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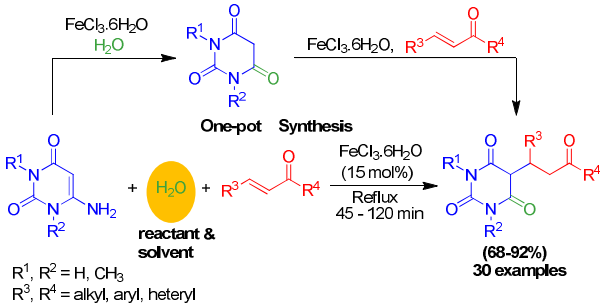
Graphical Abstract

Water as both reactant and solvent in a $FeCl_3.6H_2O$ catalyzed domino reaction towards 5-monoalkylbarbiturates is described.



Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

$FeCl_3.6H_2O$ catalyzed aqueous media domino synthesis of 5-monoalkylbarbiturates: Water as both reactant and solvent

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

A novel, simple and straightforward route to 5-monoalkylbarbiturates by $FeCl_3.6H_2O$ catalyzed domino reactions of 6-aminouracils, water and α,β-unsaturated ketones, where water plays a key dual role as both reactant and solvent, is described. Significantly, all the reactions efficiently furnished exclusively 5-monoalkylbarbiturates and not pyrido[2,3-*d*]pyrimidines as generally produced from the reactions of 6-aminouracils and α,β-unsaturated carbonyls.

Introduction

In recent years, the development of greener synthetic methods has been highly prioritized in view of the adverse implications of various chemical processes. Especially, taking into account the undesirable impacts of organic solvents, efforts to accomplish efficient organic synthesis in aqueous medium present a focal point of research in current synthetic chemistry. Because, water is not only the most abundant and non-toxic solvent, it also enables novel reactivity, accelerates reaction by the hydrophobic and 'on water' effects.[1] Meanwhile, multi-component reactions (MCRs)[2] and auto-tandem catalysis[3] have become powerful strategies towards convergent synthesis for the facts that the former allows flexible, convergent, pot, atom and step economic synthesis while the latter provides maximum catalyst utilization efficiency by catalyzing two or more mechanistically different organic transformations. However, the development of multi-component reactions in aqueous environments is a recent endeavour that has receieved relatively little attention and consequently requires greater emphasis.[1a,g,4]

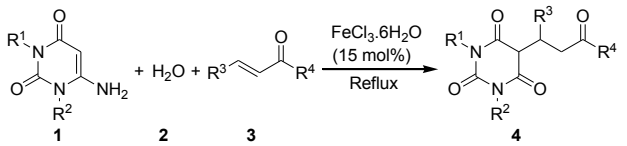
In these developments, iron catalysts have emerged as a center of renewed interest both in homogeneous and heterogeneous catalysis. Well known for their wide range of tolerance, iron catalysts are diversely applied in addition, substitution, cycloaddition and polymerization reactions to name a few.[5] In particular, $FeCl_3.6H_2O$ has received tremendous applications in organic syntheses whose applicability has been further advantaged by its cost effectiveness, ease of handling and environmental benignity.[5,6] Thus, iron catalyzed organic transformations are highly applicable approaches in organic syntheses.

5-Alkylbarbiturates are an intriguing and re-emerging privileged class of compounds in medicinal chemistry which have broad range of activities such as anticonvulsant,[7] sedative,[8] immunomodulating and antitumor properties;[9] whilst a number of them also have found wide applications in the manufacture of dyes,[10] non linear optical study[11] and in supramolecular chemistry.[12] Further synthetic interest on 5-alkylbarbiturates has been elevated with the development of highly potent antibacterial PNU-286607(-)-1[13] and inhibitors of matrix metalloproteinase (MMP)[14] and mutant SOD1-dependent protein aggregation.[15] Classically, 5-alkylbarbiturates can be synthesized by condensation of alkylated malonic esters and urea in the presence of sodium alkoxide.[16] However, the yields of this reaction are often modest due to the presence of side reactions such as hydrolysis of the malonate, decarbethoxylation, transesterification, and urea degradation. Moreover, the need for dry solvents and high temperature in addition to the requirement of inert atmosphere and metallic sodium limits the use of this classical method in the perspective of combinatorial purposes and diversity-oriented synthetic programs. Alternatively, 5-alkylation of unsubstituted barbituric acid could be a strategy towards 5-alkylbarbiturates.[17] But, in particular, direct construction of 5-monoalkylbarbiturates by alkylation of barbituric acid derivatives still remains a difficult and an inspiring task.

A common challenge en route to 5-monoalkylbarbiturates is the specific 5-monoalkylation of barbituric acid derivatives. For decades, there was no simple procedure for this strategy until, lately, Jursic and co-workers developed an effective reductive alkylation procedure in the presence of platinum and palladium catalysts.[18] More recently, Löfberg and group have described Ir(III) catalyzed reaction of barbituric acid and alcohols as an alternative route to 5-monoalkylbarbiturates.[19] Another method for 5-monoalkylbarbiturates *via* ring opening of spiro[2.5]barbiturates was also described by Singh and Paul.[20] Although these protocols are useful, the use of expensive catalysts and complex reaction conditions rather limits their applicability. The only multi-component strategy showing a prospect towards 5-monoalkylbarbiturates was developed recently by Volonterio and Zanda.[21] On the other hand, the highly viable route to 5-monoalkylbarbiturates by Michael addition of barbituric acid to α,β-unsaturated carbonyls has been highly

underrepresented since the first report given by Zalukaev and Trostyanetskaya[22] and the compounds were characterized only on the basis of IR spectral data. And, to the best of our knowledge on literature survey, there is only another report describing Michael addition of barbituric acid to α,β-unsaturated carbonyls.[23]

Therefore, in view of the need to design effective synthetic route for 5-monoalkylbarbiturates, and in conjunction with our continued pursuit on environment friendly synthetic developments,[24] we report herein the application of $FeCl_3.6H_2O$ catalyzed domino reactions of 6-aminouracils, water and α,β-unsaturated ketones as a straightforward route to 5-monoalkylbarbiturates, where water significantly serves as both reactant and solvent (Scheme 1). This tandem reaction involves an initial $FeCl_3.6H_2O$ and water mediated amine hydrolysis of the 6-aminouracil to barbituric acid followed by Michael type addition to α,β-unsaturated ketones. To the best of our knowledge, 6-aminouracils have not been explored for direct synthesis of 5-monoalkylbarbiturates. And at this point it can be noted that the general reactivity of 6-aminouracils with α,β-unsaturated carbonyls gives pyrido[2,3-*d*]pyrimidines,[25] whereas this new found reaction produced solely 5-monoalkylbarbiturates as the final products. Thus, a new reactivity role of 6-aminouracils as valuable substrates towards 5-monoalkylbarbiturates is also discovered.

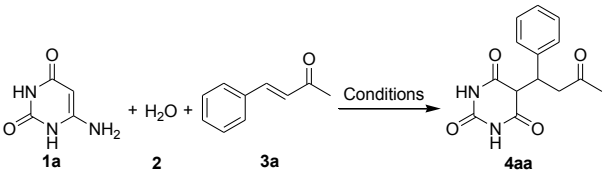


Scheme 1. Domino synthesis of 5-monoalkylbarbiturates.

