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A Clean, Highly Efficient and One-Pot Green Synthesis of Aryl/Alkyl/Heteroaryl-Substituted Bis(6-amino-1,3-dimethyluracil-5-yl)methanes in Water

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A highly efficient green synthesis of aryl/alkyl/heteroaryl-substituted bis(6-amino-1,3-dimethyluracil-5-yl)methanes by the condensation of 6-amino-1,3-dimethyluracil with aldehydes (aromatic, aliphatic and heterocyclic) in water at room temperature is described. No dehydrating agent, heat, catalyst, surfactant or additive was used. The structures of the compounds were established by spectroscopic methods and single-crystal X-ray crystallography.

Introduction

The general belief is that life started from organic compounds in an aqueous environment. Szent-Gyorgyi rightly dubbed water the "matrix of life"[1] and it is regarded as a universal solvent. Mimicking nature and bearing in mind environmentally friendly protocols, the use of water as a remarkable solvent with a difference in organic synthesis has received considerable attention in recent times.[2] The reason behind this is that water is the solvent of choice from not only an ecological but also from an economic point of view. Water is cheap, safe, natural, non-flammable, abundant, available and environmentally benign, that is, it is a green solvent[3] associated with easy reaction work-up. Compared with common organic solvents, the unique and unusual physical (low viscosity, high specific heat, high surface tension, high dielectric constant, large cohesive energy density etc.) and chemical properties (ability to form hydrogen bonds, its amphoteric nature etc.) of liquid water help to increase the reactivity and selectivity of chemical reactions.[4] Moreover, hydrophobic interactions are also responsible for reactivity. In spite of these potential advantages, water has not found use as a common organic solvent because most organic compounds are insoluble in water according to the assumption "*corpora non agunt nisi solute*" (substances do not interact unless dissolved). Regardless of this, however, there are many examples of aqueous media reactions,[5] water used as a co-solvent or on-water[6] reactions performed without dissolving the organic compounds (coined as the "on-water-effect"). Efforts have been made to dissolve organic compounds in water by adding additives like surfactants[7] and applying heat.[8] Rideout and Breslow's seminal observation that Diels–Alder reactions could be greatly accelerated by using a water suspension rather than solution instead of organic solvents established the importance of water in organic synthesis.[9] Since then, this area of research has burgeoned. On the other hand, organic solvents contribute the lion's part to the pollution problem in practical chemistry,[10] both in the laboratory as well as in industry. Hence, the search for efficient synthetic methodologies for organic reactions without the use of organic solvents is an important challenge in reducing the amount of waste generated.[11] An ideal organic reaction demands that it would proceed neat, that is, with no solvent, or in an environmentally benign solvent such as water.

Uracil, a nucleobase of the pyrimidine family, is one of the major motifs present in the biopolymer RNA[12] and it plays several roles in our life cycle.[13] The versatility of the uracil scaffold and its derivatives, as exhibited by their wide range of biological activities, has brought chemists[14] and biologists together.[15] Several patents also report promising pharmaceutical agents of uracil origin for the treatment of cancer and viral diseases.[16] To name but a few, uracil derivatives are also useful as bronchodilators and anticancer agents,[17] antiallergic compounds,[17,18a] antiviral agents,[18b] antihypertensive agents[19] and adenosine receptor antagonists.[20] In addition, 5-substituted uracils and their nucleosides are widely used in the chemotherapy of cancer.[21] Pyrimidine derivatives have also been used in coordination chemistry.[22] In view of the biological significance of pyrimidine compounds, we have been focussing on the design and synthesis of such pyrimidine derivatives.[23]

Results and Discussion

Thus, bearing in mind the importance of water and the uracil moiety together, herein we report a clean, highly efficient and one-pot green method for the synthesis of bis-uracil compounds **3** by the reaction of 6-amino-1,3-dimeth-

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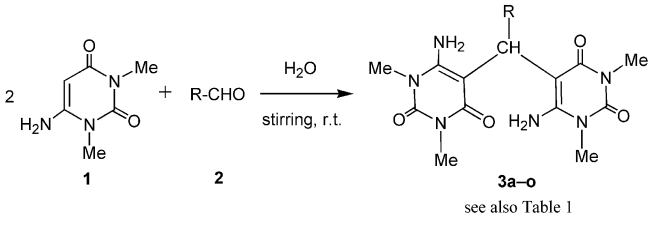
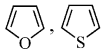
yluracil (**1**; at the 5-position) and aldehydes **2** in water at room temperature without using any catalyst, surfactant, additive, dehydrating agent, heat or organic solvent (Scheme 1).



R = Ph, CH=CH-Ph, *p*-$OCH_3C_6H_4$, *p*-ClC_6H_4, *p*-OHC_6H_4, *o*-OHC_6H_4, *p*-$CH_3C_6H_4$, *p*-$NO_2C_6H_4$,

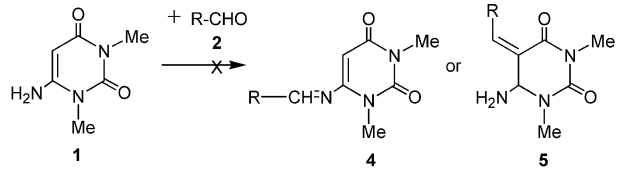
m-$NO_2C_6H_4$, H, CH_3, $CH_3(CH_2)_3$, $CH_3(CH_2)_2$, 

Scheme 1. Synthesis of bis-uracil derivatives **3**.

