acid (30 mol%) in acetonitrile (5 ml) was heated at reflux for the indicated time required to complete the reaction (Table 2). Upon completion of the reaction, monitored by TLC (eluent system – petroleum ether/ethyl acetate, 96:4), the mixture was cooled to room temperature. The precipitated product was separated by filtration, washed three times with water and acetonitrile, and dried at 60–70°C. The corresponding products were analytically pure without recrystallization.

7-(4-Nitrophenyl)-7,14-dihydro-6H-benzo[4,5]imidazo[1,2-*a*]chromeno[4,3-*d*]pyrimidin-6-one (6a). Yellow powder; mp 259–260°C. IR spectrum, ν, cm^{-1}: 3415, 3122, 1676, 1609, 1554, 1518, 1397. ^{1}H NMR spectrum, δ, ppm: 9.92 (1H, s, NH); 8.00–7.94 (4H, m, H Ar); 7.93–7.61 (4H, m, H Ar); 7.59–7.30 (2H, m, H Ar); 7.29–7.19 (2H, m, H Ar); 6.32 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 173.3; 162.9; 156.9; 151.0; 138.0; 132.7; 131.6; 131.3; 131.1; 128.4; 128.1; 125.0; 123.6; 123.5; 123.1; 122.5; 120.9; 116.9; 115.5; 104.7; 54.2. Mass spectrum, *m/z* (I_{rel}, %): 411 $[M+1]^+$ (15), 279 (72), 133 (100), 120 (70), 93 (64), 65 (18). Found, %: C 67.42; H 3.51; N 13.71. $C_{23}H_{14}N_4O_4$. Calculated, %: C 67.31; H 3.44; N 13.65.

7-(3-Nitrophenyl)-7,14-dihydro-6H-benzo[4,5]imidazo[1,2-*a*]chromeno[4,3-*d*]pyrimidin-6-one (6b). White powder; mp 222–224°C. IR spectrum, ν, cm^{-1}: 3412, 3123, 1675, 1596, 1532, 1448, 1350. ^1H NMR spectrum, δ, ppm: 9.90 (1H, s, NH); 8.40–8.36 (1H, m, H Ar); 8.18–8.16 (1H, m, H Ar); 7.98–7.91 (2H, m, H Ar); 7.71–7.30 (4H, m, H Ar); 7.27–7.25 (2H, m, H Ar); 7.18–7.10 (2H, m, H Ar); 6.41 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 173.5; 163.1; 156.8; 151.7; 137.1; 132.6; 131.6; 131.5; 131.4; 128.5; 128.2; 125.3; 123.8; 123.5; 123.2; 122.4; 120.8; 116.6; 116.3; 115.4; 112.1; 104.6; 54.0. Mass spectrum, *m/z* (I_{rel}, %): 410 $[M]^+$ (15), 336 (10), 279 (70), 133 (100), 120 (75), 93 (60), 65 (20). Found, %: C 67.46; H 3.59; N 13.44. $C_{23}H_{14}N_4O_4$ Calculated, %: C 67.31; H 3.44; N 13.65.

7-(1-Naphthyl)-7,14-dihydro-6H-benzo[4,5]imidazo[1,2-*a*]chromeno[4,3-*d*]pyrimidin-6-one (6c). White powder; mp 222–224°C. IR spectrum, ν, cm^{-1}: 3322, 3052, 1676. ^1H NMR spectrum, δ, ppm: 9.85 (1H, s, NH); 8.55–8.52 (1H, m, H Ar); 7.98–7.90 (4H, m, H Ar); 7.90–7.43 (5H, m, H Ar); 7.27–7.05 (5H, m, H Ar); 5.75 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 173.1; 163.8; 154.5; 151.1; 137.8; 134.1; 131.7; 131.3; 130.9; 129.1; 128.1; 127.7; 127.0; 126.4; 126.1; 125.9; 125.6; 125.5; 125.0; 124.1; 123.8; 123.3; 123.1; 116.5; 112.3; 98.6; 52.4. Mass spectrum, *m/z* (I_{rel}, %): 415 $[M]^+$ (15), 341 (15), 284 (78), 133 (100), 120 (65). Found, %: C 78.15; H 4.31; N 10.27. $C_{27}H_{17}N_3O_2$. Calculated, %: C 78.06; H 4.12; N 10.11.

