A Facile and Clean Synthesis of Pyrimidine Derivatives via Three-component Reaction in Aqueous Media

Shi, Daqing*,[a](史达清) Shi, Jingwen[b](拾景文) Rong, Shaofeng[b](荣少烽)

[a] *College of Chemistry, Chemical Engineering and Materials Science, Key Laboratory of Organic Synthesis of Jiangsu Province, Soochow University, Suzhou, Jiangsu 215123, China*

[b] *College of Chemistry and Chemical Engineering, Xuzhou Normal University, Xuzhou, Jiangsu 221116, China*

A series of 5-benzylidenepyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione and 5,5'-(arylmethylene) bis[6-aminopyrimidine-2,4(1*H*,3*H*)-dione] derivatives were synthesized via the three-component reactions of aromatic aldehyde, 6-aminopyrimidine-2,4-dione and Medrum's acid in aqueous media in the presence of triethylbenzylammonium chloride. The structures of the products were affected by substituents of aromatic aldehydes.

Keywords 5-benzylidenepyrimidine-2,4,6-trione, 5,5'-(arylmethylene)bis(6-amino-pyrimidine-2,4-dione), aqueous media, multicomponent reactions, heterocycles

Introduction

The importance of uracil and its annelated derivatives is well recognized by synthetic[1] as well as biological[2] chemists. With the development of clinically useful anticancer and antiviral drugs,[3] there has recently been remarkable interest in the synthetic manipulations of uracils.[4]

Multi-component reactions (MCRs), in which multiple reactions are combined into one synthetic operation, have been used extensively to form carbon-carbon bonds in synthetic chemistry.[5] Such reactions offer a wide range of possibilities for the efficient construction of highly complex molecules in a single procedural step, avoid the complicate purification operations and allow savings of both solvents and reagents. In the past decade there have been tremendous development in three- and four-component reactions and great efforts continue to be made to develop new MCRs.[6-13]

The need to reduce the amount of toxic waste and by-product arising from chemical processes requires increasing emphasis on the use of less toxic and environmentally compatible materials in the design of new synthetic methods. One of most promising approaches is using water as the reaction media. Breslow,[14] who showed that hydrophobic effects could strongly enhance the rate of several organic reactions, rediscovered the use of water as a solvent in organic chemistry in the 1980's. There has been growing recognition that water is an attractive medium for many organic reactions.[15] Recently, many MCRs in aqueous medium have been reported.[16] As part of our current studies on the developments of new routes to heterocyclic system,[17] we now report an efficient and clean synthetic route to pyrimidine derivatives in aqueous media.

Results and discussion

When the three-component of aromatic aldehyde **1**, 6-aminopyrimidine-2,4-dione (**2**) and Medrum's acid **3** were treated in water in the presence of triethylbenzylammonium chloride (TEBAC) at 90 ℃ for 18—32 h, the desired product—5-aryl-5,6-dihydropyrido[2,3-*d*]-pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione (**4**) were not obtained and the unexpected products 5-benzylidene-pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (**5**) and 5,5'-(arylmethylene)bis(6-aminopyrimidine-2,4(1*H*,3*H*)-dione) (**6**) were obtained (Scheme 1).

Choosing an appropriate solvent is of crucial importance for the successful organic synthesis. To search for the optimal solvent, the reaction of 4-dimethylaminobenzaldehyde (**1a**), 6-amino-1,3-dimethylpyrimidine-2,4-dione (**2a**) and Meldrum's acid (**3**) was examined using water, ethanol, acetone, chloroform, acetic acid and DMF, respectively, at different temperature for the synthesis of **5a**. The results are summarized in Table 1.

It can be seen from the Table 1 that the best results were obtained when the reaction was carried out in water at 90 ℃ in the presence of TEBAC (10 mol%) (Table 1, Entry 2). Water was chosen as the solvent for all further reactions as it is environmentally friendly and the toxic organic solvents can be avoided. Under these optimized reaction conditions, two series of pyrimidine derivatives **5** and **6** were synthesized. The results are summarized in Table 2.