In 1986, Lam and Pridgen first reported the reaction of unsubstituted uracil with aromatic aldehydes in aqueous mineral acids (e.g., concd. HCl, HBr, HI or H_2SO_4) at reflux.[24] Depending on the nature of substituents on the aldehydes, they obtained a mixture of (hydroxymethyl)uracil and bis-uracil adducts. The condensation reaction of substituted 6-aminouracils and aromatic aldehydes in ethanol at reflux or under microwave irradiation wetted by DMSO afforded bis-uracil compounds.[25] However, in both the cases, the reaction failed with aliphatic and heteroaromatic aldehydes. Another report presented the synthesis of bis-uracil compounds from aromatic aldehydes only in methanol and acetic acid.[26] Hlavác and co-workers in 2007 further explored the reaction of unsubstituted uracil with 4-nitrobenzaldehyde and obtained 5-[chloro(4-nitrophenyl)-methyl]uracil at reflux in aqueous mineral acids and continued the generalization for the synthesis of 5-[alkoxy(4-nitrophenyl)methyl]uracils from 5-[chloro(4-nitrophenyl)-methyl]uracil. They also studied the anticancer activity of the synthesized compounds.[27] Bazgir and co-workers in 2007 reported the formation of fused pyrimidine derivatives via bis-uracil as intermediate in a three-component reaction of 6-amino-1,3-dimethyluracil, aldehydes and urea catalysed by acetic acid under microwave irradiation.[28] Again, this method is limited to aromatic aldehydes only. During the preparation of this manuscript, an interesting report from Shi et al.[29] showed that the three-component reaction of aromatic aldehyde, 6-aminopyrimidine-2,4-dione and Meldrum's acid in water in the presence of triethylbenzylammonium chloride (TEBAC) at 90 °C for 18–32 h led to the formation 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]. However, none of these reported methods are general covering all types of aldehydes: aliphatic, aromatic and heterocyclic. Moreover, the use of mineral acid, acetic acid, additives, microwave irradiation or reflux conditions in common organic solvents are necessary for the synthesis of such substituted or unsubstituted bis-uracil adducts. Thus, a general and "green" method is required. Our method eliminates all of the above-mentioned drawbacks with an added advantage.

Bis-uracil and their analogues have also been isolated from marine sea hare *Dolabella auricularia*.[30] Semenov and co-workers have been actively working on the synthesis of *N*-substituted bis-uracil analogues and the bioactivities of the synthesized compounds.[31]

In an attempt to synthesize imines **4** from 6-amino-1,3-dimethyluracil (**1**) and benzaldehyde **2** (R = Ph) (Scheme 2) we tested several reaction conditions, both conventional and non-conventional, using a catalyst or in the absence of catalyst and in the presence or absence of solvent. However, all the attempts were in vain and we observed the following interesting results.



Scheme 2. Synthesis of imine **4** or alkene **5**.

As a model reaction, when we simply stirred 6-amino-1,3-dimethyluracil (**1**) and benzaldehyde (**2a**; R = Ph) in water at room temperature, we ended up with the formation of 5,5′-phenylmethylenebis(1,3-dimethyl-6-aminopyrimidine-2,4-dione) (**3a**) within 1 h in 95% yield (Scheme 1). The reaction was monitored by TLC. The reaction was very clean providing only one product, that is, **3a**. We did not observe the formation of product **4** nor the other possible product **5** (Scheme 2). As the reaction progressed, we observed that the product started to precipitate from the aqueous solution and simple filtration afforded the product. The structure was confirmed by IR, ^1H and ^{13}C NMR spectroscopy, mass spectrometry and elemental analyses.

The ^1H NMR peaks at δ = 3.27 (3 H), 3.34 (3 H) and 3.44 (6 H) ppm are due to the four *N*-methyl groups, the peak at δ = 5.79 ppm is due to the >CH proton, the broad singlet peaks at δ = 6.48 and 6.96 ppm are due to the two $-NH_2$ protons and the peaks at δ = 7.14–7.25 ppm are due to five aromatic protons. The two $-NH_2$ groups were confirmed by shaking with D_2O, that is, the $-NH_2$ peak disappeared from the ^1H NMR spectrum upon shaking with D_2O. The structure was further confirmed by single-crystal X-ray analysis. Suitable crystals were obtained by slow evaporation from ethanol solution.

Encouraged by this result, to study the scope and limitations of the reaction further, we extended the reaction to other differently substituted aromatic, aliphatic and heterocyclic aldehydes and ketones (**2a**–**r**) under the same optimized reaction conditions. The results are summarized in Table 1 (entries **a**–**r**). All the aldehydes (entries **a**–**o**, Table 1) reacted with equal ease within short times to furnish the bis-uracils **3a**–**o** in good-to-excellent yields (73–99%) and with no side-products.

Table 1. Synthesis of bis-uracil derivatives **3a**–**o**.

	Carbonyl compound **2**	Time [h]	M.p. [°C]	Yield of **3** [%][a]
a	C_6H_5CHO	1	296–299	95
b	$C_6H_5CH{=}CHCHO$	4	265–269	93
c	*p*-$MeOC_6H_4CHO$	3	273–275	91
d	*p*-ClC_6H_4CHO	0.25	268–270	99
e	*p*-HOC_6H_4CHO	7	245–248	75
f	*o*-HOC_6H_4CHO	7	247–249	73
g	*p*-MeC_6H_4CHO	0.25	276–279	99
h	*p*-$NO_2C_6H_4CHO$	10	228–229	73
i	*m*-$NO_2C_6H_4CHO$	5	224–225	82
j	2-furaldehyde	1	246–250	99
k	thiophene-2-carbaldehyde	6	309–312	87
l	paraformaldehyde	1	328–334	91
m	CH_3CHO	3	253–256	92
n	$CH_3(CH_2)_2CHO$	3	232–233	93
o	$CH_3(CH_2)_3CHO$	3	159–162	90
p	$(CH_3)_2CO$	48	–	–[b]
q	CH_3COPh	48	–	–[b]
r	PhCOPh	48	–	–[b]

[a] Isolated yield. [b] No product found.