7-(4-Fluorophenyl)-7,14-dihydro-6H-benzo[4,5]imidazo[1,2-*a*]chromeno[4,3-*d*]pyrimidin-6-one (6d). White powder; mp 236–237°C. IR spectrum, ν, cm^{-1}: 3334, 3105, 1676, 1598. ^1H NMR spectrum, δ, ppm: 10.38 (1H, s, NH); 7.90–7.82 (3H, m, H Ar); 7.58–7.43 (2H, m, H Ar); 7.38–7.18 (3H, m, H Ar); 7.16–7.05 (4H, m, H Ar); 6.19 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 173.2; 164.1; 157.1 (d, $^1J_{C–F}$ = 245.2); 153.2; 137.1; 132.6; 131.5; 130.4; 129.0; 128.2; 127.1; 126.8; 126.5; 125.5; 125.2; 123.4; 120.6; 120.1; 119.3; 118.2; 111.3; 105.5; 54.0. Mass spectrum, *m/z* (I_{rel}, %): 383 $[M]^+$ (15), 309 (10), 252 (68), 133 (100), 120 (70). Found, %: C 72.32; H 3.44; N 10.80. $C_{23}H_{14}FN_3O_2$. Calculated, %: C 72.06; H 3.68; N 10.96.

7-(4-Methylphenyl)-7,14-dihydro-6H-benzo[4,5]imidazo[1,2-*a*]chromeno[4,3-*d*]pyrimidin-6-one (6e). Yellow powder; mp 242–243°C. IR spectrum, ν, cm^{-1}: 3420, 3061, 1665, 1563. ^1H NMR spectrum, δ, ppm: 9.95 (1H, s, NH); 7.90–7.85 (2H, m, H Ar); 7.53–7.43 (7H, m, H Ar); 7.28–7.20 (2H, m, H Ar); 7.12–7.00 (1H, m, H Ar); 6.20 (1H, s, CH); 2.05 (3H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 173.5; 162.3; 154.5; 139.1; 137.8; 134.3; 133.9; 129.3; 128.8; 127.9; 127.4; 126.9; 126.4; 125.9; 125.8; 125.0; 124.7; 124.1; 112.2; 101.3; 54.3; 20.9. Mass spectrum, *m/z* (I_{rel}, %): 379 $[M]^+$ (15), 305 (15), 248 (70), 133 (100), 120 (70). Found, %: C 76.30; H 4.24; N 10.91. $C_{24}H_{17}N_3O_2$. Calculated, %: C 75.98; H 4.52; N 11.07.

7-(4-Methoxylphenyl)-7,14-dihydro-6H-benzo[4,5]imidazo[1,2-*a*]chromeno[4,3-*d*]pyrimidin-6-one (6f). Pale-yellow powder; mp 250–251°C. IR spectrum, ν, cm^{-1}: 3390, 3073, 1682, 1564. ^1H NMR spectrum, δ, ppm: 9.94 (1H, s, NH); 8.19–8.17 (1H, m, H Ar); 7.86–7.78 (4H, m, H Ar); 7.53–7.40 (2H, m, H Ar); 7.37–7.28 (3H, m, H Ar); 7.15–7.10 (2H, m, H Ar); 6.22 (1H, s, CH); 3.80 (3H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 173.1; 164.1; 155.0; 154.2; 133.8; 133.2; 131.1; 128.0; 127.4; 125.9; 125.1; 124.5; 123.9; 123.1; 122.9; 120.6; 118.6; 117.8; 112.3; 99.9; 54.3; 53.8. Mass spectrum, *m/z* (I_{rel}, %): 395 $[M]^+$ (10), 321 (10), 264 (65), 133 (100), 120 (70). Found, %: C 73.22; H 4.49; N 10.93. $C_{24}H_{17}N_3O_3$. Calculated, %: C 72.90; H 4.33; N 10.63.

