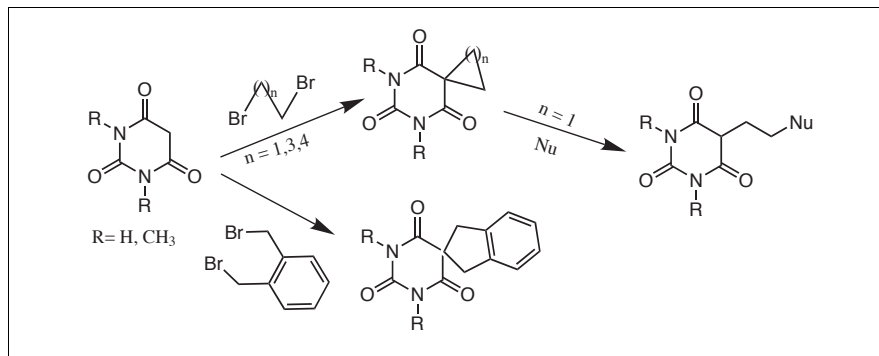


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The single step reactions of N,N'- substituted/-unsubstituted barbituric acids with various alkyl dihalides under phase transfer catalytic conditions using DMF-K₂CO₃ (base), TBAHSO₄ (catalyst) provide spirobarbituric acids in moderate to high yields. Irrespective of the existence of C₅-monoalkylated compounds in the enolic form (confirmed by the isolation of some of its analogues), the second alkylation predominantly takes place at C₅. The underlying mechanism for the reaction is discussed. The 5,7-dimethyl-5,7-diaza-spiro[2.5]octane-4,6,8-trione undergoes ring opening with NaCN, PhSH, HS(CH₂)₂OH and Br₂ to provide 5-monoalkylated barbiturates which are otherwise difficult to prepare by the usual alkylation of barbituric acids.

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Barbituric acid owes its significance due to similar type of H-bonding as thymine in the biological systems and its presence in many pharmaceutically important molecules [1]. The spirobarbiturates, exhibiting the characteristic feature of conformation locking [2] (common in spiro compounds), are biologically important molecules used as anticonvulsant [3], narcotic and analgesic agents [4], as dihydroorotate dehydrogenase inhibitors [5] and in the construction of modified oligonucleotides [6].

The widespread applications of barbituric acid based spiro compounds in biology and their use as synthons for C₅-monosubstituted barbituric acids prompted us to develop a simple synthetic methodology for spirocycloalkylbarbituric acids. A few reports for the synthesis of spirocycloalkylbarbituric acids are available which involve the condensation of 1,1-cycloalkanedicarboxylate diester and urea in the presence of a base [3,5,7]. However, these reactions mainly suffer from low yields, especially in the case of spirocyclopropanobarbiturate (10%). The available routes for procuring 5-monoalkylated barbituric acids are by the reaction of monoalkyl malonic esters with urea [8], reaction of barbituric acid with aldehydes [9,10] / α,β -unsaturated ketones [11] or by using 5-acylbarbituric acids as synthons [12].

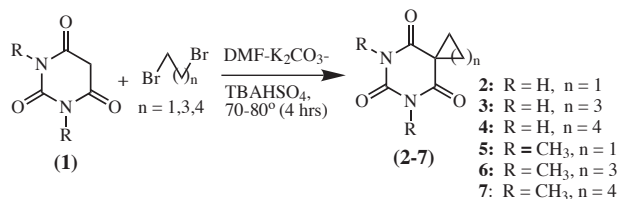
We report herein the synthesis of spiro[2.5], spiro[4.5], spiro[5.5]barbituric acids in a single step by the reaction of N,N'-unsubstituted/-substituted barbituric acids with respective dihalo-alkanes/ arenes under phase transfer catalytic conditions. The reaction mechanism for dialkylation at C₅ has been explained on the basis of tautomeric forms of first alkylated intermediate. Further, C₅-monoalkylated barbituric acids are synthesized by the ring opening of spiro[2.5]barbituric acid with NaCN, PhSH, HS(CH₂)₂OH and Br₂.