As illustrated in Table 1 (entries **a**–**o**), it is evident that aromatic, aliphatic and heterocyclic aldehydes are equally effective for the synthesis of bis-uracil **3**. We also obtained very good yields (>90%) with aliphatic aldehydes (entries **l**–**o**, Table 1). With paraformaldehyde (entry **l**, Table 1), 6-amino-1,3-dimethyluracil (**1**) afforded the bis-uracil adduct **3l**, 6,6′-diamino-1,1′,3,3′-tetramethyl-5,5′-methylenebis[pyrimidine-2,4(1*H*,3*H*)-dione] (91% yield). However, under both acidic and basic conditions, unsubstituted uracil reacted with paraformaldehyde to produce 5-hydroxymethyluracil, as reported by Kong et al.[32] This is in sharp contrast to the report[28] in which the reaction with aliphatic aldehydes was not mentioned. We performed the reaction with another three aliphatic aldehydes (entries **m**–**o**, Table 1) with different carbon chain lengths and all the products were confirmed by NMR (^1H and ^{13}C) and FTIR spectroscopy, mass spectrometry, elemental analyses and single-crystal X-ray analysis. ORTEP diagrams for compounds **3d** and **3l** are shown in Figures 1 and 2, respectively. From these ORTEP diagrams, it is clear that both the amino groups and the two uracil rings are oriented oppositely and hence they exist in different magnetic environments.

Our approach is also equally effective for heterocyclic compounds. 2-Furaldehyde (entry **j**) and thiophene-2-carbaldehyde (entry **k**) provided the desired products **3j** and **3k** in 99 and 87% yields, respectively. 2-Furaldehyde reacted within 1 h, but thiophene-2-carbaldehyde required a longer reaction time (6 h). No other products were detected. The structures of the products were confirmed by NMR (both ^1H and ^{13}C) and FTIR spectroscopy, mass spectrometry, elemental analysis and single-crystal X-ray analysis. The ORTEP diagram of compound **3j** is shown in Figure 3.

On the other hand, in the case of *ortho*- and *para*-hydroxy-substituted benzaldehydes (entries **e** and **f**, respectively), low yields (75 and 73%, respectively) of the products were obtained probably due to the formation of intermolecular hydrogen-bonding with water.

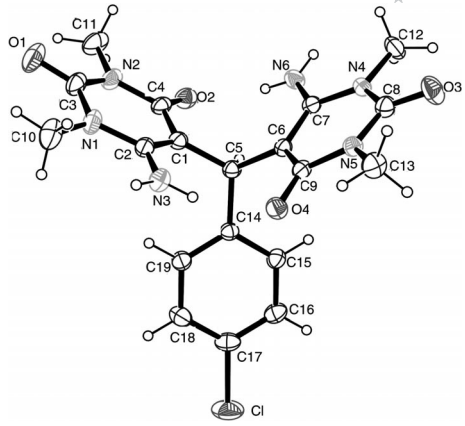


Figure 1. ORTEP diagram of compound **3d**.

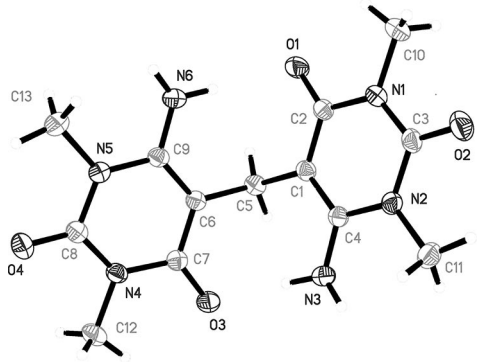


Figure 2. ORTEP diagram of compound **3l**.

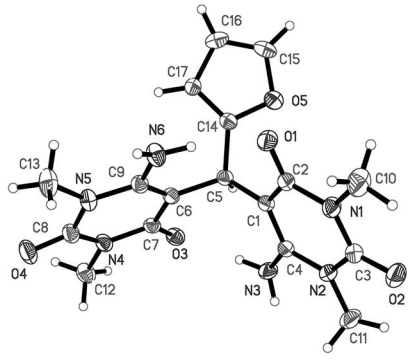
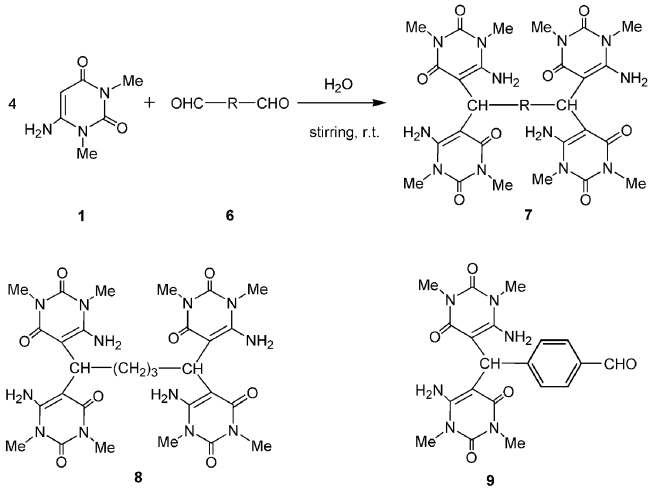


Figure 3. ORTEP diagram of compound **3j**.

Realizing the difference in reactivity of aldehydes and ketones, we also studied the reaction of 6-amino-1,3-dimethyluracil (**1**) with ketones (Scheme 1, Table 1, entries **p**–**r**). However, the reaction failed to proceed even after a long time (24 h), which shows the chemoselectivity of the reaction, and all the starting materials were recovered. This chemoselectivity was also established in a competitive experiment involving benzaldehyde (**2a**; 0.5 mmol), benzophenone (**2r**; 0.5 mmol) and uracil **1** (2.0 mmol). Benzaldehyde reacted as described in Scheme 1, whereas benzophenone did not react at all. Unreacted benzophenone (**2r**) and uracil **1** were recovered along with the desired product **3a**.

To extend the scope of the reaction further, we also studied the reaction of 6-amino-1,3-dimethyluracil (**1**) with dicarbaldehyde **6** (Scheme 3). The results are reported in Table 2 (entries **a** and **b**). In the case of an aliphatic dicarbaldehyde, glutaraldehyde (entry **b**, Table 2) we obtained the tetrakis-uracil adduct **8**, but in the case of *p*-benzenedicarbaldehyde (entry **a**, Table 2) we obtained the bis-uracil adduct **9** instead of the tetrakis-uracil adduct, as evidenced by the appearance of the aldehydic peak at δ = 9.96 ppm in the ^{1}H NMR spectrum and at δ = 192.04 ppm in the ^{13}C NMR spectrum of **9**.