6-[(2-Hydroxyphenyl)carbonyl]-7-(4-nitrophenyl)-6,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidin-5(4H)-one (7a). Pale-yellow powder; mp 210–211°C. IR spectrum, ν, cm^{-1}: 3419, 3243, 3113, 1660, 1600, 1523, 1415, 1347. ^1H NMR spectrum, δ, ppm: 10.25 (1H, s, OH); 9.45 (1H, s, NH); 8.51–8.36 (2H, m, H Ar); 8.25–8.23 (1H, m, H Ar); 8.15–8.13 (1H, m, H Ar); 7.90–7.88 (1H, m, H Ar); 7.61 (1H, s, CH); 7.45–7.43 (1H, m, H Ar); 7.37–7.32 (2H, m, H Ar); 6.43 (1H, s, CH); 5.80 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 193.2; 168.7; 165.2; 153.4; 152.4; 146.2; 140.2; 132.1; 131.5; 124.9; 124.0; 123.9; 120.5; 116.4; 85.0; 61.0. Mass spectrum, *m/z* (I_{rel}, %): 379 $[M]^+$ (15), 297 (18), 296 (20), 135 (82), 121 (100), 93 (87), 65 (27). Found, %: C 57.22; H 3.59; N 18.67. $C_{18}H_{13}N_5O_5$. Calculated, %: C 56.99; H 3.45; N 18.46.

6-[(2-Hydroxyphenyl)carbonyl]-7-(3-nitrophenyl)-6,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidin-5(4H)-one (7b). Yellow powder; mp 213–214°C. IR spectrum, ν, cm^{-1}: 3423, 3247, 3137, 1697, 1592, 1531, 1481, 1433, 1348. ^1H NMR spectrum, δ, ppm: 10.11 (1H, s, OH); 9.40 (1H, s, NH); 8.50–8.47 (1H, m, H Ar); 8.30–8.24 (2H, m, H Ar); 7.96–7.90 (2H, m, H Ar); 7.74–7.60 (1H, m, H Ar); 7.61 (1H, s, CH); 7.55–7.46 (2H, m,

H Ar); 6.30 (1H, s, CH); 5.91 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 192.9; 168.8; 165.2; 153.4; 152.2; 146.5; 146.1; 140.1; 132.2; 131.2; 125.1; 125.0; 123.9; 123.8; 120.5; 116.3; 84.2; 61.2. Mass spectrum, *m/z* (I_{rel}, %): 379 $[M]^+$ (5), 352 (10), 297 (20), 296 (25), 135 (80), 121 (100), 93 (90), 65 (25). Found, %: C 57.29; H 3.13; N 18.19. $C_{18}H_{13}N_5O_5$. Calculated, %: C 56.99; H 3.45; N 18.46.

7-(4-Hydroxyphenyl)-6-[(2-hydroxyphenyl)carbonyl]-6,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidin-5(4H)-one (7c). Yellow powder; mp 207–209°C. IR spectrum, ν, cm^{-1}: 3407, 3076, 1661, 1608, 1562. ^{1}H NMR spectrum, δ, ppm: 10.10 (2H, s, OH); 9.45 (1H, s, NH); 7.80–7.75 (1H, m, H Ar); 7.70 (1H, s, CH); 7.65–7.59 (2H, m, H Ar); 7.56–7.53 (1H, m, H Ar); 7.15–7.10 (2H, m, H Ar); 7.10–7.03 (2H, m, H Ar); 6.32 (1H, s, CH); 6.01 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 192.1; 169.0; 165.6; 153.0; 152.1; 150.1; 141.0; 132.4; 131.4; 124.8; 124.0; 122.8; 121.9; 117.1; 85.2; 59.9. Mass spectrum, *m/z* (I_{rel}, %): 350 $[M]^+$ (5), 323 (10), 268 (15), 267 (20), 135 (80), 121 (100), 51 (17). Found, %: C 62.00; H 4.22; N 15.61. $C_{18}H_{14}N_4O_4$. Calculated, %: C 61.71; H 4.03; N 15.99.