Results and Discussion

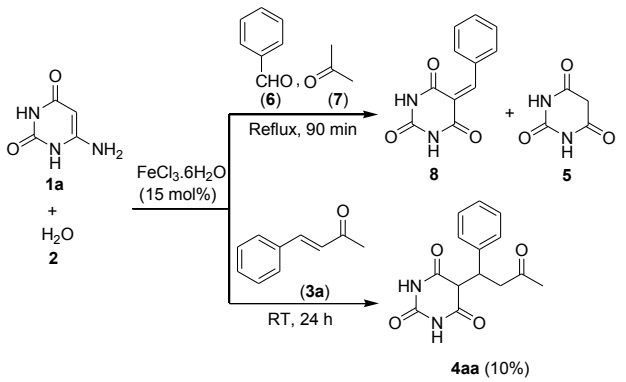
Initially we refluxed 6-aminouracil (**1a**, 1 mmol), water (**2**, 10 mL) and benzylideneacetone (**3a**, 1 mmol) in the presence of $FeCl_3.6H_2O$ (10 mol%) for sixty minutes (Table 1, entry 1). To our delight, the reaction gave 5-(3-oxo-1-phenylbutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (**4aa**) in 80% yield. Much to our satisfaction, the reaction was then set for optimization as shown in Table 1. Fortunately, optimization of the $FeCl_3.6H_2O$ catalyst was arrived at 15 mol% which afforded the highest yield of **4aa** in 92% yield (Table 1, entry 2). Further, to get the best effect of the reaction, some potential Lewis acid catalysts and a number of solvents were screened (Table 1, entries 5-12). Interestingly, the reaction was found to work only with water and $FeCl_3.6H_2O$. Even solvents such as EtOH and DMSO or reactions performed under solventless condition failed to furnish the desired product (Table 1, entries 8-13). In an attempt to succeed the reaction at room temperature (≈ 24 °C), the process was not satisfactory and gave **4aa** only in 10% yield, even after stirring for 24 hours (Table 1, entry 14) (Scheme 2). In another process, simultaneous mixing of 6-aminouracil (**1a**), benzaldehyde (**6**) and acetone (**7**) in the presence of $FeCl_3.6H_2O$ and water did not yield the desired 5-monoalkylbarbiturate, and only barbituric acid (**5**) and benzylidenebarbituric acid (**8**) were isolated (Scheme 2). We observed that, although barbituric acid was formed in the process, the rate of formation of **8** greatly exceeded the rate of generation of benzylideneacetone (**3a**). Nevertheless, these results indicated that $FeCl_3.6H_2O$ and water were specifically essential to obtain 5-monoalkylbarbiturates through this protocol.

Table 1 Optimization of the reaction under different conditions.[a]



Entry	Catalyst (mol%)	Solvent[b]	Temp (°C)	Time (min)	Yield (%)[c]
1	$FeCl_3.6H_2O$ (10)	H_2O	Reflux	60	80
2	$FeCl_3.6H_2O$ (15)	H_2O	Reflux	45	92
3	$FeCl_3.6H_2O$ (20)	H_2O	Reflux	45	92
4	$FeCl_3.6H_2O$ (25)	H_2O	Reflux	45	92
5	$CuCl_2.2H_2O$ (15)	H_2O	Reflux	60	0
6	$NiCl_2.6H_2O$ (15)	H_2O	Reflux	60	0
7	$CoCl_2.6H_2O$ (15)	H_2O	Reflux	60	0
8	$FeCl_3.6H_2O$ (15)	EtOH	Reflux	60	0
9	$FeCl_3.6H_2O$ (15)	CH_3CN	Reflux	60	0
10	$FeCl_3.6H_2O$ (15)	$CHCl_3$	Reflux	60	0
11	$FeCl_3.6H_2O$ (15)	Toluene	Reflux	60	0
12	$FeCl_3.6H_2O$ (15)	DMSO	Reflux	60	0
13	$FeCl_3.6H_2O$ (15)	—	heat	50	0
14	$FeCl_3.6H_2O$ (15)	H_2O	RT[d]	1440	10

[a] Reaction scale: **1a** (1 mmol), **2** (10 mL) and **3a** (1 mmol). [b] 10 mL. [c] Isolated yield. [d] RT ≈ 24 °C.

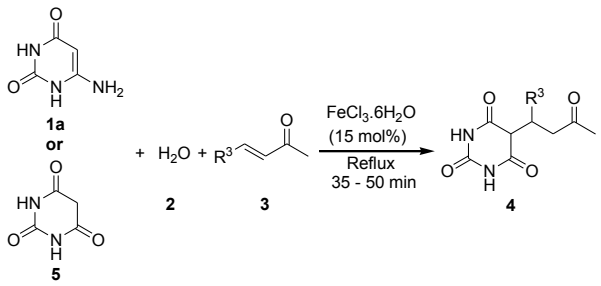


Scheme 2. Reaction study towards 5-monoalkylbarbiturates.

Next, a comparative study on the substrate prospect of 6-aminouracil (**1a**) versus barbituric acid (**5**) towards 5-monoalkylbarbiturates was investigated by executing some parallel reactions with selected arylideneacetones (**3**) under the same reaction conditions (Table 2). Interestingly, both the reactions showed almost equal competency for 5-monoalkylbarbiturates yielding similar yields without significant differences in reaction times. Thus, this observation described that 6-aminouracil could be an equally competent and alternative substrate towards 5-monalkylbarbiturates.

Subsequently, under the optimized conditions, we then explored the scope of the reaction. As shown in Table 3, a wide array of 5-monoalkylbarbiturates was prepared from the reaction of 6-aminouracil (**1a**), water (**2**) and various α,β-unsaturated ketones (**3**). It was found that, the presence of electron withdrawing or donating groups in the *ortho*, *meta*- or *para*-positions of the benzene ring of various arylideneacetones (**3a-f**) or chalcones (**3g-k**) had no significant impact on the reaction and

Table 2 Comparative substrate prospect of 6-aminouracil (**1a**) versus barbituric acid (**5**) towards 5-monoalkylbarbiturates (**4**).[a]

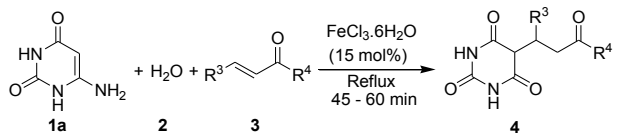


Entry	R^3	Product	Time (min)		Yield (%)[b]	
			1a	**5**	**1a**	**5**
1	C_6H_5	**4aa**	45	40	92	92
2	3-$OCH_3C_6H_4$	**4ad**	50	45	85	85
3	4-ClC_6H_4	**4ae**	45	41	92	93
4	4-$NO_2C_6H_4$	**4af**	45	40	89	89
5	2-thiophenyl	**4am**	50	45	81	82

[a] All reactions were carried out using **1** mmol each of **1a**/**5**, **3** and 10 mL of **2**. [b] Isolated yield.

they were conveniently transformed to their corresponding 5-monoalkylbarbiturates (Table 3, entries 1-11; 76-92%). To our delight, heterylideneacetones (**3l** and **3m**) and heterylideneacetophenones (**3n** and **3o**) also participated well in the reaction and provided their corresponding products in good to high yields (Table 3, entries 12-15; 76-81%). Other substituted alken-2-ones (**3p-r**) also responded moderately to the reaction and their resultant 5-monoalkylbarbiturates were successfully obtained although the reactions were slightly sluggish (Table 3, entries 16-18; 71-74%).

Table 3 $FeCl_3.6H_2O$ catalyzed aqueous media domino synthesis of 5-monoalkylbarbiturates.[a]

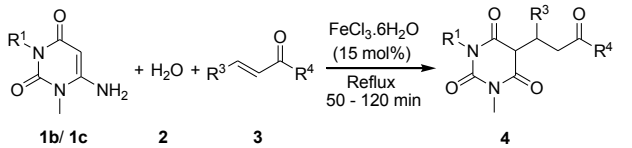


Entry	**3**			Time (min)	Product	Yield (%)[b]
	R^3	R^4				
1	C_6H_5	CH_3	**3a**	45	**4aa**	92
2	2-ClC_6H_4	CH_3	**3b**	45	**4ab**	88
3	3-ClC_6H_4	CH_3	**3c**	50	**4ac**	85
4	3-$OCH_3C_6H_4$	CH_3	**3d**	50	**4ad**	85
5	4-ClC_6H_4	CH_3	**3e**	45	**4ae**	92
6	4-$NO_2C_6H_4$	CH_3	**3f**	45	**4af**	89
7	C_6H_5	C_6H_5	**3g**	45	**4ag**	87
8	2-ClC_6H_4	C_6H_5	**3h**	45	**4ah**	90
9	3-$OCH_3C_6H_4$	C_6H_5	**3i**	50	**4ai**	83
10	4-ClC_6H_4	C_6H_5	**3j**	45	**4aj**	90
11	3,5-$(OCH_3)_2C_6H_3$	C_6H_5	**3k**	50	**4ak**	76
12	2-furyl	CH_3	**3l**	45	**4al**	78
13	2-thiophenyl	CH_3	**3m**	50	**4am**	81
14	2-furyl	C_6H_5	**3n**	60	**4an**[c]	76
15	2-thiophenyl	C_6H_5	**3o**	50	**4ao**	80
16	Ethyl	CH_3	**3p**	50	**4ap**[c]	71
17	Butyl	CH_3	**3q**	50	**4aq**[c]	73
18	Butyl	C_6H_5	**3r**	50	**4ar**[c]	74

[a] Reaction scale: **1a** (1 mmol), **2** (10 mL) and **3** (1 mmol). [b] Isolated yield. [c] Purified by column chromatography.