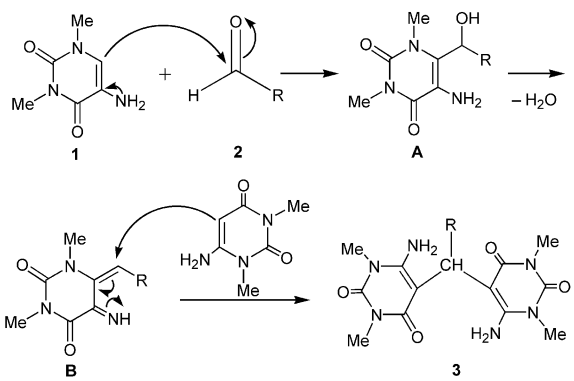
Scheme 3. Synthesis of tetrakis-uracil derivatives.

Table 2. Synthesis of the bis- and tetrakis-uracil derivatives **8** and **9**.

	Carbonyl compound **6**	Time [h]	M.p. [°C]	Yield [%][a]
a	*p*-(CHO)C_6H_4(CHO)	7	301–303	86
b	$CHO(CH_2)_5CHO$	7	194–195	89

[a] Isolated yield.

Only a few examples of the nucleophilic nature[33] of the 5-position of uracil and its metal-binding capacity have been reported.[34] Indole also shows similar nucleophilic behaviour at the 3-position and reacts with the carbonyl moiety to produce bis-indolyl compounds.[35]



Scheme 4.

At this stage, the detailed mechanism is not fully understood. A plausible mechanism for the reaction is shown in Scheme 4. Mechanistically, the nucleophilic 5-position of 6-amino-1,3-dimethyluracil (**1**) attacks the carbon centre of the aldehyde **2** and is followed by elimination of a water molecule. A second molecule of **1** then reacts at the nucleophilic 5-position to afford the product **3**.

6-Amino-1,3-dimethyluracil (**1**) is water-soluble. When the aldehyde, which is insoluble, is added to an aqueous solution of uracil **1** the reaction probably occurs at the interface. As soon as the product forms, it precipitates owing to its hydrophobic nature, which might be the driving force for the reaction.

Conclusions

The experimental procedure for the electrophilic substitution is remarkably simple without the need for dry solvents, an inert atmosphere or reflux conditions. The product was purified by simple filtration without the need for any further separation technique, that is, neither chromatography (TLC/column chromatography) nor extraction using organic solvent. Importantly, the separation step in any synthesis involves most of the capital and operating costs (60–80%) of the overall cost. Different steps (reaction, separation and purification) contribute to the environmental footprint of the process.[36] Hence, our method is environmentally benign (eliminating the use of organic solvents in both the reaction and purification), safe and cost effective. Note that no dehydrating agent, heat (hence energy is saved), catalyst, surfactant or additive is required. Moreover, protection of the $-NH_2$ group is also not required. The present method opens a new avenue for the synthesis of bis-uracils, which might be useful for exploring bioactivities.

In conclusion, we have developed a mild, chemoselective, highly efficient, clean and truly "green" methodology for the synthesis of aryl/alkyl/heteroaryl bis(6-amino-1,3-dimethyluracil-5-yl)methanes by condensation of 6-amino-1,3-dimethyluracil with all types of aldehydes (aromatic, aliphatic and heterocyclic) in water at room temperature.

Further exploration of "in water" reactions, both in terms of applications and mechanism (experimentally and theoretically), are in progress in our laboratory.

Experimental Section

General: Melting points were determined with a Büchi 504 apparatus. IR spectra were recorded as KBr pallets with a Nicolet (Impact 410) FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded with a JNM ECS 400 MHz NMR spectrophotometer (JEOL) using tetramethylsilane (TMS) as the internal standard. X-ray intensity data were collected with a Bruker SMART APEX CCD area-detector diffractometer with Mo-K_α radiation (λ = 0.71073 Å). The structures were solved by SHELX97 and refined by full-matrix least-squares on *F2* (SHELX97).[37] Reactions were monitored by thin-layer chromatography using aluminium sheets with silica gel 60 F_{254} (Merck). Elemental analyses were carried out

with a Perkin–Elmer CHN analyser (2400 series II). Mass spectra were recorded with a Waters Q-TOF Premier and Aquity UPLC spectrometer. All the chemicals were used as received.

General Procedure for the Synthesis of Bis-uracil 3: Distilled water (30 mL) was added to 6-amino-1,3-dimethyluracil (**1**; 155 mg, 1 mmol) in a 100 mL round-bottomed flask and the mixture was stirred at room temperature until all the 6-amino-1,3-dimethyluracil had dissolved. Benzaldehyde (54 mg, 0.5 mmol) was added dropwise to the 6-amino-1,3-dimethyluracil solution with constant stirring and then after a few minutes the product appeared as a white precipitate and stirring was continued for a further 1 h so that all of the reactants were converted into product. The white precipitate was filtered and collected to provide the pure product **3a** in 95% yield. A small amount of the product was dissolved in distilled ethanol (98%) and then warmed. Then the solution was filtered, allowed to cool and evaporated at room temp. to give square-shaped white shining transparent crystals. The crystals were collected and dried; m.p. 296–299 °C. The crystals are stable at room temp. and also in an open environment for several days.

The same procedure was followed for the other substrates.

General Procedure for the Synthesis of Bis- and Tetrakis-uracil 8 and 9: Distilled water (30 mL) was added to 6-amino-1,3-dimethyluracil (**1**; 155 mg, 1 mmol) in a 100 mL round-bottomed flask and the mixture was stirred at room temperature until all the 6-amino-1,3-dimethyluracil had dissolved. Then glutaraldehyde (25 mg, 0.25 mmol; entry **6b**, Table 2) was added dropwise to the 6-amino-1,3-dimethyluracil solution with constant stirring. After 3 h a yellowish white precipitate appeared and stirring was continued for a further 4 h so that all of the reactants were converted into product. The yellowish white precipitate was filtered and collected. On drying we obtained the product **8** in 89% yield. A small amount of the product was dissolved in distilled ethanol (98%) and warmed. Then the solution was filtered, allowed to cool and evaporated at room temp. to give square-shaped yellow shining transparent crystals. The crystals were collected and dried; m.p. 194–195 °C. The crystals are stable at room temp. and also in an open environment for several days.