Barbituric acid **1** (R=H) on reaction with 1.2 equivalents of dibromoethane in DMF using K₂CO₃ as base (2 equiv) and TBAHSO₄ (Tetrabutylammonium hydrogen sulphate) as catalyst (0.01 equiv) gave a solid compound (63%, 50% of the consumed barbituric acid) while 20% barbituric acid was recovered unchanged. The solid compound [M⁺+1 m/z 155, m.p. 320° (dec), lit. [7] m.p. 320-25°] has been assigned structure **2**. Earlier this compound [7] has been synthesized only in 10% yield where 1,1-cyclopropanedicarboxylic diester was condensed with urea in the presence of a base. In these reported reactions base promoted cyclopropane ring opening before condensation with urea might be the cause of low yield for spiro compound. Similarly, **1** (R=H) on reaction with 1,4-dibromobutane and 1,5-dibromopentane

gave compounds **3** (55%, lit. [7] 53%) and **4** (55%, lit.[4] 33 %) respectively (scheme-1).

Under similar reaction conditions *N,N'*-dimethylbarbituric acid (**1**, R=CH₃) on reaction with 1.2 equivalents of dibromoethane gave a white solid (87%, 70% of consumed barbituric acid), m.p. 265-67° and 20% starting barbituric acid is recovered unchanged. In ¹H NMR spectrum, it shows a 4H singlet at δ 2.23 and a 6H singlet at δ 3.22. In ¹³C/DEPT-135 NMR spectrum, it shows a -ve signal at δ 27.86 (CH₂), a +ve signal at δ 28.96 (CH₃), and quaternary carbon signals at δ 48.76, 150.8 and 171.71 due to C₅, C₂ and C₄/C₆ respectively. ¹H and ¹³C NMR spectra corroborate a symmetrical structure **5** for this compound (scheme 1).

Scheme I

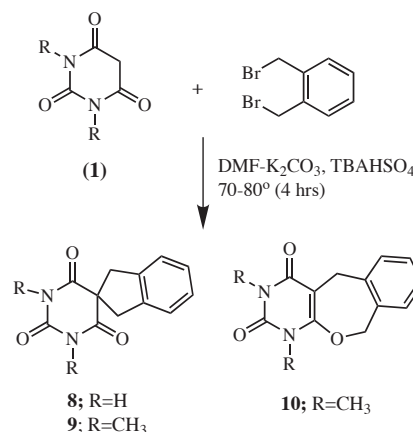


1 (R=CH₃) on reaction with 1,4-dibromobutane and 1,5-dibromopentane gave spiro[4.5] and spiro[5.5]-barbituric acids **6** and **7**. Therefore, the dialkylation with alkyl dihalides at C-5 of barbituric acids provided a straightforward method for synthesizing spirocycloalkyl-barbituric acids in higher yields than the reported ones.

Keeping in mind the role of π - π interactions in the various enzyme-inhibitor complexes, the above synthetic methodology was extended to the reactions of barbituric acids **1** with 1,2-bis[bromomethyl]benzene. **1** (R=H) on reaction with 1,2-bis[bromomethyl]benzene in DMF using K_2CO_3 as base and $TBAHSO_4$ as catalyst provided compound **8** (60%, $M^+ + 1$ m/z 231). The reaction of **1** (R=CH₃) with 1,2-bis[bromomethyl]benzene gave two compounds. The first one, 60%, $M^+ + 1$ m/z 259 in 1H NMR spectrum shows a 6H singlet at δ 3.33, a 4H singlet at δ 3.61 and 4H multiplet at δ 7.20-7.26 has been assigned structure **9**. The second compound (20%, $M^+ + 1$ m/z 258) in 1H NMR spectrum shows two 3H singlets at δ 3.35 and 3.39, two 2H singlets at δ 4.07 and 5.49 along with 4H multiplet at δ 7.33-7.38, has been assigned structure **10** (scheme II).