The scope of the reaction was also extended towards 1-methyl-6-aminouracil (**1b**) and 1,3-dimethyl-6-aminouracil (**1c**) under the same conditions and the results are shown in Table 4. Gratifyingly, all reactions of **1b** or **1c** with various α,β-unsaturated ketones (**3**) and water (**2**) proceeded successfully without much complexity and furnished their 5-monoalkylbarbiturates (68-91%). However, in the case of 1,3-dimethyl-6-aminouracil (**1c**), conversions were found to be relatively slower than when 6-aminouracil (**1a**) or 1-methyl-6-aminouracil (**1b**) was employed. This may be due to the presence of electron releasing methyl group/s which impeded hydrolysis of the amine to form barbituric acid. And, unlike those reactions with 6-aminouracil (**1a**), most of the reactions involving 1-methyl-6-aminouracil (**1b**) and 1,3-dimethyl-6-aminouracil (**1c**) were slightly sluggish. Thus, a reactivity aptitude: 6-aminouracil (**1a**) > 1-methyl-6-aminouracil (**1b**) > 1,3-dimethyl-6-aminouracil (**1c**) was observed in this study. Furthermore, the 5-monoalkylbarbiturates (**4bi-4bl**) obtained from reactions involving 1-methyl-6-aminouracil (**1b**) showed their existence as diastereoisomers as revealed by ^1H and ^{13}C NMR spectra. Meanwhile, to further supplement the structural characterization, a single crystal X-ray diffraction study was probed upon **4bb** whose X-ray structure is depicted in Figure 1.

Table 4 Substituted 6-aminouracils towards 5-monoalkylbarbiturates.[a]



Entry	**1b**/**1c**	**3**			Time (min)	Product	Yield (%)[b]
	R^1	R^3	R^4				
1	CH_3	C_6H_5	CH_3	**3a**	90	**4ba**[c]	83
2	CH_3	2-ClC_6H_4	CH_3	**3b**	120	**4bb**	87
3	CH_3	3-ClC_6H_4	CH_3	**3c**	120	**4bc**[c]	78
4	CH_3	3-$OCH_3C_6H_4$	CH_3	**3d**	120	**4bd**[c]	85
5	CH_3	3-$NO_2C_6H_4$	CH_3	**3s**	120	**4be**[c]	84
6	CH_3	4-BrC_6H_4	CH_3	**3t**	90	**4bf**[c]	87
7	CH_3	4-OHC_6H_4	CH_3	**3u**	120	**4bg**	68
8	CH_3	4-$NO_2C_6H_4$	CH_3	**3f**	105	**4bh**[c]	84
9	H	2-ClC_6H_4	CH_3	**3b**	60	**4bi**[c,d]	88
10	H	2-FC_6H_4	C_6H_5	**3v**	60	**4bj**[c,d]	85
11	H	3-ClC_6H_4	CH_3	**3c**	60	**4bk**[c,d]	88
12	H	4-BrC_6H_4	CH_3	**3w**	50	**4bl**[c,d]	91

[a] All reactions were carried out using **1** (1 mmol), **2** (10 mL) and **3** (1 mmol). [b] Isolated yield. [c] Purified by column chromatography. [d] Combined diastereomeric yield.

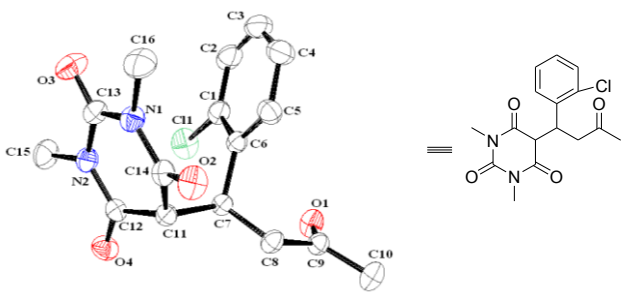
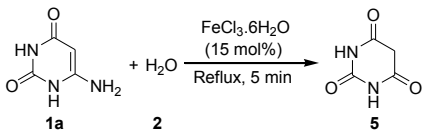


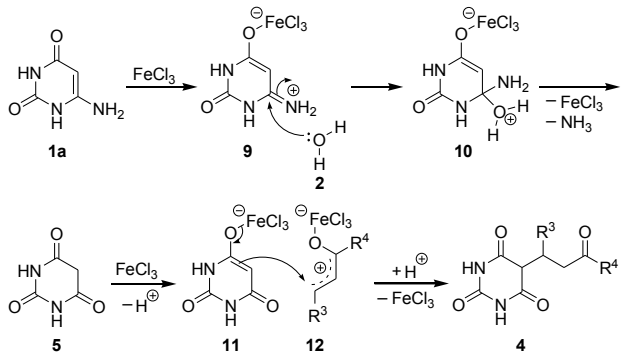
Figure 1. X-Ray crystal structure of **4bb** (CCDC 959094).[26]

To probe the reaction mechanism, 6-aminouracil (**1a**) was refluxed alone in water in the presence of $FeCl_3.6H_2O$. The reaction completed swiftly within minutes and yielded barbituric

acid (Scheme 3). Furthermore, when barbituric acid and benzylideneacetone were refluxed without any catalyst for 45 minutes, the product **4aa** was resulted but only in 20% yield, which was indicative that $FeCl_3.6H_2O$ also has catalytic role in the addition step. Thus, based upon literature reports[20,6b,c,e,27] and our results, a possible mechanism is proposed in Scheme 4. The coordination of 6-aminouracil with $FeCl_3$ facilitated amine hydrolysis by water and generated barbituric acid (**5**) *via* **9** and **10**. The *in situ* formed barbituric acid further underwent complexation with $FeCl_3$ to give intermediate **11** while, apparently, α,β-unsaturated ketone (**3**) also gets activated with $FeCl_3$ to **12**. Subsequent addition of the activated complex **11** to **12** followed by protonation finally led to the formation of 5-monoalkylbarbiturate **4**.



Scheme 3. Barbituric acid from 6-aminouracil.



Scheme 4. Proposed reaction mechanism.

Conclusions

In summary we have developed, for the first time, a simple, general and environment friendly protocol for synthesis of 5-monoalkybarbiturates directly through $FeCl_3.6H_2O$ catalyzed domino reaction of 6-aminouracils, water and α,β-unsaturated ketones. Significantly, this study has also demonstrated the key role of water as both reactant and solvent in achieving the synthesis, which further exemplifies for wider applications of aqueous media organic synthesis. Moreover, while barbituric acid has served as common substrate for 5-monalkylbarbiturates thus far, our study has now demonstrated that 6-aminouracils can be also alternative and equally competent reactants towards obtaining the same compounds. Therefore, provided by the versatility of the catalyst, wide substrate scope and mild reaction conditions, the protocol is highly facile which remarkably expands the procedural scopes for the synthesis of a huge library of important 5-monoalkylbarbiturates, suitable as well for combinatorial synthetic study.