6-[(2-Hydroxyphenyl)carbonyl]-7-phenyl-6,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidin-5(4H)-one (7d). White powder; mp 217–219°C. IR spectrum, ν, cm^{-1}: 3394, 3264, 1684, 1598, 1569. ^{1}H NMR spectrum, δ, ppm: 10.10 (1H, s, OH); 9.45 (1H, s, NH); 7.61 (1H, s, CH); 7.35–7.31 (2H, m, H Ar); 7.25–7.21 (2H, m, H Ar); 7.20–7.17 (2H, m, H Ar); 7.15–7.13 (1H, m, H Ar); 7.10–7.00 (2H, m, H Ar); 6.00 (1H, s, CH); 5.90 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 192.1; 168.8; 165.0; 153.5; 152.5; 140.2; 132.9; 132.4; 132.0; 124.5; 124.1; 122.9; 120.0; 117.2; 84.8; 61.2. Mass spectrum, *m/z* (I_{rel}, %): 334 $[M]^+$ (10), 307 (15), 252 (15), 251 (20), 135 (80), 121 (100), 51 (15). Found, %: C 64.39; H 4.11; N 16.81. $C_{18}H_{14}N_4O_3$. Calculated, %: C 64.66; H 4.22; N 16.76.

7-(4-Chlorophenyl)-6-[(2-hydroxyphenyl)carbonyl]-6,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidin-5(4H)-one (7e). Pale-yellow powder; mp 229–230°C. IR spectrum, ν, cm^{-1}: 3241, 3081, 1670, 1603, 1564. ^{1}H NMR spectrum, δ, ppm: 10.00 (1H, s, OH); 8.92 (1H, s, NH); 7.77 (1H, s, CH); 7.85–7.51 (2H, m, H Ar); 7.39–7.33 (2H, m, H Ar); 7.32–7.29 (1H, m, H Ar); 7.21–7.10 (3H, m, H Ar); 6.21 (1H, s, CH); 5.95 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 193.0; 167.8; 166.1; 153.3; 151.9; 140.2; 133.0; 132.5; 131.8; 128.1; 126.4; 123.8; 123.1; 118.0; 84.5; 61.2. Mass spectrum, *m/z* (I_{rel}, %): 368/370 $[M]^+$ (5), 341 (10), 286 (20), 285 (25), 135 (85), 121 (100), 51 (20). Found, %: C 58.89; H 4.19; N 15.51. $C_{18}H_{13}ClN_4O_3$. Calculated, %: C 58.62; H 3.55; N 15.19.

7-(2-Furyl)-6-[(2-hydroxyphenyl)carbonyl]-6,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidin-5(4H)-one (7f). Gray powder; mp 250–251°C. IR spectrum, ν, cm^{-1}: 3372, 3250, 3122, 1693. ^{1}H NMR spectrum, δ, ppm: 10.11 (1H, s, OH); 9.90 (1H, s, NH); 7.68 (1H, s, CH); 7.75–7.67 (1H, m, H Ar); 7.56–7.51 (1H, m, H Ar); 7.50–7.47 (1H, m, H Ar); 7.43–7.38 (1H, m, H Ar); 7.13–7.05 (2H, m, H Ar); 6.90–6.88 (1H, m, H Ar); 6.22 (1H, s, CH); 6.01(1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 192.8; 168.9; 166.8; 154.4; 152.7; 149.2; 135.6; 133.0; 132.5; 124.1; 122.4; 121.8; 119.3; 118.0; 85.1; 62.2. Mass spectrum, *m/z* (I_{rel}, %): 324 $[M]^+$ (10), 242 (15), 241 (20), 135 (80), 121 (100), 51 (20). Found, %: C 58.99; H 4.05; N 17.76. $C_{16}H_{12}N_4O_4$. Calculated, %: C 59.26; H 3.73; N 17.28.