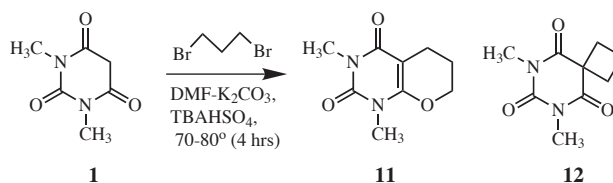
The reactivity behaviour of **1** towards 1,3-dibromopropane is quite different where instead of the formation of spiro compounds, pyranopyrimidines are formed. *N,N'*-Dimethylbarbituric acid on reaction with 1,3-dibromopropane gave a solid product (60%), m.p. 122° which in its ¹H NMR spectrum shows a 2H quintet at δ 1.98, 2H triplet at δ 2.48, 3H singlet at δ 3.34, 3H singlet at δ 3.35

Scheme II



and a 2H triplet at δ 4.35. The downfield triplet at δ 4.35 seems to be due to a methylene group linked to oxygen. In ^{13}C NMR spectrum, the C-5 quaternary carbon has been shifted downfield in comparison to C-5 of compound **5**. From this spectral data along with $^{13}\text{C}/\text{DEPT}$ -135 NMR spectra, the structure **11** has been assigned to this compound and the expected compound **12** ($\text{R}=\text{CH}_3$) was not formed (Scheme III). The non-formation of compound **12** may be attributed to the preferred formation of six membered ring in compound **11** over the four membered ring in **12**.

Scheme III

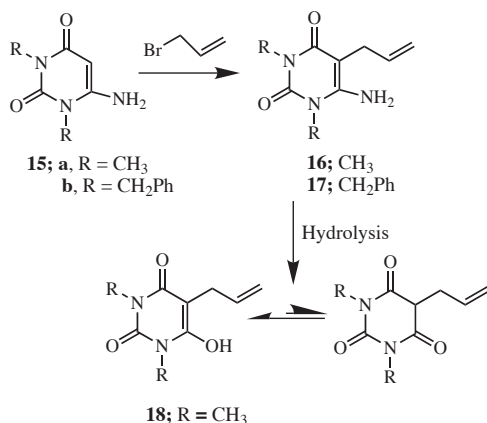


As per the literature reports [13,14], the ^1H NMR spectrum of *N,N'*-dimethylbarbituric acid shows 2H singlet at δ 3.2 along with a 6H singlet corresponding to two CH_3 groups. The complete absence of olefinic proton at C-5 in the region δ 4-5 indicates the existence of this barbituric acid in triketo- form **1** [15]. Due to the presence of active methylene group at C-5, the first alkylation in barbituric acids takes place at C-5 and not at NH (in case of **1**, R=H). The result of first alkylation is intermediate **13**, which could exist in two tautomeric forms **13a** and **13b** (scheme V).

The enolic form of **13** has been confirmed by the synthesis of its analogue 5-allyl-1,3-dimethylbarbituric acid **18** (Scheme IV).

¹H NMR spectrum of **18** shows complete absence of C₅-H and its ¹³C NMR spectrum shows the presence of C₅ as quaternary carbon at δ 75.9.

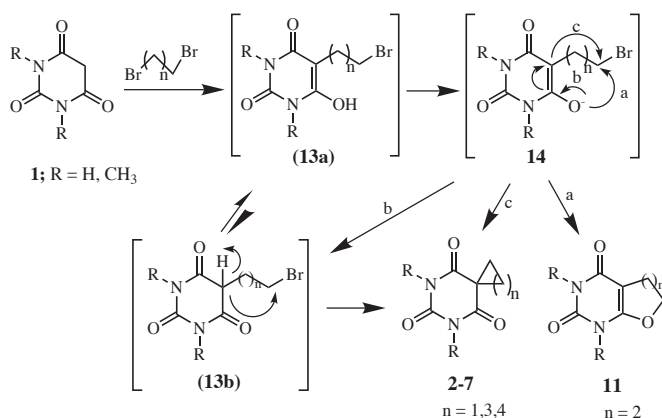
Scheme IV



The presence of **13** in the enolic form is in favour of the possibility of second alkylation to take place at OH instead of C₅. Moreover, it is controlled by the ease of electron transfer from C₆-O⁻ towards C-5 and the stabilization of the annulated ring to be formed.

Intermediate **14** (Scheme V) formed by deprotonation of OH, gets transformed to the product through three routes: i) reaction of oxide ion at CH₂-Br via **a** forming compound **11**, ii) concerted cyclisation via **c** forming compounds **2-7** and iii) formation of keto form **13b** via **b**. The stability of 6 membered ring in **11** favours route **a** over **b** and **c** while in other cases for the formation of compounds **2-7**, either route **b** followed by cyclization is adopted or route **c** is followed (Scheme V).