* E-mail: dqshi@suda.edu.cn
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Scheme 1

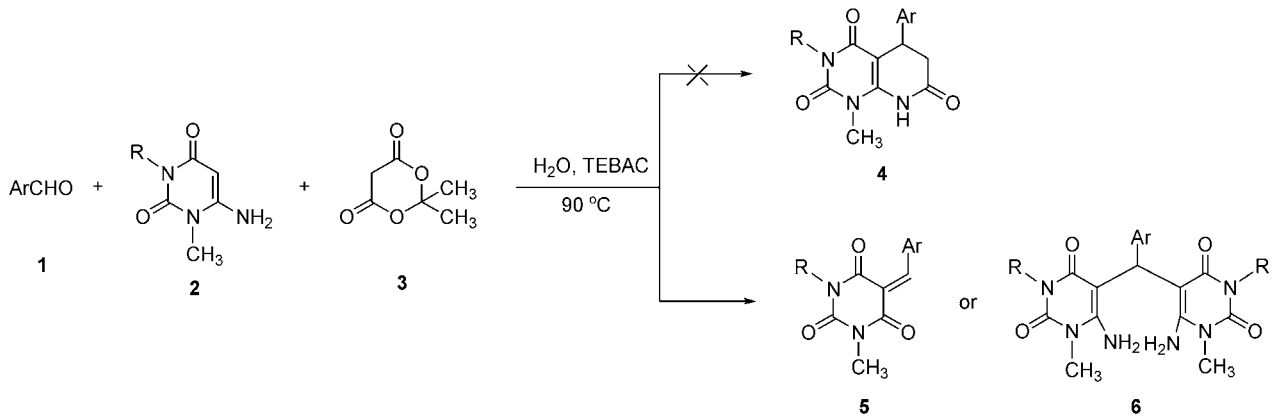

Table 1 Solvent optimization for the synthesis of **5a**

Entry	Solvent	Reaction temperature/℃	Time/h	Yield/%
1	H_2O	90	24	64
2	H_2O+TEBAC (10 mol%)	90	24	75
3	Ethanol	Reflux	24	67
4	Acetone	Reflux	24	39
5	$CHCl_3$	Reflux	24	63
6	HOAc	80	24	70
7	DMF	80	24	45

Table 2 The synthesis of pyrimidine derivatives **5** and **6** in aqueous media

Entry	Product	Ar	R	Time/h	Yield/%
1	**5a**	4-$(CH_3)_2NC_6H_4$	CH_3	24	75
2	**5b**	4-$CH_3OC_6H_4$	CH_3	22	78
3	**5c**	3,4-$OCH_2OC_6H_3$	CH_3	25	73
4	**5d**	4-HOC_6H_4	CH_3	20	65
5	**5e**	3,4-$(CH_3)_2C_6H_3$	CH_3	25	74
6	**5f**	3,4-$(CH_3O)_2C_6H_3$	CH_3	27	70
7	**5g**	4-$(CH_3)_2NC_6H_4$	H	18	70
8	**5h**	4-$CH_3OC_6H_4$	H	24	65
9	**5i**	3,4-$OCH_2OC_6H_3$	H	30	77
10	**5j**	4-HOC_6H_4	H	32	61
11	**5k**	3,4-$(CH_3O)_2C_6H_3$	H	26	72
12	**6a**	3,4-$Cl_2C_6H_3$	CH_3	26	94
13	**6b**	2,4-$Cl_2C_6H_3$	CH_3	27	95
14	**6c**	4-$NO_2C_6H_4$	CH_3	24	90
15	**6d**	4-FC_6H_4	CH_3	22	60
16	**6e**	4-BrC_6H_4	CH_3	20	88
17	**6f**	4-BrC_6H_4	H	24	96
18	**6g**	3,4-$Cl_2C_6H_3$	H	25	98
19	**6h**	2,4-$Cl_2C_6H_3$	H	22	95

As shown in Table 2, the structures of the products were affected by the electronic nature of substituents in aromatic aldehydes. When the aromatic aldehydes with electron-donoring groups (Table 2, Entries 1—11) were used, the products **5** were obtained. While the aromatic aldehydes with electron-withdrawing groups (Table 2, Entries 12—19) were used, the products **6** were obtained with excellent yields under the same reaction conditions. For compounds **5g**—**5k** two isomers—*E* and *Z* configurations were observed.

The structures of products **5** and **6** were identified by their spectroscopy analysis. The structure of **5b** was further confirmed by X-ray diffraction analysis.[18] The molecular structure of **5b** is shown in Figure 1.