The same procedure was followed for **6a**.

The following compounds were also prepared according to the general procedure.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(benzylidene)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3a): Colour: white shining transparent crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3453.37, 3383.38, 3197.94, 2993.08, 1695.96, 1654.14, 1587.29 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.27 (s, 3 H, NCH_3), 3.36 (s, 3 H, NCH_3), 3.44 (s, 6 H, NCH_3), 5.79 (s, 1 H, CH), 6.48 (br. s, 2 H, NH_2), 6.69 (br. s, 2 H, NH_2), 7.14–7.25 (m, 5 H, arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.4 (NCH_3), 28.8 (NCH_3), 29.1 (NCH_3), 29.4 (NCH_3), 35.7 (CH), 87.4 and 88.8 (C-5 and C′-5), 125.7 (C-4, arom.), 126.6 (C-3 and C-5, arom.), 127.9 (C-2 and C-6, arom.), 138.1 (C-1, arom.), 150.9 (C-6 and C′-6), 153.1 and 154.4 (C-2 and C′-2), 163.2 and 164.8 (C-4 and C′-4) ppm. MS: *m*/*z* = 398 $[M]^+$. $C_{19}H_{22}N_6O_4$ (398.42): calcd. C 57.28, H 5.57, N 21.07; found C 57.31, H 5.56, N 21.01.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(cinnamylidene)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3b): Colour: yellowish transparent crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3390.54, 3214.46, 3097.30, 2941.31, 1688.03, 1594.43, 1497.32 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.33 (s, 3 H, NCH_3), 3.35 (s, 3 H, NCH_3), 3.37 (s, 3 H, NCH_3), 3.39 (s, 3 H, NCH_3), 4.16 (d, *J* = 11.2 Hz, 1 H, CH=CH), 4.83 (d, *J* = 13.2 Hz, 1 H, CH=CH), 5.09 (s, 1 H, CH), 6.15 (br. s, 1 H, NH_2), 6.19 (br. s, 1 H, NH_2), 7.21–7.48 (m, 5 H, arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.0 (NCH_3), 28.1 (NCH_3), 29.1 (NCH_3), 29.2 (NCH_3), 34.2 (CH), 36.1 (CH=CH), 39.3 (CH=CH), 86.3 and 86.8 (C-5 and C′-5), 126.2 (C-4, arom.), 128.4 (C-3 and C-5, arom.), 128.9 (C-2 and C-6, arom.), 137.7 (C-1, arom.), 145.3 (C-6 and C′-6), 150.5 and 150.9 (C-2 and C′-2), 162.1 and 165.0 (C-4 and C′-4) ppm. MS: *m*/*z* = 424 $[M]^+$. $C_{21}H_{24}N_6O_4$ (424.46): calcd. C 59.42, H 5.70, N 19.80; found C 59.45, H 5.75, N 19.78.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(4-methoxybenzylidene)bis-[pyrimidine-2,4(1*H*,3*H*)-dione] (3c): Colour: white crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3358.89, 3195.07, 3083.58, 2952.68, 1688.34, 1593.50, 1503.18, 1448.50 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.29 (s, 3 H, NCH_3), 3.36 (s, 3 H, NCH_3), 3.45 (s, 6 H, NCH_3), 3.77 (s, 3 H, OCH_3), 5.74 (s, 1 H, CH), 6.49 (br. s, 2 H, NH_2), 6.70 (br. s, 2 H, NH_2), 6.80 (d, *J* = 8.72 Hz, 2 H, arom.), 7.04 (d, *J* = 8.24 Hz, 2 H, arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.2 (NCH_3), 29.3 (NCH_3), 29.3 (NCH_3), 29.4 (NCH_3), 35.1 (CH), 55.2 (OCH_3), 87.9 and 89.1 (C-5 and C′-5), 113.4 (C-1, arom.), 127.7 (C-3 and C-5, arom.), 129.9 (C-2 and C-6, arom.), 151.0 (C-6 and C′-6), 153.4 and 154.6 (C-2 and C′-2), 157.6 (C-4, arom.), 163.3 and 165.2 (C-4 and C′-4) ppm. MS: *m*/*z* = 393 $[M]^+$. $C_{20}H_{24}N_6O_5$ (428.45): calcd. C 56.07, H 5.65, N 19.62; found C 56.10, H 5.68, N 19.65.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(4-chlorobenzylidene)bis-[pyrimidine-2,4(1*H*,3*H*)-dione] (3d): Colour: white transparent crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3346.99, 3156.01, 3040.98, 2951.22, 1692.61, 1589.72, 1495.72 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.27 (s, 3 H, NCH_3), 3.38 (s, 3 H, NCH_3), 3.45 (s, 6 H, NCH_3), 5.74 (s, 1 H, CH), 6.48 (br. s, 2 H, NH_2), 6.68 (br. s, 2 H, NH_2), 7.08 (d, *J* = 21.08 Hz, 2 H, arom.), 7.26 (d, *J* = 21.08 Hz, 2 H, arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.2 (NCH_3), 29.3 (NCH_3), 29.4 (NCH_3), 29.7 (NCH_3), 35.6 (CH), 88.5 and 88.6 (C-5 and C′-5), 127.9 (C-4, arom.), 128.1 (C-3 and C-5, arom.), 131.4 (C-2 and C-6, arom.), 136.8 (C-1, arom.), 150.9 (C-6 and C′-6), 153.2 and 154.5 (C-2 and C′-2), 163.3 and 164.6 (C-4 and C′-4) ppm. MS: *m*/*z* = 432 $[M]^+$. $C_{19}H_{21}ClN_6O_4$ (432.87): calcd. C 52.72, H 4.89, N 19.42; found C 52.73, H 4.86, N 19.38.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(4-hydroxybenzylidene)bis-[pyrimidine-2,4(1*H*,3*H*)-dione] (3e): Colour: transparent crystalline solid. Solubility: soluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3393.35, 3118.08, 2956.74, 1664.76, 1601.04, 1498.95 cm^{-1}. ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 2.98 (s, 3 H, NCH_3), 3.01 (s, 3 H, NCH_3), 3.04 (s, 3 H, NCH_3), 3.47 (s, 3 H, NCH_3), 5.69 (s, 1 H, CH), 7.16 (br. s, 2 H, NH_2), 7.41 (br. s, 2 H, NH_2), 6.72 (d, *J* = 8.72 Hz, 2 H, arom.), 6. 96 (d, *J* = 8.24 Hz, 2 H, arom.), 8.58 (s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 29.52 (2 NCH_3), 29.55 (2 NCH_3), 34.89 (CH), 114.85 (C-4, arom.), 127.52 (C-3 and C-5, arom.), 127.55 (C-2 and C-6, arom.), 129.16 (C-1, arom.), 151.07 (C-6 and C′-6), 154.79 (C-2 and C′-2) ppm. MS: *m*/*z* = 414 $[M]^+$. $C_{19}H_{22}N_6O_5$ (414.42): calcd. C 55.07, H 5.35, N 20.28; found C 55.04, H 5.33, N 20.25.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(2-hydroxybenzylidene)bis-[pyrimidine-2,4(1*H*,3*H*)-dione] (3f): Colour: transparent crystalline