6-[(2-Hydroxyphenyl)carbonyl]-5-(4-nitrophenyl)-5,8-dihydropyrido[2,3-*d*]pyrimidine-2,4,7(1H,3H,6H)-trione (8a). Yellow powder; mp > 300°C. IR spectrum, ν, cm^{-1}: 3405, 3345, 3178, 1718, 1627, 1518, 1460, 1394. ^{1}H NMR spectrum, δ, ppm: 10.68 (1H, s, NH); 10.49 (1H, s, NH); 10.16 (1H, s, NH); 10.14 (1H, s, OH); 8.20–8.17 (2H, m, H Ar); 8.15–8.10 (2H, m, H Ar); 7.54–7.51 (2H, m, H Ar); 7.45–7.42 (2H, m, H Ar); 6.26 (1H, s, CH); 4.50 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 191.0; 165.1; 164.3; 164.0; 156.0; 151.8; 150.6; 149.7; 146.1; 142.4; 130.3; 128.8; 124.5; 120.4; 119.7; 109.1; 75.0; 33.9. Mass spectrum, *m/z* (I_{rel}, %): 422 $[M]^+$ (5), 336 (17), 297 (22), 269 (34), 121 (65), 86 (100). Found, %: C 57.09; H 3.48; N 13.38. $C_{20}H_{14}N_4O_7$. Calculated, %: C 56.88; H 3.34; N 13.27.

6-[(2-Hydroxyphenyl)carbonyl]-5-(3-nitrophenyl)-5,8-dihydropyrido[2,3-*d*]pyrimidine-2,4,7(1H,3H,6H)-trione (8b). Yellow powder; mp > 300°C. IR spectrum, ν, cm^{-1}: 3405, 3346, 3180, 1710, 1628, 1465, 1396. ^{1}H NMR spectrum, δ, ppm: 10.80 (1H, s, NH); 10.51 (1H, s, NH); 10.20 (1H, s, NH); 10.14 (1H, s, OH); 8.40–8.33 (1H, m, H Ar); 8.20–8.00 (2H, m, H Ar); 7.74–7.72 (1H, m, H Ar); 7.70–7.68 (2H, m, H Ar); 7.55–7.52 (1H, m,

H Ar); 7.51–7.48 (1H, m, H Ar); 6.22 (1H, s, CH); 4.55 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 192.0; 165.5; 164.5; 163.5; 156.9; 152.5; 150.9; 150.0; 147.0; 143.2; 129.9; 128.9; 127.9; 127.1; 126.0; 120.4; 120.1; 111.1; 74.6; 33.7. Mass spectrum, *m/z* (I_{rel}, %): 422 $[M]^+$ (10), 336 (20), 297 (25), 269 (35), 121 (65), 86 (100). Found, %: C 56.55; H 3.14; N 13.09. $C_{20}H_{14}N_4O_7$. Calculated, %: C 56.88; H 3.34; N 13.27.

6-[(2-Hydroxyphenyl)carbonyl]-5-(4-methylphenyl)-5,8-dihydropyrido[2,3-*d*]pyrimidine-2,4,7(1H,3H,6H)-trione (8c). Pale-yellow powder; mp > 300°C. IR spectrum, ν, cm^{-1}: 3415, 3317, 3170, 1714, 1625. ^{1}H NMR spectrum, δ, ppm: 10.80 (1H, s, NH); 10.52 (1H, s, NH); 10.21 (1H, s, NH); 10.15 (1H, s, OH); 7.80–7.72 (2H, m, H Ar); 7.61–7.58 (2H, m, H Ar); 7.37–7.35 (1H, m, H Ar); 7.14–7.12 (1H, m, H Ar); 7.07–7.05 (2H, m, H Ar); 6.20 (1H, s, CH); 4.56 (1H, s, CH); 2.15 (3H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 192.8; 165.0; 164.1; 163.8; 156.0; 151.1; 150.5; 148.0; 145.9; 140.6; 130.5; 129.2; 126.5; 119.9; 118.8; 110.0; 75.1; 32.5; 22.4. Mass spectrum, *m/z* (I_{rel}, %): 391 $[M]^+$ (10), 305 (20), 266 (25), 238 (25), 121 (62), 86 (100). Found, %: C 64.14; H 4.71; N 10.48. $C_{21}H_{17}N_3O_5$. Calculated, %: C 64.45; H 4.38; N 10.74.