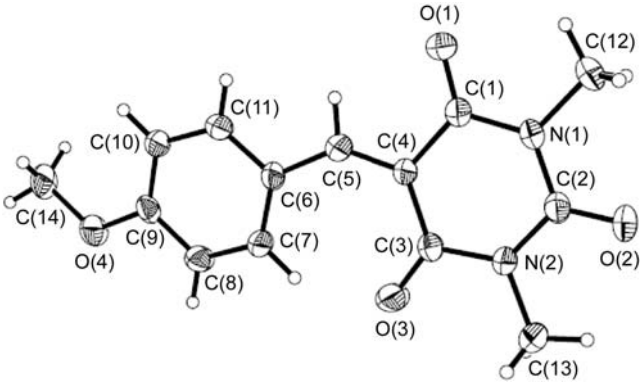

Figure 1 ORTEP diagram of **5b**.

Though the detailed mechanism of this reaction has not been fully clarified, the formation of **5** and **6** can be explained by the possible mechanism presented in Scheme 2. The reaction occurs via an initial formation

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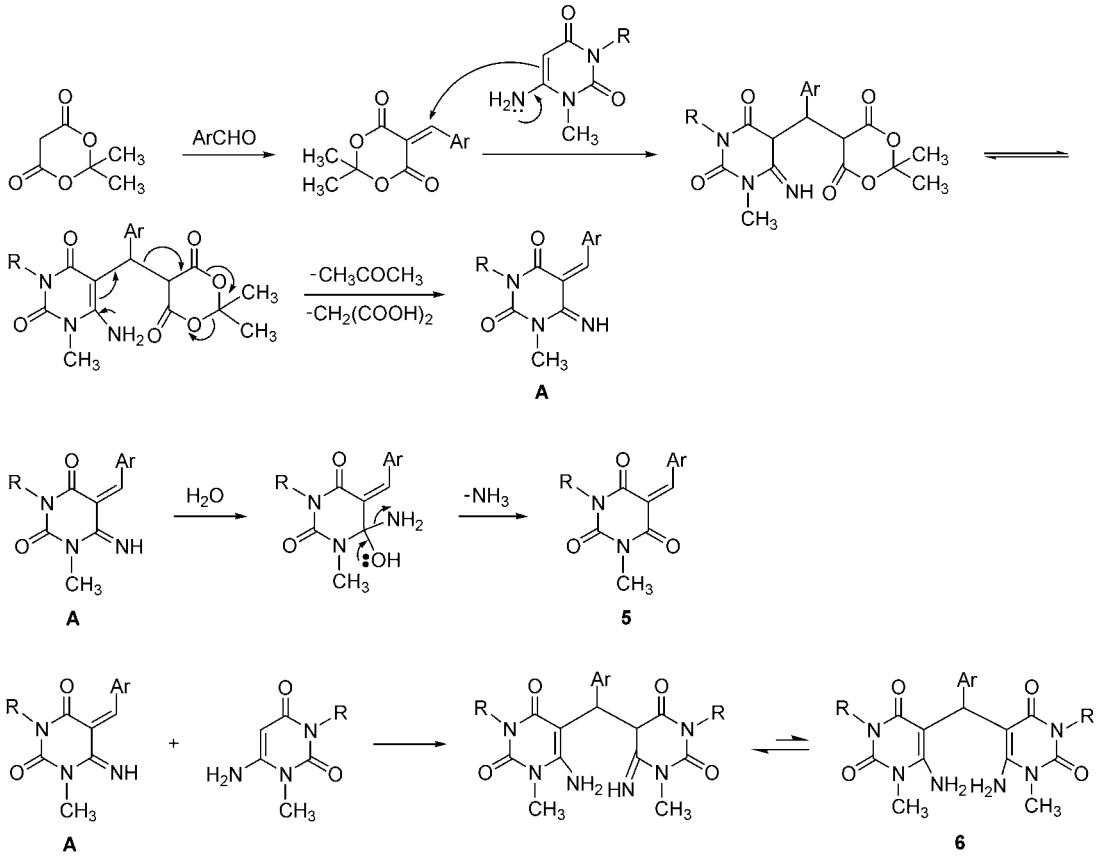
Scheme 2



of the α,β-unsaturated Meldrum's acid from the condensation of aldehyde and Meldrum's acid, which suffers nucleophilic attack by 6-aminopyrimidine-2,4-dione and loses acetone and malonic acid to give the intermediate **A**. When the substituents in aromatic aldehydes are electron-donoring groups, the intermediate is more stable, which was hydrolyzed in water finely to give the products **5**. When the substituents in aromatic aldehydes are electron-withdrawing groups, the intermediate is more active. The Michael addition between intermediate **A** and 6-aminopyrimidine-2,4-dione took place, the products **6** were given. In this reaction, the Meldrum's acid took part in the reaction, when no Meldrum's acid was added the reaction did not take place. In the reaction mixture no Meldrum's acid was detected. Moreover, when the catalytic amount of Meldrum's acid (10 mol%) was used, the yield of the desired product **5** was very poor.