Experimental Section

All reagents were purchased from commercial suppliers and were used without further purification. The α,β-unsaturated ketones were prepared according to literature procedure.[28] IR spectra were recorded on a SHIMADZU infrared spectrometer as KBr pellets with absorption in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 or MeOH-d_4 on 300 MHz Bruker NMR spectrometer at ≈ 25 °C and resonances (δ) are given in ppm relative to tetramethylsilane. Data are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, ‡ = double signal), coupling constants (Hz) and integration. LCMS were obtained on Waters ZQ 4000 and equipped with ESI source. Melting points were determined using Veego VMP-D and not corrected. The X-ray crystal structure determination was done on a Bruker, SMART APEX II CCD system. Elemental analysis was done on Perkin Elmer Series II Analyzer 2400. Column chromatography was performed on silica gel (200–300 mesh) using ethyl acetate:hexane (6:4) as the eluent. Thin Layer Chromatography (TLC) was performed using Merck pre-coated silica gel or Silica gel G and the components were visualized under a UV or an iodine chamber.

General procedure for the synthesis of 5-monoalkylbarbiturates (4aa-4ar and 4ba-4bl) from 6-aminouracils, water and α,β-unsaturated ketones

A mixture of 6-aminouracil (**1a**/**1b**/**1c**, 1 mmol), α,β-unsaturated ketone (**3**, 1 mmol) in water (**2**, 10 mL) was refluxed in the presence of $FeCl_3.6H_2O$ (15 mol%) as catalyst for appropriate time (Tables 3 & 4). On completion of the reaction, as indicated by TLC, the crude reaction mass was cooled and was extracted with ethyl acetate (10 mL x 4). After drying with anhydrous Na_2SO_4 and evaporation under reduced pressure, the crude product was purified suitably either by recrystallization from DCM:ethanol (6:4) solvent mixture or ethanol or column chromatography on silica gel using ethyl acetate:hexane (6:4) as the eluent to afford 5-monoalkylbarbiturates.

General procedure for the synthesis of 5-monoalkylbarbiturates from barbituric acid and α,β-unsaturated ketones (Table 2)

A mixture of barbituric acid (**5**, 1 mmol) and α,β-unsaturated ketone (**3**, 1 mmol) was refluxed in the presence of $FeCl_3.6H_2O$ (15 mol%) in water (10 mL) for appropriate time. On completion of the reactions, as indicated by TLC, the reaction mass was cooled and extracted with ethyl acetate (10 mL x 4) and dried over anhydrous Na_2SO_4. After concentrated under reduced pressure, the obtained crude solids were further purified by recrystallization from DCM:ethanol (6:4) solvent mixture to afford the 5-monoalkylbarbiturates.

Procedure for the synthesis of barbituric acid from 6-aminouracil

6-Aminouracil (**1a**, 1 mmol) was refluxed in water (**2**, 10 mL) in the presence of $FeCl_3.6H_2O$ (15 mol%) for 5 minutes. On completion of the reaction, as indicated by TLC, the reaction mass was cooled and extracted with ethyl acetate (10 mL x 4). The organic extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The obtained solid product was purified by recrystallization from ethanol:water (1:9). The physical and chemical properties are identical to that reported in the literature.[29]

5-(3-oxo-1-phenylbutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4aa).[30]

Yield 0.252 g (92%). White solid, mp 152-154 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.08 (s, 3H), 3.05-3.14 (m, 1H), 3.31-3.40 (m, 1H), 3.65 (d, 1H, J = 3.9 Hz), 3.88-3.95 (m, 1H), 7.04-7.13 (m, 2H), 7.18-7.27 (m, 3H), 11.03 (s, 1H), 11.09 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d6): δ_C (ppm) 30.7, 41.8, 45.6, 52.2, 127.8, 128.1, 128.8, 139.7, 150.9, 170.2, 170.7, 207.4; IR (KBr) (ν_{max}/cm^{-1}) 3392, 2923, 1729, 1704, 1681, 1664; MS (ESI): *m/z* Calcd for $C_{14}H_{14}N_2O_4$: 274.10; Found 275.10 $[M+H]^+$, 297.00 $[M+Na]^+$; Anal. Calcd for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.14; N, 10.21. Found: C, 61.44; H, 5.26; N, 10.08.

5-(1-(2-chlorophenyl)-3-oxobutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ab)

Yield, 0.271 g (88%). White solid, mp 102-104 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.10 (s, 3H), 2.90-2.94 (m, 1H), 3.24-3.33 (m, 1H), 3.84 (d, 1H, J = 3.3 Hz), 4.68 (m, 1H), 7.08-7.39 (m, 4H), 9.46 (s, 1H), 9.58 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 30.0, 36.6, 44.5, 50.8, 127.4, 128.7, 128.9, 129.9, 133.6, 137.9, 150.5, 168.8, 169.0, 208.8; IR (KBr) (ν_{max}/cm^{-1}) 3410, 3011, 2924, 1719, 1701, 1687, 1659, 1551; MS (ESI): *m/z* Calcd for $C_{14}H_{13}ClN_2O_4$: 308.06; Found 308.92 $[M+H]^+$, 331.04 $[M+Na]^+$; Anal. Calcd for $C_{14}H_{13}ClN_2O_4$: C, 54.47; H, 4.24; N, 9.07. Found: C, 54.69; H, 4.09; N, 9.19.

5-(1-(3-chlorophenyl)-3-oxobutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ac)

Yield, 0.262 g (85%). White solid, mp 103-105 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.18 (s, 3H), 2.90-2.98 (m, 1H), 3.51-3.61 (m, 1H), 3.89 (d, 1H, J = 3.3 Hz), 4.09-4.16 (m, 1H), 7.09-7.27 (m, 4H), 9.10 (s, 1H), 9.16 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 30.3, 40.8, 45.1, 51.3, 126.3, 128.1, 130.2, 134.6, 141.2, 149.8, 168.8, 208.2; IR (KBr) (ν_{max}/cm^{-1}) 3232, 3109, 2924, 1728, 1701, 1693, 1647, 1554; MS (ESI): *m/z* Calcd for $C_{14}H_{13}ClN_2O_4$: 308.06; Found 308.92 $[M+H]^+$, 331.01 $[M+Na]^+$; Anal. Calcd for $C_{14}H_{13}ClN_2O_4$: C, 54.47; H, 4.24; N, 9.07. Found: C, 54.71; H, 4.06; N, 9.25.

5-(1-(3-methoxyphenyl)-3-oxobutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ad)

Yield, 0.258 g (85%). White solid, mp 141-143 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.15 (s, 3H), 2.90-2.97 (m, 1H), 3.45-3.55 (m, 1H), 3.68 (s, 3H), 3.81 (d, 1H, J = 3.9 Hz), 4.03-4.12 (m, 1H), 6.69-6.78 (m, 3H), 7.10-7.15 (m, 1H), 9.39 (s, 1H), 9.47 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 30.2, 41.8, 45.2, 51.4, 55.1, 113.1, 113.8, 120.1, 129.9, 140.1, 150.2, 159.5, 169.4, 169.6, 208.3; IR (KBr) (ν_{max}/cm^{-1}) 3437, 3082, 2924, 1723, 1708, 1684, 1668, 1546; MS (ESI): *m/z* Calcd for $C_{15}H_{16}N_2O_5$: 304.11; Found 304.79 $[M + H]^+$, 323.76 $[M+H_2O]^+$; Anal. Calcd for $C_{15}H_{16}N_2O_5$: C, 59.21; H, 5.30; N, 9.21. Found: C, 59.35; H, 5.45; N, 9.05.

5-(1-(4-chlorophenyl)-3-oxobutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ae)

Yield, 0.284 g (92%). White solid, mp 247-249 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.15 (s, 3H), 2.91-2.97 (m, 1H), 3.48-3.57 (m, 1H), 3.86 (d, 1H, J = 3.0 Hz), 4.10-4.12 (m, 1H), 7.09 (d, 2H, J = 8.4 Hz), 7.18 (d, 2H, J = 8.4 Hz), 9.67 (s, 1H), 9.71 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 30.3, 40.7, 45.2, 51.3, 129.0, 129.4, 133.6, 137.4, 150.4, 169.3, 169.5, 208.4; IR (KBr) (ν_{max}/cm^{-1}) 3347, 3011, 2924, 1721, 1703, 1681, 1661, 1557; MS (ESI): *m/z* Calcd for $C_{14}H_{13}ClN_2O_4$: 308.06; Found 309.10 $[M+H]^+$, 331.01 $[M+Na]^+$; Anal. Calcd for $C_{14}H_{13}ClN_2O_4$: C, 54.47; H, 4.24; N, 9.07. Found: C, 54.70; H, 4.07; N, 9.21.