solid. Solubility: soluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3457.17, 3297.16, 3195.14, 2973.08, 1694.16, 1657.21, 1583.23 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.09 (s, 3 H, NCH_3), 3.32 (s, 3 H, NCH_3), 3.48 (s, 3 H, NCH_3), 3.57 (s, 3 H, NCH_3), 4.84 (s, 1 H, CH), 5.75 (s, 1 H, OH), 6.41 (br. s, 4 H, NH_2), 7.05–7.25 (m, 5 H, arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.6 (NCH_3), 28.1 (NCH_3), 29.2 (NCH_3), 29.3 (NCH_3), 30.1 (CH), 87.8 and 93.3 (C-5 and C′-5), 115.5 (C-4, arom.), 123.4 and 125.2 (C-3 and C-5, arom.), 127.8 and 128.3 (C-2 and C-6, arom.), 150.4 and 150.5 (C-6 and C′-6), 151.3 and 151.5 (C-2 and C′-2), 154.3 (C-1, arom.), 161.2 and 164.0 (C-4 and C′-4) ppm. MS: *m*/*z* = 414 $[M]^+$. $C_{19}H_{22}N_6O_5$ (414.42): calcd. C 55.07, H 5.35, N 20.28; found C 55.10, H 5.33, N 20.22.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(4-methylbenzylidene)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3g): Colour: transparent crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3358.52, 3152.81, 3053.07, 2929.70, 1690.23, 1591.04, 1498.48, 1447.64 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, CH_3), 3.28 (s, 3 H, NCH_3), 3.37 (s, 3 H, NCH_3), 3.45 (s, 6 H, NCH_3), 5.75 (s, 1 H, CH), 6.49 (br. s, 2 H, NH_2), 6.69 (br. s, 2 H, NH_2), 7.01–7.08 (m, 4 H, arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.8 (CH_3), 28.3 (NCH_3), 28.3 (NCH_3), 29.6 (NCH_3), 29.6 (NCH_3), 35.6 (CH), 86.8 and 88.4 (C-5 and C′-5), 126.4 (C-4, arom.), 128.4 (C-3 and C-5, arom.), 134.4 (C-2 and C-6, arom.), 135.5 (C-1, arom.), 150.9 (C-6 and C′-6), 153.5 and 154.5 (C-2 and C′-2), 163.2 and 164.4 (C-4 and C′-4) ppm. MS: *m*/*z* = 412 $[M]^+$. $C_{20}H_{24}N_6O_4$ (412.45): calcd. C 58.24, H 5.87, N 20.38; found C 58.21, H 5.84, N 20.31.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(4-nitrobenzylidene)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3h): Colour: brown transparent crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3394.02, 3189.69, 1676.16, 1615.01, 1505.16 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.30 (s, 3 H, NCH_3), 3.36 (s, 3 H, NCH_3), 3.39 (s, 3 H, NCH_3), 3.42 (s, 3 H, NCH_3), 5.84 (s, 1 H, CH), 6.53 (br. s, 2 H, NH_2), 6.68 (br. s, 2 H, NH_2), 8.08 (d, *J* = 8.72 Hz, 2 H, arom.), 8.40 (d, *J* = 8.72 Hz, 2 H, arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.6 (NCH_3), 29.1 (NCH_3), 29.4 (NCH_3), 29.7 (NCH_3), 35.9 (CH), 86.7 and 88.2 (C-5 and C′5), 122.1 (C-2 and C-6, arom.), 128.1 (C-3 and C-5, arom.), 141.2 (C-1, arom.), 148.6 (C-4, arom.), 150.9 (C-6 and C′-6), 153.4 and 154.9 (C-2 and C′-2), 163.3 and 165.1 (C-4 and C′-4) ppm. MS: *m*/*z* = 443 $[M]^+$. $C_{19}H_{21}N_7O_6$ (443.42): calcd. C 51.47, H 4.77, N 22.11; found C 51.43, H 4.78, N 22.13.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(3-nitrobenzylidene)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3i): Colour: brown transparent crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3396.10, 3196.67, 1681.06, 1607.07, 1503.67, 1451.58 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.36 (s, 3 H, NCH_3), 3.45 (s, 3 H, NCH_3), 3.50 (s, 3 H, NCH_3), 3.52 (s, 3 H, NCH_3), 5.81 (s, 1 H, CH), 6.51 (br. s, 2 H, NH_2), 6.69 (br. s, 2 H, NH_2), 7.23–7.24 (m, 1 H, arom.), 7.41–7.46 (m, 2 H, arom.), 7.95–8.08 (m, 1 H, arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.6 (NCH_3), 29.1 (NCH_3), 29.4 (NCH_3), 29.7 (NCH_3), 35.9 (CH), 86.7 and 88.2 (C-5 and C′-5), 121.2 (C-4, arom.), 122.1 (C-2, arom.), 128.9 (C-5, arom.), 133.3 (C-6, arom.), 141.2 (C-1, arom.), 148.6 (C-3, arom.), 151.0 (C-6 and C′-6), 153.4 and 154.9 (C-2 and C′-2), 163.4 and 165.1 (C-4 and C′-4) ppm. MS: *m*/*z* = 443 $[M]^+$. $C_{19}H_{21}N_7O_6$ (443.42): calcd. C 51.47, H 4.77, N 22.11; found C 51.42, H 4.74, N 22.11.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(2-furyl)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3j): Colour: transparent crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3351.56, 3190.48, 3074.22, 2951.20, 1698.55, 1592.24, 1497.74 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.29 (s, 3 H, NCH_3), 3.42 (s, 9 H, NCH_3), 5.65 (s, 1 H, CH), 5.98 (1 H, furan), 6.28 (1 H, furan), 6.51 (br., s, 2 H, NH_2), 6.63 (br., s, 2 H, NH_2), 7.24 (1 H, furan) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.6 (NCH_3), 28.6 (NCH_3), 29.3 (NCH_3), 29.3 (NCH_3), 31.8 (CH), 87.6 (C-5 and C′5), 105.9 (C-3, furan), 110.2 (C-4, furan), 141.0 (C-6 and C′-6), 150.9 (C-5, furan), 152.4 and 153.5 (C-2 and C′-2), 164.1 (C-4 and C′-4) ppm. MS: *m*/*z* = 388 $[M]^+$. $C_{17}H_{20}N_6O_5$ (388.38): calcd. C 52.57, H 5.19, N 21.64; found C 52.55, H 5.20, N 21.62.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(2-thienyl)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3k): Colour: transparent crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3361.56, 3327.33, 3057.73, 2982.55, 1681.87, 1632.89, 1573.09 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.31 (s, 1 H, NCH_3), 3.33 (s, 1 H, NCH_3), 3.42 (s, 1 H, NCH_3), 3.45 (s, 1 H, NCH_3), 5.93 (s, 1 H, CH), 6.54 (br. s, 2 H, NH_2), 6.68 (1 H, thiophene), 6.87 (1 H, thiophene), 6.91 (br. s, 2 H, NH_2), 7.13 (1 H, thiophene) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.32 (NCH_3), 29.38 (NCH_3), 29.41 (NCH_3), 29.44 (NCH_3), 33.3 (CH), 89.0 and 89.3 (C-5 and C′5), 123.4 and 124.0 (C-6 and C′-6), 126.3 (C-3, thiophene), 144.4 (C-4, thiophene), 150.9 (C-5, thiophene), 153.2 and 153.9 (C-2 and C′-2), 163.5 and 164.5 (C-4 and C′-4) ppm. MS: *m*/*z* = 404.13 $[M]^+$. $C_{17}H_{20}N_6O_4S$ (404.44): calcd. C 50.48, H 4.98, N 20.78; found C 50.46, H 4.99, N 20.77.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(methylene)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3l): Colour: white transparent crystalline solid. Solubility: insoluble in water, common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3386.70, 3155.75, 2927.21, 1682.97, 1619.94, 1504.20 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 3.19 (s, 3 H, NCH_3), 3.28 (s, 3 H, NCH_3), 3.37 (s, 6 H, NCH_3), 4.13 (s, 2 H, CH_2), 7.51 (br. s, 2 H, NH_2), 7.70 (br. s, 2 H, NH_2) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 19.53 (CH_2), 29.96 (2 NCH_3), 30.07 (2 NCH_3), 85.2 and 85.41 (C-5 and C′-5), 151.08 (C-6 and C′-6), 154.30 and 154.36 (C-2 and C′-2), 164.00 (C-4 and C′-4) ppm. MS: *m*/*z* = 322 $[M]^+$. $C_{13}H_{18}N_6O_4$ (322.32): calcd. C 48.44, H 5.63, N 26.07; found C 48.42, H 5.61, N 26.08.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(ethylidene)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3m): Colour: white transparent crystalline solid. Solubility: insoluble in water, soluble in common organic volatile solvents. IR (KBr): $\tilde{\nu}_{max}$ = 3410.87, 3172.15, 2997.44, 2949.39, 1680.66, 1621.14, 1493.60 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.66 (3 H, CH_3), 3.31 (s, 6 H, NCH_3), 3.46 (s, 6 H, NCH_3), 4.43–4.45 (m, 1 H, CH), 6.48 (br. s, 2 H, NH_2), 6.91 (br. s, 2 H, NH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.1 (CH_3), 26.3 (CH), 28.3 (NCH_3), 28.8 (NCH_3), 29.2 (NCH_3), 29.5 (NCH_3), 90.1 and 91.3 (C-5 and C′-5), 151.0 (C-6 and C′-6), 152.9 and 153.6 (C-2 and C′-2), 164.2 and 164.4 (C-4 and C′-4) ppm. MS: *m*/*z* = 336.15 $[M]^+$. $C_{14}H_{20}N_6O_4$ (336.35): calcd. C 49.99, H 5.99, N 24.99; found C 49.99, H 5.98, N 24.97.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(butylidene)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3n): Colour: white transparent crystalline solid. Solubility: insoluble in water, soluble in common organic volatile solvents. IR (KBr): $\tilde{\nu}_{max}$ = 3401.23, 3146.61, 2955.29, 1666.63, 1606.54, 1493.54 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.91–0.93