Conclusion

In conclusion, a series of 5-benzylidenepyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione and 5,5'-(arylmethylene)bis(6-aminopyrimidine-2,4(1*H*,3*H*)-dione) were synthesized by three-component reaction of aromatic aldehydes, 6-aminopyrimidine-2,4-dione and Meldrum's acid in aqueous media. The advantages of this method are easier work-up, milder reaction conditions, environmentally benign procedure and wide scope.

Experimental

Melting points were determined on an XT-5 microscopic melting point instrument and uncorrected. IR spectra were recorded on a Tensor 27 spectrometer in KBr with absorptions in cm^{-1}. ^1H NMR was measured on a Bruker DPX 400 MHz spectrometer in DMSO-d_6 with TMS as internal standard. Microanalyses were carried out on Perkin-Elmer 2400 II instruments. X-ray diffraction was recorded on Smart-1000 diffractometer.

Typical procedure for the synthesis of 5-benzylidenepyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5) and 5,5'-(arylmethylene) bis(6-aminopyrimidine-2,4(1*H*,3*H*)-dione) (6) in aqueous media

A mixture of an aromatic aldehyde **1** (2 mmol), 6-aminopyrimidine-2,4-dione (**2**) (2 mmol), Meldrum's acid **3** (2 mmol) and TEBAC (0.15 g) in water (10 mL) was stirred for 18—32 h at 90 ℃, then the reaction mixture was cooled to room temperature. The crystalline powder formed was collected by filtration, washed with water and purified by recrystallization from the mixture of DMF and water to give **5** or **6**

1,3-Dimethyl-5-[4-(dimethylamino)benzylidene]-pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5a) m.p. 240—242 ℃ (Lit.[19] 242 ℃); ^1H NMR (DMSO-d_6, 400 MHz)

δ: 3.14 (s, 6H, 2×CH_3), 3.22 (s, 6H, 2×CH_3), 6.81 (d, J=8.8 Hz, 2H, ArH), 8.23 (s, 1H, CH=), 8.43 (d, J=8.8 Hz, 2H, ArH); IR (KBr) ν: 1713, 1659, 1608, 1572, 1535, 1468, 1442, 1411, 1362, 1234, 1193, 1160, 998, 971, 940, 786, 752 cm^{-1}.

1,3-Dimethyl-5-(4-methyoxybenzylidene)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5b) m.p. 149—151 ℃ (Lit.[20] 152 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.21 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 3.87 (s, 3H, CH_3O), 7.08 (d, J=9.2 Hz, 2H, ArH), 8.32 (s, 1H, CH=), 8.34 (d, J=9.2 Hz, 2H, ArH); IR (KBr) ν: 1717, 1664, 1603, 1569, 1463, 1433, 1406, 1382, 1229, 1185, 850, 817, 790, 752 cm^{-1}.

1,3-Dimethyl-5-(3,4-methylenedioxybenzylidene)-pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5c) m.p. 202—204 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.22 (s, 3H, CH_3), 3.24 (s, 3H, CH_3), 6.19 (s, 2H, OCH_2O), 7.09 (d, J=8.4 Hz, 1H, ArH), 7.74 (dd, J=1.6, 8.4 Hz, 1H, ArH), 8.17 (d, J=1.6 Hz, 1H, ArH), 8.29 (s, 1H, CH=); IR (KBr) ν: 1728, 1657, 1596, 1553, 1363, 1344, 1148, 887, 814, 787, 752 cm^{-1}. Anal. calcd for $C_{14}H_{12}N_2O_5$: C 58.33, H 4.20, N 9.72; found C 58.59, H 4.02, N 9.85.