5-(1-(4-nitrophenyl)-3-oxobutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4af)

Yield, 0.284 g (89%). White solid mp 214-216 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.02 (s, 3H), 3.03-3.12 (m, 1H), 3.73-3.77 (m, 1H), 3.84 (d, 1H, J = 3.6 Hz), 4.08-4.11 (m, 1H), 7.37-7.48 (m, 2H), 8.09-8.20 (m, 2H), 11.24 (s, 1H), 11.30 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 24.4, 42.4, 49.4, 70.6, 117.1, 123.5, 124.3, 139.3, 143.5, 164.4, 166.0, 200.4; IR (KBr) (ν_{max}/cm^{-1}) 3437, 3078, 2924, 1710, 1703, 1682, 1658, 1558; MS (ESI): *m/z* Calcd for $C_{14}H_{13}N_3O_6$: 319.08; Found 319.92 $[M+H]^+$, 342.01 $[M+Na]^+$; Anal. Calcd for $C_{14}H_{13}N_3O_6$: C, 52.67; H, 4.10; N, 13.16. Found: C, 52.86; H, 3.95; N, 13.39.

5-(1-(4-nitrophenyl)-3-oxobutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4af)

Yield, 0.284 g (89%). White solid, mp 214-216 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.02 (s, 3H), 3.03-3.12 (m, 1H), 3.73-3.77 (m, 1H), 3.84 (d, 1H, J = 3.6 Hz), 4.08-4.11 (m, 1H), 7.37-7.48 (m, 2H), 8.09-8.20 (m, 2H), 11.24 (s, 1H), 11.30 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 24.4, 42.4, 49.4, 70.6, 117.1, 123.5, 124.3, 139.3, 143.5, 164.4, 166.0, 200.4; IR (KBr) (ν_{max}/cm^{-1}) 3437, 3078, 2924, 1710, 1703, 1682, 1658, 1558; MS (ESI): *m/z* Calcd for $C_{14}H_{13}N_3O_6$: 319.08; Found 319.92 $[M+H]^+$, 342.01 $[M+Na]^+$; Anal. Calcd for $C_{14}H_{13}N_3O_6$: C, 52.67; H, 4.10; N, 13.16. Found: C, 52.83; H, 3.95; N, 13.29.

5-(3-oxo-1,3-diphenylpropyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ag)[23]

Yield, 0.292 g (87%). White solid, mp 176-178 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 3.58-3.66 (m, 1H), 3.79 (d, 1H, J = 3.6 Hz), 4.00-4.09 (m, 1H), 4.13-4.19 (m, 1H), 7.23 (d, 2H, J = 9.0 Hz), 7.28-7.31 (m, 3H), 7.53 (t, 2H, J = 7.3 Hz), 7.65 (t, 1H, J = 6.9 Hz), 7.98 (d, 2H, J = 7.5 Hz), 11.06 (s, 1H), 11.11 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 45.8, 46.8, 56.9, 132.6, 133.0, 133.1, 133.6, 134.0, 138.6, 141.8, 144.7, 155.7, 175.1, 175.5, 203.5; IR (KBr) (ν_{max}/cm^{-1}) 3424, 3017, 2923, 1721, 1705, 1682, 1662, 1561; MS (ESI): *m/z* Calcd for $C_{19}H_{16}N_2O_4$: 336.11; Found 337.01 $[M+H]^+$, 359.01 $[M+Na]^+$; Anal. Calcd for $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.79; N, 8.33. Found: C, 67.71; H, 4.67; N, 8.49.

5-(1-(2-chlorophenyl)-3-oxo-3-phenylpropyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ah)[23]

Yield, 0.333 g (90%). White solid, mp 196-198 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 3.55-3.64 (m, 1H), 3.73-3.82 (m, 1H), 3.88 (d, 1H, J = 3.6 Hz), 4.65-4.71 (m, 1H), 7.21-7.29 (m, 2H), 7.40 (d, 2H, J = 7.2 Hz), 7.48-7.53 (m, 2H), 7.63 (t, 1H, J = 7.2 Hz), 7.93 (d, 2H, J = 7.2 Hz), 11.10 (s, 1H), 11.13 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C

(ppm) 30.3, 41.2, 45.1, 120.2, 121.3, 122.0, 122.8, 123.5, 127.1, 127.6, 130.4, 132.7, 144.8, 145.9, 161.9, 192.9; IR (KBr) (ν_{max}/cm^{-1}) 3411, 3071, 2923, 1720, 1709, 1688, 1664, 1552; MS (ESI): *m/z* Calcd for $C_{19}H_{15}ClN_2O_4$: 370.07; Found 371.00 $[M+H]^+$, 393.10 $[M+Na]^+$; Anal. Calcd for $C_{19}H_{15}ClN_2O_4$: C, 61.55; H, 4.08; N, 7.56. Found: C, 61.64; H, 3.93; N, 7.67.

5-(1-(3-methoxyphenyl)-3-oxo-3-phenylpropyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ai)

Yield, 0.304 g (83%). White solid, mp 167-169 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 3.44-3.52 (m, 1H), 3.71 (s, 3H), 3.97 (d, 1H, *J* = 3.6 Hz), 4.09-4.18 (m, 1H), 4.34-4.37 (m, 1H), 6.75- 6.84 (m, 3H), 7.14-7.20 (m, 1H), 7.37-7.57 (m, 3H), 7.94-7.99 (m, 2H), 8.88 (s, 1H), 8.94 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 40.5, 42.2, 51.6, 55.2, 113.1, 114.0, 120.2, 128.1, 128.6, 130.0, 133.4, 136.5, 140.5, 149.5, 159.6, 168.9, 169.0, 198.7; IR (KBr) (ν_{max}/cm^{-1}) 3391, 3019, 2924, 1719, 1702, 1682, 1660, 1559; MS (ESI): *m/z* Calcd for $C_{20}H_{18}N_2O_5$: 366.12; Found 367.10 $[M+H]^+$, 389.00 $[M+Na]^+$; Anal. Calcd for $C_{20}H_{18}N_2O_5$: C, 65.57; H, 4.95; N, 7.65. Found: C, 65.69; H, 5.12; N, 7.53.

5-(1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4aj)

Yield, 0.333 g (90%). White solid, mp 175-177 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 3.47-3.55 (m, 1H), 4.01 (d, 1H, *J* = 3.6 Hz), 4.10-4.19 (m, 1H), 4.39-4.45 (m, 1H), 7.23-7.30 (m, 4H), 7.45-7.50 (m, 2H), 7.57-7.62 (m, 1H), 7.97 (d, 2H, *J* = 8.1 Hz), 8.21 (s, 1H), 8.25 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 40.5, 41.2, 51.6, 128.1, 128.7, 129.2, 129.4, 133.6, 134.0, 137.7, 148.4, 152.4, 153.7, 168.1, 203.6; IR (KBr) (ν_{max}/cm^{-1}) 3380, 3067, 2924, 1719, 1705, 1687, 1661, 1552; MS (ESI): *m/z* Calcd for $C_{19}H_{15}ClN_2O_4$: 370.07; found 370.93 $[M+H]^+$, 393.00 $[M+Na]^+$; Anal. Calcd for $C_{19}H_{15}ClN_2O_4$: C, 61.55; H, 4.08; N, 7.56. Found: C, 61.69; H, 3.95; N, 7.68.