(m, 3 H, CH_3), 1.25–1.27 (m, 2 H, CH_2), 2.16–2.21 (m, 2 H, CH_2), 3.31 (s, 3 H, NCH_3), 3.35 (s, 3 H, NCH_3), 3.45 (s, 6 H, NCH_3), 4.20 (t, J = 8 Hz, 1 H, CH), 6.54 (br. s, 2 H, NH_2), 6.67 (br. s, 2 H, NH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7 (CH_3), 21.7 (CH), 27.8 (CH_2), 28.4 (NCH_3), 28.7 (NCH_3), 29.1 (NCH_3), 31.3 (NCH_3), 31.6 (CH_2), 88.6 and 89.6 (C-5 and C′-5), 150.6 and 150.7 (C-6 and C′-6), 152.5 and 153.6 (C-2 and C′-2), 163.7 and 164.3 (C-4 and C′-4) ppm. MS: m/z = 364.19 $[M]^+$. $C_{16}H_{24}N_6O_4$ (364.40): calcd. C 52.74, H 6.64, N 23.06; found C 52.72, H 6.66, N 23.08.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(pentylidene)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (3o): Colour: white transparent crystalline solid. Solubility: insoluble in water, soluble in common organic volatile solvents. IR (KBr): $\tilde{\nu}_{max}$ = 3396.53, 3106.74, 2952.08, 2859.75, 1661.83, 1606.21, 1490.77 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84–0.88 (m, 3 H, CH_3), 1.26–1.30 (m, 4 H, CH_2CH_2), 2.05–2.21 (m, 2 H, CH_2), 3.34 (s, 3 H, NCH_3), 3.36 (s, 3 H, NCH_3), 3.46 (s, 3 H, NCH_3), 3.47 (s, 3 H, NCH_3), 4.13–4.18 (m, 1 H, CH), 6.52 (br. s, 2 H, NH_2), 6.94 (br. s, 2 H, NH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.3 (CH_3), 21.8 (CH), 27.4 (CH_2), 27.9 (CH_2), 28.2 (NCH_3), 28.4 (NCH_3), 28.6 (NCH_3), 30.4 (NCH_3), 31.4 (CH_2), 88.2 and 89.2 (C-5 and C′-5), 150.1 and 150.2 (C-6 and C′-6), 151.9 and 153.0 (C-2 and C′-2), 163.2 and 163.8 (C-4 and C′-4) ppm. MS: m/z = 378.2 $[M]^+$. $C_{17}H_{26}N_6O_4$ (378.43): calcd. C 53.96, H 6.93, N 22.21; found C 53.97, H 6.93, N 22.20.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(glutarylidene)bis[pyrimidine-2,4(1*H*,3*H*)-dione] (8): Colour: yellow transparent crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3409.63, 3215.74, 2938.88, 1664.95, 1603.34, 1495.23, 1446.66 cm^{-1}. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 0.81–0.94 (m, 2 H, CH_2), 1.22–1.34 (m, 4 H, 2 CH_2), 3.09 (s, 3 H, NCH_3), 3.25 (s, 3 H, NCH_3), 3.34 (s, 18 H, NCH_3), 3.94 (s, 1 H, CH), 4.12 (s, 1 H, CH), 6.78 (br. s, 2 H, NH_2), 6.88 (br. s, 2 H, NH_2), 7.19 (br. s, 2 H, NH_2), 7.67 (br. s, 2 H, NH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + [D_6]DMSO): δ = 22.7 (CH), 23.5 (CH), 27.4 (CH_2), 27.7 (CH_2), 28.0 (NCH_3), 28.3 (NCH_3), 28.7 (NCH_3), 29.2 (NCH_3), 29.4 (NCH_3), 29.5 (NCH_3), 29.7 (NCH_3), 30.1 (NCH_3), 31.7 (CH_2), 85.9, 87.9, 89.3 and 89.4 (C-5, C-5, C′-5 and C′-5), 128.2, 128.6, 129.7 and 130.8 (C-6, C-6, C′-6 and C′-6), 150.8, 150.9, 153.0 and 154.2 (C-2, C-2, C′-2 and C′-2), 162.8, 163.4 and 164.0 (C-4, C-4, C′-4 and C′-4) ppm. MS: m/z = 684.31 $[M]^+$. $C_{29}H_{40}N_{12}O_8$ (684.71): calcd. C 50.87, H 5.89, N 24.55; found C 50.88, H 5.90, N 24.54.