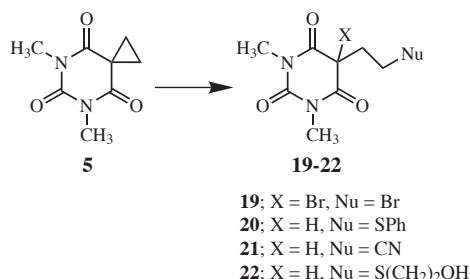
Scheme V



Therefore, the existence of C₅-monalkylated barbituric acids in enolic forms creates a competition between C-/O-alkylation and reaction going through the participation of intermediate **14** is predominantly controlled by the stability of the product.

The cyclopropane ring present at C-5 of spirobarbiturates (**2** and **5**) is important because of its reactivity pattern equivalent to carbon-carbon double bond. Compound **5** when taken in ethanol decolorize bromine water and on usual work up gave a thick liquid that has been identified as **19**. The reaction of **5** with thiophenol, NaCN and 2-mercaptoethanol in ethanol gave C₅-monoalkylated products **20** (55%), **21** (52%) and **22** (55%) respectively (Scheme VI).

Scheme VI



All the new compounds have been characterized by various spectral (¹H NMR, ¹³C NMR and mass) techniques and elemental analysis. The formation of compounds **20** and **22** paves the way for these compounds to act as thymidylate synthase inhibitors.

It is concluded that a synthetic methodology (in better yields relative to literature reports) has been developed for the spirobarbiturates except the formation of compound **11** where the preferred formation of six membered ring over four membered ring leads to the formation of pyranopyrimidine. In spirocyclopropanobarbituric acid **5** the reactivity of cyclopropane ring helps in the synthesis of C-5 monoalkylated barbituric acids which otherwise are not possible because the C-5 alkylation of barbituric acids is always plagued by dialkylation.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. ¹H and ¹³C NMR spectra in CDCl₃/DMSO-*d*₆ were run on JEOL JNM-AL FT NMR 300 MHz and 75 MHz spectrometer, respectively using TMS as an internal standard (chemical shifts in δ, ppm). Column chromatography was performed using silica gel (60-120 mesh) using ethyl acetate-hexane as eluents. Mass spectra were recorded at Electrospray Ionization Interface in the +ve mode. C, H, N analysis were recorded at RSIC, Lucknow.

General Method for Synthesis of Compounds **2-11**.

A mixture of barbituric acid (1.56 g / 1.86 g, 10 mmol), dibromoalkane (2.22 g, 12 mmol), K₂CO₃ (2.76 g, 20 mmol) and TBAHSO₄ (catalyst, 0.1 mmol) in DMF was stirred at 70-80° for 4 hrs. On completion of reaction (TLC), it was filtered. After

removing the solvent under reduced pressure, the residue was purified by column chromatography using ethyl acetate and hexane as eluents. Recrystallization from ethanol obtained analytically pure product. The yields are reported with respect to consumed barbituric acid.

5,7-Diaza-spiro[2.5]octane-4,6,8-trione (2).

This compound was obtained as whitish solid (ethanol); 63%, mp 320° (dec.); ir (KBr): CO 1670, 1693 cm⁻¹; ¹H nmr (CDCl₃+DMSO-*d*₆): δ 2.26 (s, 4H, 2xCH₂); ¹³C nmr (normal/DEPT-135): δ 28.2 (-ve, CH₂), 47.8 (C-5), 151.9 (C-2), 171.7 (C-4, C-6); ms: m/z 155 (M⁺+1).

Anal. Calcd. for C₆H₆N₂O₃: C, 46.76; H, 3.92; N, 18.18. Found: C, 47.03; H, 4.02; N, 17.92.

7,9-Diaza-spiro[4.5]decane-6,8,10-trione (3).

This compound was obtained as whitish solid (ethanol); 55%; mp 259°; ir (KBr): CO 1645, 1660 cm⁻¹; ¹H nmr (CDCl₃+DMSO-*d*₆): δ 1.95 (m, 4H, 2xCH₂), 2.24 (t, 4H, 2xCH₂, J=6.6 Hz); ¹³C nmr (normal/DEPT-135): δ 28.0 (-ve, CH₂), 39.6 (-ve, CH₂), 57.0 (C-5), 160 (C-2), 174.1 (C-4, C-6); ms: m/z 183 (M⁺+1).