1,3-Dimethyl-5-(4-hydroxybenzylidene)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5d) m.p. 293—295 ℃ (Lit.[21] 297—299 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.21 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 6.89 (d, J=8.4 Hz, 2H, ArH), 8.29 (d, J=8.4 Hz, 2H, ArH), 8.33 (s, 1H, CH=), 10.84 (s, 1H, OH); IR (KBr) ν: 3200, 1705, 1667, 1639, 1602, 1470, 1420, 1397, 1385, 1298, 1252, 1235, 885, 827, 789, 753 cm^{-1}.

1,3-Dimethyl-5-(3,4-dimethylbenzylidene)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5e) m.p. 210—212 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.28 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.21 (s, 3H, CH_3), 3.24 (s, 3H, CH_3), 7.28 (d, J=8.0 Hz, 1H, ArH), 7.94 (s, 1H, ArH), 7.97 (d, J=8.0 Hz, 1H, ArH), 8.31 (s, 1H, CH=); IR (KBr) ν: 1722, 1665, 1574, 1555, 1506, 1448, 1420, 1361, 1241, 1224, 1178, 987, 965, 917, 845, 792, 752, 723 cm^{-1}. Anal. calcd for $C_{15}H_{16}N_2O_3$: C 66.16, H 5.92, N 10.29; found C 66.04, H 6.08, N 10.51.

1,3-Dimethyl-5-(3,4-dimethoxybenzylidene)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5f) m.p. 226—228 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.23 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 3.83 (s, 3H, CH_3O), 3.90 (s, 3H, CH_3O), 7.13 (d, J=8.4 Hz, 1H, ArH), 7.92 (d, J=8.4 Hz, 1H, ArH), 8.29 (s, 1H, ArH), 8.34 (s, 1H, CH=); IR (KBr) ν: 1720, 1657, 1598, 1556, 1360, 1334, 1170, 1033, 922, 804, 771, 753 cm^{-1}. Anal. calcd for $C_{15}H_{16}N_2O_5$: C 59.21, H 5.30, N 9.21; found C 59.36, H 5.12, N 9.09.

1-Methyl-5-(4-(dimethylamino)benzylidene)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5g) m.p. 268—270 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.12 (s, 6H, 2×CH_3), 3.17 (s, 3H, CH_3), 6.82 (d, J=8.8 Hz, 2H, ArH), 8.21 (s, 1H, CH=), 8.43 (d, J=8.8 Hz, 2H, ArH), 11.17 (s) and 11.27 (s) (1H, NH); IR (KBr) ν: 3225, 1713, 1659, 1608, 1572, 1468, 1442, 1362, 1318, 1160, 998, 940, 830, 786, 752 cm^{-1}. Anal. calcd for $C_{14}H_{15}N_3O_3$: C 61.53, H 5.53, N 15.38; found C 61.74, H 5.40, N 15.57.

1-Methyl-5-(4-methoxybenzylidene)pyrimidine-2,-4,6(1*H*,3*H*,5*H*)-trione (5h) m.p. 242—244 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.15 (s) and 3.18 (s) (3H, CH_3), 3.88 (s, 3H, CH_3O), 7.06—7.08 (m, 2H, ArH), 8.27 (s) and 8.30 (s) (1H, CH=), 8.34—8.39 (m, 2H, ArH), 11.41 (s) and 11.52 (s) (1H, NH); IR (KBr) ν: 3230, 1723, 1693, 1604, 1571, 1550, 1388, 1348, 1188, 1147, 983, 842, 756 cm^{-1}. Anal. calcd for $C_{13}H_{12}N_2O_4$: C 60.00, H 4.65, N 10.76; found C 60.21, H 4.53, N 10.89.

1-Methyl-5-(3,4-methylenedioxybenzylidene)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5i) m.p. 287—289 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.15 (s) and 3.17 (s) (3H, CH_3), 6.19 (s, 2H, OCH_2O), 7.09 (d, J=8.4 Hz, 1H, ArH), 7.75 (s, 1H, ArH), 8.18—8.26 (m, 2H and CH=), 11.44 (s) and 11.54 (s) (1H, NH); IR (KBr) ν: 3225, 1731, 1641, 1548, 1503, 1359, 1260, 1029, 978, 908, 783, 752 cm^{-1}. Anal. calcd for $C_{13}H_{10}N_2O_5$: C 56.94, H 3.68, N 10.22; found C 56.81, H 3.53, N 10.41.