5-(4-Hydroxyphenyl)-6-[(2-hydroxyphenyl)carbonyl]-5,8-dihydropyrido[2,3-*d*]pyrimidine-2,4,7-(1H,3H,6H)-trione (8d). Yellow powder; mp > 300°C. IR spectrum, ν, cm^{-1}: 3408, 3340, 3174, 1709, 1627. ^{1}H NMR spectrum, δ, ppm: 10.83 (1H, s, NH); 10.52 (1H, s, NH); 10.30 (1H, s, NH); 10.21 (2H, s, OH); 7.80–7.70 (1H, m, H Ar); 7.66–7.64 (1H, m, H Ar); 7.60–7.53 (2H, m, H Ar); 7.37–7.34 (1H, m, H Ar); 7.24–7.21 (1H, m, H Ar); 7.18–7.00 (2H, m, H Ar); 6.22 (1H, s, CH); 4.68 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 194.3; 166.8; 165.5; 161.1; 153.9; 151.8; 150.8; 138.3; 132.2; 131.2; 127.9; 127.0; 122.8; 119.0; 118.0; 109.5; 74.6; 32.7. Mass spectrum, *m/z* (I_{rel}, %): 393 $[M]^+$ (5), 307 (15), 268 (20), 240 (38), 121 (60), 86 (100). Found, %: C 61.25; H 4.08; N 10.36. $C_{20}H_{15}N_3O_6$. Calculated, %: C 61.07; H 3.84; N 10.68.

5-(Furan-2-yl)-6-[(2-hydroxyphenyl)carbonyl]-5,8-dihydropyrido[2,3-*d*]pyrimidine-2,4,7(1H,3H,6H)-trione (8e). Grey powder; mp > 300°C. IR spectrum, ν, cm^{-1}: 3403, 3327, 3127, 1709, 1622, 1396. ^{1}H NMR spectrum, δ, ppm: 10.58 (1H, s, NH); 10.40 (1H, s, NH); 10.28 (1H, s, NH); 10.18 (1H, s, OH); 7.50–7.44 (1H, m, H Ar); 7.38–7.35 (1H, m, H Ar); 7.25–7.20 (2H, m, H Ar); 7.18–7.15 (1H, m, H Ar); 7.10–7.05 (2H, m, H Ar); 6.18 (1H, s, CH); 4.41 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 192.1; 166.0; 164.1; 160.2; 151.1; 150.5; 148.0; 146.9; 140.6; 130.3; 120.9; 120.3; 120.1; 119.2; 117.8; 109.1; 75.0; 34.3. Mass spectrum, *m/z* (I_{rel}, %): 367 $[M]^+$ (5), 281 (20), 242 (25), 214 (30), 121 (59), 86 (100). Found, %: C 59.01; H 3.88; N 11.61. $C_{18}H_{13}N_3O_6$. Calculated, %: C 58.86; H 3.57; N 11.44.

5-(3-Bromophenyl)-6-[(2-hydroxyphenyl)carbonyl]-5,8-dihydropyrido[2,3-*d*]pyrimidine-2,4,7-(1H,3H,6H)-trione (8f). Yellow powder; mp > 300 °C. IR spectrum, ν, cm^{-1}: 3405, 3346, 3162, 1711, 1627, 1529, 1465. ^{1}H NMR spectrum, δ, ppm: 10.75 (1H, s, NH); 10.42 (1H, s, NH); 10.25 (1H, s, NH); 10.19 (1H, s, OH); 7.85–7.79 (1H, m, H Ar); 7.60–7.53 (3H, m, H Ar); 7.31–7.25 (1H, m, H Ar); 7.18–7.11 (1H, m, H Ar); 7.06–7.00 (2H, m, H Ar); 6.20 (1H, s, CH); 4.60 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 192.2; 167.2; 165.4; 161.5; 154.2; 151.6; 150.5; 144.4; 138.3; 130.3; 129.9; 128.0; 126.2; 124.3; 120.4; 120.1; 119.0; 111.5; 75.4; 33.5. Mass spectrum, *m/z* (I_{rel}, %): 455/457 $[M]^+$ (15), 369 (20), 329 (20), 301 (35), 121 (60), 86 (100). Found, %: C 52.89; H 3.28; N 9.56. $C_{20}H_{14}BrN_3O_5$. Calculated, %: C 52.65; H 3.09; N 9.21.

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