5-(1-(3,5-dimethoxyphenyl)-3-oxo-3-phenylpropyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ak)

Yield, 0.301 g (76%). White solid, mp 206-208 °C (from EtOH). ^{1}H NMR (300 MHz, Methanol-d_4): δ_H (ppm) 3.56-3.69 (m, 1H), 3.74 (s, 6H), 3.82 (m, 1H), 4.05-4.12 (m, 1H), 4.23-4.26 (m, 1H), 6.38 (s, 1H), 6.71 (s, 2H), 7.51-7.54 (m, 2H), 7.60-7.63 (m, 1H), 8.03-8.05 (m, 2H); ^{13}C NMR (75 MHz, Methanol-d_4): δ_C (ppm) 34.2, 36.9, 48.0, 92.9, 99.3, 121.2, 122.1, 126.7, 130.8, 134.5, 154.4, 161.5, 206.5; IR (KBr) (ν_{max}/cm^{-1}) 3384, 3066, 2924, 1714, 1701, 1686, 1656, 1542; MS (ESI): *m/z* Calcd for $C_{21}H_{20}N_2O_6$: 396.13; Found 397.21 $[M+H]^+$, 419.14 $[M+Na]^+$; Anal. Calcd for $C_{21}H_{20}N_2O_6$: C, 63.63; H, 5.09; N, 7.07. Found: C, 63.77; H, 5.26; N, 6.92.

5-(1-(furan-2-yl)-3-oxobutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4al)[31]

Yield, 0.206 g (78%). Yellow solid, mp 186-188 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.12 (s, 3H), 3.13-3.25 (m, 2H), 3.71 (m, 1H), 4.01-4.06 (m, 1H), 6.03 (m, 1H), 6.30 (m, 1H), 7.46 (m, 1H), 11.09 (s, 1H), 11.20 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 24.1, 28.4, 37.9, 44.0, 100.3, 104.5, 136.1, 144.7, 147.6, 163.3, 163.8, 200.6; IR (KBr) (ν_{max}/cm^{-1}) 3205, 3001, 2916, 1720, 1705, 1690, 1655, 1522; MS (ESI): *m/z* Calcd for $C_{12}H_{12}N_2O_5$: 264.07; Found 264.90 $[M+H]^+$, 286.90 $[M+Na]^+$; Anal. Calcd for $C_{12}H_{12}N_2O_5$: C, 54.55; H, 4.58; N, 10.60. Found: C, 54.44 H, 4.70; N, 10.75.

5-(3-oxo-1-(thiophen-2-yl)butyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4am)

Yield, 0.227 g (81%). Yellow solid, mp 77-79 °C (from EtOH). ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.11 (s, 3H), 3.15-3.24 (m, 1H), 3.32-3.35 (m, 1H), 3.77 (d, 1H, *J* = 3.0 Hz), 4.24-4.30 (m, 1H), 6.76-6.77 (m, 1H), 6.90-6.93 (m, 1H), 7.35-7.37 (m, 1H), 11.18 (s, 1H), 11.22 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 29.0, 34.9, 45.5, 50.8, 123.4, 124.1, 125.6, 140.9, 149.4, 168.3, 168.8, 205.4; IR (KBr) (ν_{max}/cm^{-1}) 3310, 3012, 2919, 1716, 1702, 1677, 1658, 1551; MS (ESI): *m/z* Calcd for $C_{12}H_{12}N_2O_4S$: 280.05; Found 281.00 $[M+H]^+$, 303.00 $[M+Na]^+$; Anal. Calcd for $C_{12}H_{12}N_2O_4S$: C, 51.42; H, 4.32; N, 9.99. Found: C, 51.31; H, 4.47; N, 9.91.

5-(1-(furan-2-yl)-3-oxo-3-phenylpropyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4an)[31]

Yield, 0.247 g (76%). Brown gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 3.50-3.55 (m, 1H), 3.97-4.13 (m, 2H). 4.51 (m, 1H), 6.09-6.18 (m, 2H), 6.93-7.51 (m, 4H), 7.94-7.96 (m, 2H), 9.39 (s, 1H), 9.53 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 35.6, 39.1, 49.8, 107.1, 110.5, 128.1, 128.6, 133.4, 136.3, 142.2, 150.3, 152.5, 168.7, 169.1, 198.1; IR (KBr) (ν_{max}/cm^{-1}) 3410, 3078, 2921, 1721, 1709, 1688, 1654, 1556; MS (ESI): *m/z* Calcd for $C_{17}H_{14}N_2O_5$: 326.09; Found 326.91 $[M+H]^+$, 348.90 $[M+Na]^+$; Anal. Calcd for $C_{17}H_{14}N_2O_5$: C, 62.57; H, 4.32; N, 8.59. Found: C, 62.71; H, 4.42; N, 8.44.

5-(3-oxo-3-phenyl-1-(thiophen-2-yl)propyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ao)

Yield, 0.273 g (80%). Brown solid, mp > 300 °C (from EtOH); ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 3.68-3.76 (m, 1H), 3.91 (m, 1H), 3.97-4.05 (m, 1H), 4.50 (m, 1H), 6.84-6.91 (m, 2H), 7.33-7.35 (m, 1H), 7.53-7.64 (m, 3H), 7.95-7.97 (m, 2H), 11.16 (s, 1H), 11.22 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 35.9, 41.8, 51.4, 124.3, 125.0, 126.3, 127.4, 128.3, 132.9, 136.0, 141.8, 150.0, 169.1, 169.4, 197.4; IR (KBr) (ν_{max}/cm^{-1}) 3380, 3078, 2919, 1718, 1702, 1689, 1657, 1547; MS (ESI): *m/z* Calcd for $C_{17}H_{14}N_2O_4S$: 342.07; Found 343.11 $[M+H]^+$, 365.09 $[M+Na]^+$; Anal. Calcd for $C_{17}H_{14}N_2O_4S$: C, 59.64; H, 4.12; N, 8.18. Found: C, 59.77; H, 3.98; N, 8.30.

5-(5-oxohexan-3-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ap)

Yield, 0.160 g (71%). Red gummy solid (afer column chromatography). ^{1}H NMR (300 MHz, Methanol-d_4): δ_H (ppm) 0.83-0.96 (m, 3H), 1.55-1.60 (m, 2H), 2.16 (s, 3H), 2.51-2.59 (m, 1H), 2.71-2.77 (m, 2H), 3.59 (m, 1H), 11.03 (s, 2H); ^{13}C NMR (75 MHz, Methanol-d_4): δ_C (ppm) 13.5, 22.7, 26.5, 30.8, 37.8, 84.1, 145.3, 161.7, 203.5; IR (KBr) (ν_{max}/cm^{-1}) 3391, 2924, 1719, 1702, 1682, 1655; MS (ESI): *m/z* Calcd for $C_{10}H_{14}N_2O_4$: 226.10; Found 226.23 $[M]^+$, 249.01 $[M+Na]^+$; Anal. Calcd for $C_{10}H_{14}N_2O_4$: C, 53.09; H, 6.24; N, 12.38. Found: C, 52.97; H, 6.11; N, 12.51.

5-(2-oxooctan-4-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4aq)

Yield, 0.185 g (73%). Red gummy solid (after column chromatography). ^{1}H NMR (300 MHz, Methanol-d_4): δ_H (ppm) 0.91 (m, 3H), 1.31-1.59 (m, 6H), 2.16 (s, 3H), 2.68-2.72 (m, 1H), 2.86-2.91 (m, 2H), 3.59-3.65 (m, 1H), 10.94 (s, 2H); ^{13}C NMR (75 MHz, Methanol-d_4): δ_C (ppm) 6.8, 22.6, 22.7, 24.7, 29.0, 32.1, 38.1, 84.5, 150.2, 161.7, 164.2, 203.4; IR (KBr) (ν_{max}/cm^{-1}) 3127, 2923, 1721, 1708, 1682, 1670; MS (ESI): *m/z* Calcd for $C_{12}H_{18}N_2O_4$: 254.13; Found 255.10 $[M+H]^+$, 277.01 $[M+Na]^+$; Anal. Calcd for $C_{12}H_{18}N_2O_4$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.81; H, 7.00; N, 10.89.