1-Methyl-5-(4-hydroxybenzylidene)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5j) m.p.>300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.16 (s) and 3.17 (s) (3H, CH_3), 6.89 (d, J=7.6 Hz, 2H, ArH), 8.23 (s) and 8.26 (s) (1H, CH=), 8.31—8.35 (m, 2H, ArH), 10.84 (s, 1H, OH), 11.36 (s) and 11.47 (s) (1H, NH); IR (KBr) ν: 3228, 1716, 1690, 1649, 1609, 1537, 1389, 1217, 1176, 985, 956, 844, 790, 756 cm^{-1}. Anal. calcd for $C_{12}H_{10}N_2O_4$: C 58.54, H 4.09, N 11.38; found C 58.78, H 3.86, N 11.51.

1-Methyl-5-(3,4-dimethoxybenzylidene)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5k) m.p. 265—267 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.16 (s) and 3.17 (s) (3H, CH_3), 3.81—3.88 (m, 6H, 2×CH_3O), 7.11 (d, J=8.8 Hz, 2H, ArH), 7.87—7.94 (m, 1H, CH=), 8.26—8.41 (m, 2H, ArH), 11.41 (s) and 11.51 (s) (1H, NH); IR (KBr) ν: 3210, 1732, 1687, 1658, 1549, 1509, 1357, 1289, 1014, 930, 892, 801, 751 cm^{-1}. Anal. calcd for $C_{14}H_{14}N_2O_5$: C 57.93, H 4.86, N 9.65; found C 58.04, H 4.79, N 9.83.

5,5'-(3,4-Dichlorophenylmethylene)bis(6-amino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione) (6a) m.p. >300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.06 (s, 6H, 2×CH_3), 3.24 (s, 6H, 2×CH_3), 5.57 (s, 1H, CH), 7.10 (d, J=9.2 Hz, 1H, ArH), 7.31—7.44 (m, 5H, ArH+2×NH_2), 7.89 (s, 1H, ArH); IR (KBr) ν: 3389, 3139, 1693, 1661, 1610, 1499, 1381, 1251, 1029, 881, 822, 788, 755 cm^{-1}. Anal. calcd for $C_{19}H_{20}Cl_2N_6O_4$: C 48.83, H 4.31, N 17.98; found C 49.05, H 4.14, N 18.18.

5,5'-(2,4-Dichlorophenylmethylene)bis(6-amino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione) (6b) m.p. >300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.02 (s, 6H, 2×CH_3), 3.21 (s, 6H, 2×CH_3), 5.52 (s, 1H, CH), 7.15 (d, J=9.2 Hz, 1H, ArH), 7.28—7.40 (m, 5H, ArH+2×NH_2), 7.85 (s, 1H, ArH); IR (KBr) ν: 3379, 3130, 1695, 1661, 1605, 1496, 1380, 1193, 1029, 881, 788, 755, 717 cm^{-1}. Anal. calcd for $C_{19}H_{20}Cl_2N_6O_4$: C 48.83,

H 4.31, N 17.98; found C 49.01, H 4.46, N 18.11.

5,5'-(4-Nitrophenylmethylene)bis(6-amino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione) (6c) m.p. > 300 ℃ (Lit.[22] >300 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.15 (s, 6H, 2×CH_3), 3.29 (s, 6H, 2×CH_3), 5.49 (s, 1H, CH), 7.10 (d, J=9.2 Hz, 1H, ArH), 7.31—7.44 (m, 6H, ArH+2×NH_2), 7.90 (s, 1H, ArH); IR (KBr) v: 3456, 3331, 1694, 1667, 1596, 1505, 1344, 1245, 1148, 932, 857, 790, 762, 748 cm^{-1}.

5,5'-(4-Fluorophenylmethylene)bis(6-amino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione) (6d) m.p.> 300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.11 (s, 6H, 2×CH_3), 3.28 (s, 6H, 2×CH_3), 5.52 (s, 1H, CH), 7.10 (d, J=9.2 Hz, 1H, ArH), 7.30—7.44 (m, 6H, ArH+2×NH_2), 7.95 (s, 1H, ArH); IR (KBr) v: 3364, 3154, 1697, 1593, 1498, 1378, 1286, 1159, 846, 812, 790, 734 cm^{-1}. Anal. calcd for $C_{19}H_{21}FN_6O_4$: C 54.80, H 5.08, N 20.18; found C 54.97, H 4.93, N 20.30.