2,4-Diaza-spiro[5.5]undecane-1,3,5-trione (4):

This compound was obtained as whitish solid (ethanol); 55%; mp 279°; ir (KBr): CO 1675, 1692 cm⁻¹; ¹H nmr (CDCl₃+DMSO-*d*₆): δ 1.56-1.65 (m, 2H, CH₂), 1.72-1.83 (m, 4H, 2xCH₂), 1.98 (t, 4H, 2xCH₂, J=6.4 Hz); ¹³C nmr (normal/DEPT-135): δ 21.7 (-ve, CH₂), 25.0 (-ve, CH₂), 33.8 (-ve, CH₂), 52.1 (C-5), 162.4 (C-2), 172.8 (C-4, C-6); ms: m/z 197 (M⁺+1).

5,7-Dimethyl-5,7-diaza-spiro[2.5]octane-4,6,8-trione (5):

This compound was obtained as whitish solid (ethanol); 87%; mp 265-67°; ir (KBr): CO 1666, 1697 cm⁻¹; ¹H nmr (CDCl₃): δ 2.23 (s, 4H, 2xCH₂), 3.22 (s, 6H, N-CH₃); ¹³C nmr (normal/DEPT-135): δ 27.8 (-ve, CH₂), 28.9 (+ve, N-CH₃), 48.8 (C-5), 150.8 (C-2), 171.7 (C-4, C-6); ms: m/z 183 (M⁺+1).

Anal. Calcd. for C₈H₁₀N₂O₃: C, 52.74; H, 5.53; N, 15.38. Found: C, 52.44; H, 5.16; N, 15.22.

7,9-Dimethyl-7,9-diaza-spiro[4.5]decane-6,8,10-trione (6):

This compound was obtained as whitish solid (ethanol); 52%; mp 87°; ir (KBr): CO 1624 cm⁻¹; ¹H nmr (CDCl₃): δ 1.93 (t, 4H, 2xCH₂, J=6.6 Hz), 2.22 (t, 4H, 2xCH₂, J=6.6 Hz), 3.31 (s, 6H, N-CH₃); ¹³C nmr (normal/DEPT-135): δ 27.4 (-ve, CH₂), 28.9 (+ve, N-CH₃), 39.2 (-ve, CH₂), 56.6 (C-5), 151.5 (C-2), 173.4 (C-4, C-6); ms: m/z 212 (M⁺+1).

Anal. Calcd. for C₁₀H₁₄N₂O₃: C, 57.13; H, 6.71; N, 13.33. Found: C, 56.77; H, 6.85; N, 13.19.

2,4-Dimethyl-2,4-diaza-spiro[5.5]undecane-1,3,5-trione (7):

This compound was obtained as whitish solid (ethanol); 31%; mp 60°; ir (KBr): CO 1678, 1685 cm⁻¹; ¹H nmr (CDCl₃): δ 1.51-1.60 (m, 2H, CH₂), 1.67-1.84 (m, 4H, 2xCH₂), 1.96 (t, 4H, 2xCH₂, J=6.4 Hz), 3.30 (s, 6H, N-CH₃); ¹³C nmr (normal/DEPT-135): δ 21.2 (-ve, CH₂), 24.5 (-ve, CH₂), 28.8 (+ve, N-CH₃), 32.7 (-ve, CH₂), 50.7 (C-5), 161 (C-2), 172.4 (C-4, C-6); ms: m/z 225 (M⁺+1).

Anal. Calcd. for C₁₁H₁₆N₂O₃: C, 58.91; H, 7.19; N, 12.49. Found: C, 58.61; H, 7.37; N, 12.39.

[2.3]Benzo-7,9-diaza-spiro[4.5]decane-6,8,10-trione (8):

This compound was obtained as whitish solid (ethanol); 60%; mp 280°; ir (KBr): CO 1684, 1701 cm⁻¹; ¹H nmr (CDCl₃+DMSO-*d*₆): δ 3.73 (s, 4H, 2xCH₂), 7.25-7.36 (m, 4H, Ph); ¹³C nmr (normal/DEPT-135): δ 44.2 (-ve, CH₂), 55.9 (C-5), 124.0 (+ve, ArCH), 127.8 (+ve, ArCH), 128 (ArC), 150.9 (C-2), 175.3 (C-4, C-6); ms: m/z 231 (M⁺+1).