6,6′-Diamino-1,1′,3,3′-tetramethyl-5,5′-(terephthaldibenzylidene)-bis[pyrimidine-2,4(1*H*,3*H*)-dione] (9): Colour: transparent crystalline solid. Solubility: insoluble in water, sparingly soluble in common organic volatile solvents, soluble in aprotic polar solvents like DMF, DMSO and DMAc. IR (KBr): $\tilde{\nu}_{max}$ = 3420.99, 3110.18, 2924.07, 1683.96, 1603.00, 1496.68 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.27 (s, 3 H, NCH_3), 3.39 (s, 3 H, NCH_3), 3.47 (s, 3 H, NCH_3), 3.50 (s, 3 H, NCH_3), 5.84 (s, 1 H, CH), 6.51 (br. s, 2 H, NH_2), 6.69 (br. s, 2 H, NH_2), 7.32 (d, J = 8 Hz, 2 H, arom.), 7.78 (d, J = 8 Hz, 2 H, arom.), 9.96 (s, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.5 (NCH_3), 29.0 (NCH_3), 29.4 (NCH_3), 29.7 (NCH_3), 36.3 (CH), 86.7 and 88.7 (C-5 and C′-5), 127.4 (C-4, arom.), 129.7 (C-3 and C-5, arom.), 134.3 (C-2 and C-6, arom.), 146.3 (C-1, arom.), 150.9 (C-6 and C′-6), 153.3 and 154.8 (C-2 and C′-2), 165.1 (C-4 and C′-4), 192.0 (CHO) ppm. MS: m/z = 426.17 $[M]^+$. $C_{20}H_{22}N_6O_5$ (426.43): calcd. C 56.33, H 5.20, N 19.17; found C 56.33, H 5.21, N 19.18.

CCDC-750667 (for **3d**), -775981 (for **3l**) and -775982 (for **3j**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of all compounds.

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