5,5'-(4-Bromophenylmethylene)bis(6-amino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione) (6e) m.p.> 300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.15 (s, 6H, 2×CH_3), 3.29 (s, 6H, 2×CH_3), 5.49 (s, 1H, CH), 7.12 (d, J=9.2 Hz, 1H, ArH), 7.33—7.41 (m, 6H, ArH+2×NH_2), 8.01 (s, 1H, ArH); IR (KBr) v: 3339, 3160, 1698, 1594, 1499, 1377, 1208, 1156, 931, 849, 789, 752, 716 cm^{-1}. Anal. calcd for $C_{19}H_{21}BrN_6O_4$: C 47.81, H 4.43, N 17.61; found C 47.52, H 4.36, N 17.77.

5,5'-(4-Bromophenylmethylene)bis(6-amino-1-methylpyrimidine-2,4(1*H*,3*H*)-dione) (6f) m.p. > 300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.36 (s, 6H, 2×CH_3), 5.39 (s, 1H, CH), 7.06 (d, J=8.4 Hz, 2H, ArH), 7.36—7.38 (m, 5H, ArH+2×NH_2), 7.95 (s, 1H, ArH), 10.74—10.87 (m, 2H, 2×NH); IR (KBr) v: 3343, 3117, 1725, 1605, 1500, 1387, 1253, 1095, 900, 851, 786, 760 cm^{-1}. Anal. calcd for $C_{17}H_{17}BrN_6O_4$: C 45.45, H 3.81, N 18.71; found C 45.62, H 3.97, N 18.54.

5,5'-(3,4-Dichlorophenylmethylene)bis(6-amino-1-methylpyrimidine-2,4(1*H*,3*H*)-dione) (6g) m.p.> 300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.25 (s, 6H, 2×CH_3), 5.43 (s, 1H, CH), 7.09 (d, J=8.4 Hz, 1H, ArH), 7.30—7.45 (m, 6H, ArH+2×NH_2), 7.96 (s, 1H, ArH), 10.89—10.91 (m, 2H, 2×NH); IR (KBr) v: 3348, 3174, 1696, 1664, 1603, 1503, 1470, 1389, 1255, 889, 832, 771, 757, 735 cm^{-1}. Anal. calcd for $C_{17}H_{16}Cl_2N_6O_4$: C 46.48, H 3.67, N 19.13; found C 46.64, H 3.47, N 19.05.

5,5'-(2,4-Dichlorophenylmethylene)bis(6-amino-1-methylpyrimidine-2,4(1*H*,3*H*)-dione) (6h) m.p. > 300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.20 (s, 6H, 2×CH_3), 5.43 (s, 1H, CH), 7.05 (d, J=8.4 Hz, 1H, ArH), 7.30—7.45 (m, 6H, ArH+2×NH_2), 7.96 (s, 1H, ArH), 10.88—10.95 (m, 2H, 2×NH); IR (KBr) v: 3371, 3220, 1716, 1610, 1505, 1387, 1255, 1102, 921, 847, 821, 792, 755, 709 cm^{-1}. Anal. calcd for $C_{17}H_{16}Cl_2N_6O_4$: C 46.48, H 3.67, N 19.13; found C 46.57, H 3.72, N 19.08.

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18 Crystal data for **5b**: $C_{14}H_{14}N_2O_4$; M_r=274.27, colorless block crystals, 0.42 mm×0.39 mm×0. 35 mm, triclinic, space group P-1, a=0.7667(3) nm, b=0.8325(3) nm, c=1.0434(4) nm, α = 92.272(5)°, β = 91. 998(6)°, γ = 104.374(5)°, V=0. 6439(4) nm^3, Z=2, D_c=1.415 g/cm^3,

$F(000)=288$, μ(Mo Kα)$=0.105$ mm^{-1}. Intensity data were collected on Smart-1000 diffractometer with graphite monochromated Mo Kα radiation ($\lambda=0.071073$ nm) using ω scan mode with $2.53°<\theta<25.00°$. 2244 unique reflections were measured and 1082 reflections with $I>2\sigma(I)$ were used in the refinement. The structure was solved by direct methods and expanded using Fourier technique. The final cycle of full-matrix least squares technique refined to $R=0.0611$ and $wR=0.1557$.

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