Anal. Calcd. for C₁₂H₁₀N₂O₃: C, 62.60; H, 4.38; N, 12.17. Found: C, 62.40; H, 4.62; N, 11.92.

[2.3]Benzo-7,9-dimethyl-7,9-diaza-spiro[4.5]decane-6,8,10-trione (9).

This compound was obtained as whitish solid (ethanol); 60%; mp 120°; ir (KBr): CO 1678 cm⁻¹; ¹H nmr (CDCl₃): δ 3.33 (s, 6H, N-CH₃), 3.61 (s, 4H, 2xCH₂), 7.20-7.26 (m, 4H, Ph); ¹³C nmr (normal/DEPT-135): δ 29.0 (+ve, N-CH₃), 44.2 (-ve, CH₂), 56.1 (C-5), 124.0 (+ve, ArCH), 127.3 (+ve, ArCH), 127.9 (ArC), 151.4 (C-2), 172 (C-4, C-6); ms: m/z 259 (M⁺+1).

Anal. Calcd. for C₁₄H₁₄N₂O₃: C, 65.11; H, 5.46; N, 10.85. Found: C, 65.08; H, 5.78; N, 10.83.

1,3-Dimethyl-5,10-dihydro-1*H*-11-oxa-1,3-diaza-dibenzo[*a,b*]cycloheptene-2,4-dione (10).

This compound was obtained as whitish solid (ethanol); 20%; mp 105°; ir (KBr): CO 1681 cm⁻¹; ¹H nmr (CDCl₃): δ 3.35 (s, 3H, N-CH₃), 3.39 (s, 3H, N-CH₃), 4.07 (s, 2H, CH₂), 5.49 (s, 2H, O-CH₂), 7.33-7.38 (m, 4H, Ph); ¹³C nmr (normal/DEPT-135): δ 27.4 (-ve, CH₂), 29.0 (+ve, N-CH₃), 29.5 (+ve, N-CH₃), 72.5 (-ve, CH₂), 89.7 (C-5), 127.4 (+ve, ArCH), 128.6 (+ve, ArCH), 128.7 (+ve, ArCH), 130.3 (ArC), 150.6 (C-2), 158.3 (C-4), 164.5 (C-6); ms: m/z 258 (M⁺+1).

Anal. Calcd. for C₁₄H₁₄N₂O₃: C, 65.11; H, 5.46; N, 10.85. Found: C, 65.38; H, 5.78; N, 11.10.

1,3-Dimethyl-1*H*,5*H*-6,7-dihydro-pyrano[2,3-*d*]pyrimidine-2,4-dione (11).

This compound was obtained as whitish solid (ethanol); 60%; mp 122°; ir (KBr): CO 1610, 1631 cm⁻¹; ¹H nmr (CDCl₃): δ 1.92-2.04 (m, 2H, CH₂), 2.48 (t, 2H, CH₂, J=6.4 Hz), 3.34 (s, 3H, N-CH₃), 3.36 (s, 3H, N-CH₃), 4.35 (t, 2H, O-CH₂, J=5.2 Hz); ¹³C nmr (normal/DEPT-135): δ 17.5 (-ve, CH₂), 21.1 (-ve, CH₂), 27.8 (+ve, N-CH₃), 28.3 (+ve, N-CH₃), 69.4 (-ve, O-CH₂), 86.9 (C-5), 151 (C-2), 155.9 (C-4), 163.2 (C-6); ms: m/z 197 (M⁺+1).

Anal. Calcd. for C₉H₁₂N₂O₃: C, 55.09; H, 6.16; N, 14.28. Found: C, 55.29; H, 5.82; N, 14.10.

Synthesis of Compounds 16 and 17.

Equimolar amounts of 1,3-dialkyl-6-aminouracil (1.55g, 10 mmol) and allyl bromide (1.20 g, 10 mmol) were stirred at 70-80° in DMF (10 ml) using K₂CO₃ (2.76 g, 20 mmol) as base and TBAHSO₄ as catalyst (0.1 mmol) for 3 hrs. After filtration, solvent was removed under reduced pressure. The impure residue was purified by column chromatography using ethyl acetate hexane as eluents and recrystallized from ethanol.