5-(1-oxo-1-phenylheptan-3-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ar)

Yield, 0.234 g (74%). Red gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 0.90 (m, 3H), 1.13-1.15 (m, 2H), 1.26-1.46 (m, 4H), 3.18-3.25 (m, 1H), 3.39 (m, 1H), 3.42-3.54 (m, 1H), 3.75 (m, 1H), 7.46-7.49 (m, 2H), 7.58 (m, 1H), 7.94 (d, 2H, J = 7.5 Hz), 8.25 (s, 1H), 8.29 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 7.5, 23.3, 25.6, 33.1, 42.1, 85.0, 121.7, 122.3, 127.0, 143.1, 162.3, 162.5, 162.8, 193.7; IR (KBr) (ν_{max}/cm^{-1}) 3210, 3052, 2923, 1722, 1709, 1687, 1661, 1558; MS (ESI): *m/z* Calcd for $C_{17}H_{20}N_2O_4$: 316.14; Found 316.96 $[M+H]^+$, 339.10 $[M+Na]^+$; Anal. Calcd for $C_{17}H_{20}N_2O_4$: C, 64.54; H, 6.37; N, 8.86. Found: C, 64.68; H, 6.27; N, 9.05.

1,3-dimethyl-5-(3-oxo-1-phenylbutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ba)[30]

Yield, 0.251 g (83%). Yellow gummmy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.18 (s, 3H), 2.89-2.91 (m, 1H), 2.96 (s, 3H), 3.10 (s, 3H), 3.42-3.51 (m, 1H), 3.84 (d, 1H, J = 4.2 Hz), 4.02-4.09 (m, 1H), 6.94-6.97 (m, 2H), 7.19-7.22 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 27.8, 27.9, 30.3, 44.0, 44.7, 52.5, 127.1, 128.3, 128.4, 137.5, 150.8, 167.5, 168.2, 206.4; IR (KBr) (ν_{max}/cm^{-1}) 3072, 2924, 1710, 1701, 1688, 1658, 1553; MS (ESI): *m/z* Calcd for $C_{16}H_{18}N_2O_4$: 302.13; Found 303.12 $[M+H]^+$, 325.00 $[M+Na]^+$; Anal. Calcd for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.72; H, 5.86; N, 9.38.

5-(1-(2-chlorophenyl)-3-oxobutyl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4bb)

Yield, 0.292 g (87%). White solid, mp 93-95 °C (from EtOH/DCM). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.13 (s, 3H), 2.89-2.97 (m, 1H), 3.10 (s, 6H), 3.29-3.38 (m, 1H), 3.75 (d, 1H, J = 4.5 Hz), 4.59-4.65 (m, 1H), 7.11-7.29 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 28.2, 28.4, 30.0, 38.7, 45.5, 52.6, 126.9, 128.2, 128.7, 129.7, 133.8, 136.5, 151.8, 167.4, 167.5, 206.1; IR (KBr) (ν_{max}/cm^{-1}) 3090, 2919, 1718, 1706, 1688, 1659, 1554; MS (ESI): *m/z* Calcd for $C_{16}H_{17}ClN_2O_4$: 336.09; Found 337.01 $[M+H]^+$, 359.00 $[M+Na]^+$. Anal. Calcd for $C_{16}H_{17}ClN_2O_4$: C, 57.06; H, 5.09; N, 8.32. Found: C, 57. 18; H, 4.95; N, 8.47.

5-(1-(3-chlorophenyl)-3-oxobutyl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4bc)

Yiedl, 0.263 g (78%). Yellow gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.20 (s, 3H), 2.90-3.00 (m, 1H), 3.03 (s, 3H), 3.12 (s, 3H), 3.42-3.51 (m, 1H), 3.84 (d, 1H, J = 3.9 Hz), 4.04-4.10 (m, 1H), 6.89 (d, 1H, J = 6.9 Hz), 7.01, (s, 1H), 7.14-7.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 28.0, 28.1, 30.3, 43.2, 44.7, 52.3, 125.5, 127.4, 128.4, 129.9, 134.6, 140.0, 150.7, 167.4, 167.9, 206.1; IR (KBr) (ν_{max}/cm^{-1}) 3055, 2924, 1727, 1710, 1687, 1660, 1552; MS (ESI): *m/z* Calcd for $C_{16}H_{17}ClN_2O_4$: 336.09; Found 337.01$[M+H]^+$, 359.01 $[M+Na]^+$. Anal. Calcd for $C_{16}H_{17}ClN_2O_4$: C, 57.06; H, 5.09: N, 8.32. Found: C, 56.93; H, 4.96; N, 8.45.

5-(1-(3-methoxyphenyl)-3-oxobutyl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4bd)

Yield, 0.282 g (85%). Yellow gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.17 (s, 3H), 2.87-2.95 (m, 1H), 2.96 (s, 3H), 3.06 (s, 3H), 3.08-3.47 (m, 1H), 3.69 (s, 3H), 3.81 (d, 1H, J = 3.9 Hz), 4.01-4.02 (m, 1H), 6.50-6.53 (m, 2H), 6.72-6.74 (m, 1H), 7.09-7.14 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 27.8, 27.9, 30.2, 43.8, 44.7, 52.3, 55.0, 113.0, 113.2, 119.2, 129.5, 139.1, 150.8, 159.5, 167.5, 168.1, 206.3; IR (KBr) (ν_{max}/cm^{-1}) 3067, 2923, 1719, 1707, 1680, 1651, 1561; MS (ESI): *m/z* Calcd for $C_{17}H_{20}N_2O_5$: 332.14; Found 333.15 $[M+H]^+$; Anal. Calcd for $C_{17}H_{20}N_2O_5$: C, 61.44; H, 6.07; N, 8.43. Found: C, 61.59; H, 6.19; N, 8.27.

1,3-dimethyl-5-(1-(3-nitrophenyl)-3-oxobutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4be)

Yield, 0.291 g (84%). Yellow gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.18 (s, 3H), 2.83-2.91 (m, 1H), 3.02 (s, 3H), 3.11 (s, 3H), 3.48-3.57 (m, 1H), 3.89 (d, 1H, J = 3.9 Hz), 4.20-4.27 (m, 1H), 7.43-7.51 (m, 2H), 7.92 (s, 1H), 8.05-8.07 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 28.1, 28.2, 30.1, 42.2, 44.8, 52.0, 122.0, 122.9, 129.6, 134.1, 140.8, 148.1, 150.6, 167.1, 167.4, 206.0; IR (KBr) (ν_{max}/cm^{-1}) 3086, 2924, 1711, 1701, 1688, 1657, 1531; MS (ESI): *m/z* Calcd for $C_{16}H_{17}N_3O_6$: 347.11; Found 348.34 $[M+H]^+$, 370.15 $[M+Na]^+$; Anal. Calcd for $C_{16}H_{17}N_3O_6$: C, 55.33; H, 4.93; N, 12.10. Found: C, 55.17; H, 5.06; N, 11.98.

5-(1-(4-bromophenyl)-3-oxobutyl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4bf)

Yield, 0.331 g (87%). Yellow gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.18 (s, 3H), 2.88-2.96 (m, 1H), 3.04 (s, 3H), 3.12 (s, 3H), 3.42-3.52 (m, 1H), 3.85 (d, 1H, J = 3.9 Hz), 4.05-4.11 (m, 1H), 6.89 (d, 2H, J = 8.7 Hz), 7.34 (d, 2H, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 28.1, 28.2, 30.4, 42.8, 45.1, 52.2, 122.2, 129.1, 131.8, 137.3, 150.8, 167.5, 167.9, 206.3; IR (KBr) (ν_{max}/cm^{-1}) 3029, 2924, 1718, 1710, 1693, 1674, 1516; MS (ESI): *m/z* Calcd for $C_{16}H_{17}BrN_2O_4$: 380.04; Found 381.12 $[M+H]^+$, 403.00 $[M+Na]^+$; Anal. Calcd for $C_{16}H_{17}BrN_2O_4$: C, 50.41; H, 4.49; N, 7.35. Found: C, 50.34; H, 4.61; N, 7.21.

5-(1-(4-hydroxyphenyl)-3-oxobutyl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4bg)

Yield, 0.216 g (68%). White solid, mp 173-175 °C (from EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.04 (s, 3H), 2.88-2.93 (m, 1H), 3.02 (s, 3H), 3.10 (s, 3H), 3.38-3.47 (m, 1H), 3.83 (d, 1H, J = 3.9 Hz), 4.02-4.03 (m, 1H), 6.45 (s, 1H), 6.67 (d, 2H, J = 8.4 Hz), 6.81 (d, 2H, J = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 28.0, 28.1, 30.5, 43.6, 45.2, 52.9, 115.6, 128.4, 128.9, 151.0, 156.0, 167.7, 168.6, 207.3; IR (KBr) (ν_{max}/cm^{-1}) 3433, 3012, 2927, 1710, 1700, 1678, 1671, 1554; MS (ESI): *m/z* Calcd

for $C_{16}H_{18}N_2O_5$: 318.12; Found 318.97 $[M+H]^+$, 341.00 $[M+H]^+$; Anal. Calcd for $C_{16}H_{18}N_2O_5$: C, 60.37; H, 5.70; N, 8.80. Found: C, 60.21; H, 5.85; N, 8.97.

1,3-dimethyl-5-(1-(4-nitrophenyl)-3-oxobutyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4bh)

Yield, 0.292 g (84%). Yellow gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.19 (s, 3H), 2.83-3.00 (m, 1H), 3.08 (s, 3H), 3.15 (s, 3H), 3.50-3.59 (m, 1H), 3.91 (d, 1H, J = 3.3 Hz), 4.27-4.29 (m, 1H), 7.27 (d, 2H, J = 8.4 Hz), 8.08 (d, 2H, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 28.2, 28.3, 30.2, 42.1, 44.9, 51.9, 123.7, 128.7, 146.4, 147.3, 150.6, 167.1, 167.3, 206.1; IR (KBr) (ν_{max}/cm^{-1}) 3124, 2924, 1710, 1701, 1689, 1652, 1523; MS (ESI): *m/z* Calcd for $C_{16}H_{17}N_3O_6$: 347.11; Found 348.24 $[M+H]^+$, 370.01 $[M+Na]^+$; Anal. Calcd for $C_{16}H_{17}N_3O_6$: C, 55.33; H, 4.93; N, 12.10. Found: C, 55.19; H, 4.81; N, 12.27.

5-(1-(2-chlorophenyl)-3-oxobutyl)-1-methylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4bi)

Yield, 0.284 g (88%). Yellow gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.12/2.13 (s‡, 3H), 2.88-2.96 (m, 1H), 3.15/3.21 (s‡, 3H), 3.27-3.31/3.33-3.38 (m‡, 1H), 3.77/3.85 (d‡, 1H, J = 4.2 Hz), 4.67-4.68 (m, 1H), 7.14-7.32 (m, 4H), 9.38/9.39 (s‡, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 27.5/27.6, 29.9, 37.5/37.6, 38.9, 44.9, 126.8/126.9, 127.0/127.1, 128.3/128.4, 129.8/129.9, 133.6/133.7, 137.0/137.3, 150.4, 167.7, 168.1/168.2, 207.0/207.1; IR (KBr) (ν_{max}/cm^{-1}) 3356, 3095, 2924, 1712, 1701, 1681, 1654, 1585; MS (ESI): *m/z* Calcd for $C_{15}H_{15}ClN_2O_4$: 322.07; Found 323.09 $[M+H]^+$, 345.01 $[M+Na]^+$; Anal. Calcd for $C_{15}H_{15}ClN_2O_4$: C, 55.82; H, 4.68; N, 8.68. Found: C, 56.07; H, 4.50; N, 8.56.

5-(1-(2-fluorophenyl)-3-oxo-3-phenylpropyl)-1-methylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4bj)

Yield, 0.328 g (85%). Yellow gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 3.04/3.13 (s‡, 3H), 3.47-3.49 /3.53-3.55 (m‡, 1H), 3.95-3.97 (m, 1H), 3.99-4.03/4.05-4.09 (m‡, 1H), 4.61-4.62 (m, 1H), 6.98-7.08 (m, 2H), 7.20-7.26 (m, 2H), 7.41-7.55 (m, 3H), 7.94-7.97 (m, 2H), 9.04/9.14 (s‡, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 27.5, 37.3/37.5, 39.8/39.9, 51.9/52.0, 115.6/115.7, 115.9/116.0, 124.5, 125.6/125.8, 128.0, 128.6, 129.5/129.6, 129.7/129.8, 133.4, 136.4, 150.3/150.4, 167.8/168.0, 168.3/168.6, 197.7/197.8; IR (KBr) (ν_{max}/cm^{-1}) 3321, 3092, 2923, 1721, 1709, 1684, 1657, 1552; MS (ESI): *m/z* Calcd for $C_{20}H_{17}FN_2O_4$: 368.12; Found 369.13 $[M+H]^+$; Anal. Calcd for $C_{20}H_{17}FN_2O_4$: C, 65.21; H, 4.65; N, 7.60. Found: C, 65.35; H, 4.51; N, 7.76.

5-(1-(3-chlorophenyl)-3-oxobutyl)-1-methylpyrimidine-2,4,6(1*H*,3*H*,5*H*)trione (4bk)

Yield, 0.284 g (88%). Yellow gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.20/2.21 (s‡, 3H), 2.92-3.00 (m, 1H), 3.04/3.13 (s‡, 3H), 3.50-3.59 (m, 1H), 3.88-3.92 (m‡, 1H), 4.08-4.16 (m, 1H), 7.01-7.29 (m, 4H), 9.16/9.24 (s‡, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 27.3/27.4, 30.2, 42.0/42.1, 44.7/44.9, 51.7/51.8, 125.8/126.0, 127.7/127.8, 128.24, 130.0, 134.5, 140.5, 150.0/150.1, 167.7/168.0, 168.3/168.6, 206.9; IR (KBr) (ν_{max}/cm^{-1}) 3341, 3088, 2924, 1719, 1710, 1689, 1660, 1552; MS (ESI): *m/z* Calcd for $C_{15}H_{15}ClN_2O_4$: 322.07; Found 323.15 $[M+H]^+$, 345.10 $[M+Na]^+$; Anal. Calcd for $C_{15}H_{15}ClN_2O_4$: 55.82; H, 4.68; N, 8.68. Found: C, 55.95; H, 4.51; N, 8.74

5-(1-(4-bromophenyl)-3-oxobutyl)-1-methylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4bl)

Yield, 0.334 g (91%). Yellow gummy solid (after column chromatography). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 2.17/2.18 (s‡, 3H), 2.88-2.96 (m, 1H), 3.03/3.12 (s‡, 3H), 3.47-3.52/3.53-3.58 (m‡, 1H), 3.87-3.91 (m‡, 1H), 4.07-4.14 (m, 1H), 6.96-7.02 (m‡, 2H), 7.36-7.43 (m‡, 2H), 9.11/9.15 (s‡, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C (ppm) 28.6, 30.4, 41.8/41.9, 45.0/45.1, 51.7/ 51.8, 122.1, 129.5, 132.0, 137.5, 150.1/150.2, 167.9/168.2, 168.4/168.7, 207.2; IR (KBr) (ν_{max}/cm^{-1}): 3323, 3097, 2924, 1719, 1702, 1689, 1658, 1551; MS (ESI): *m/z* Calcd for $C_{15}H_{15}BrN_2O_4$: 366.02; Found 367.01 $[M+H]^+$, 389.00 $[M+Na]^+$; Anal. Calcd for $C_{15}H_{15}BrN_2O_4$: C, 49.06; H, 4.12; N, 7.63. Found: C, 48.91; H, 3.98; N, 7.78.

Acknowledgements

H. M. and S. J. K. thank the DST, Govt. of India for the financial assistance under the DST-INSPIRE Faculty scheme. The authors also acknowledge SAIF-GU, SAIF-NEHU and IIT-Guwahati for sample analyses.

Notes and references

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