5-Allyl-6-amino-1,3-dimethyl-1*H*-pyrimidine-2,4-dione (16).

This compound was obtained as whitish solid (ethanol); 53%; mp 165°; ¹H nmr (CDCl₃): δ 3.28 (dd, 2H, CH₂, J=8.0 Hz, J=10.0 Hz), 3.38 (s, 3H, N-CH₃), 3.49 (s, 3H, N-CH₃), 4.49 (bs,

2H, NH₂), 5.16 (dd, 2H, CH₂, J=6.0 Hz, J=8.0 Hz), 5.65 (m, 1H, CH); ¹³C nmr (normal/DEPT-135): δ 28.1 (-ve, CH₂), 28.2 (+ve, CH₃), 29.3 (+ve, CH₃), 85.0 (C-5), 115.3 (-ve, CH₂), 135.4 (+ve, CH), 151.2 (C-2), 151.4 (C-4), 162.4 (C-6); ms: m/z 196 (M⁺).

5-Allyl-6-amino-1,3-dibenzyl-1H-pyrimidine-2,4-dione (17).

This compound was obtained as yellowish oil; 42%; ¹H nmr (CDCl₃): δ 2.41 (dd, 2H, CH₂, J=6.0 Hz, J=8.0 Hz), 2.72 (dd, 2H, CH₂, J=6.0 Hz, J=8.0 Hz), 4.94 (dd, 2H, CH₂, J=4.0 Hz, J=10.0 Hz), 5.01 (s, 2H, CH₂), 5.18 (s, 2H, CH₂), 5.34 (m, 1H, CH); 7.28 (m, 10H, 2xPh); ¹³C nmr (normal/DEPT-135): δ 44.1 (-ve, CH₂), 45.0 (-ve, CH₂), 46.0 (-ve, CH₂), 54.3 (C-5), 120.7 (-ve, CH₂), 125.9 (+ve, ArCH), 127.3 (+ve, ArCH), 127.5 (+ve, ArCH), 128.3 (+ve, ArCH), 128.6 (+ve, ArCH), 128.8 (ArC), 128.9 (+ve, ArCH), 130.3 (+ve, CH), 136.6 (ArC), 150.5 (C-2), 161.5 (C-4), 170.2 (C-6).

Syntheses of 18.

Method A: 5-Allyl-6-amino-1,3-dimethyluracil (1.95 g, 10 mmol) and *m*-chloroperbenzoic acid (1.725 g, 10 mmol) were taken in CHCl₃ (10 ml) and stirred for 12 hrs at room temperature. The reaction was monitored by TLC. After the starting material is consumed, the reaction mixture was treated with saturated solution of NaHCO₃ and extracted with CHCl₃. The combined organic extractions were dried over anhydrous sodium sulphate. On removing the solvent, the crude residue was purified by column chromatography using ethyl acetate and hexane as eluents.

Method B: 5-Allyl-6-amino-1,3-dimethyluracil (1.95 g, 10 mmol) and oxone (12.30 g, 20 mmol) were stirred at 0° in Acetone-Water mixture (7:3) for 2 hrs. The reaction was monitored by TLC and after the completion of the reaction, it was extracted with CHCl₃. The impure residue obtained after the removal of solvent was purified by column chromatography with ethyl acetate-hexane mixture.

5-Allyl-6-hydroxy-1,3-dimethyl-1H-pyrimidine-2,4-dione (18):

This compound was obtained as yellowish oil; 45%; ¹H nmr (CDCl₃): δ 2.70 (d, 2H, CH₂, J=6 Hz), 3.31 (s, 6H, N-CH₃), 5.21 (dd, 2H, CH₂, J=6.0 Hz, J=8.0 Hz), 5.61 (m, 1H, CH); ¹³C nmr (normal/DEPT-135): δ 28.8 (+ve, CH₃), 46.9 (-ve, CH₂), 75.9 (C-5), 122.0 (-ve, CH₂), 128.4 (+ve, CH), 150.5 (C-2), 169.8 (C-4, C-6); ms: m/z 197 (M⁺).

General Method for Synthesis of Compounds 19-22.

A mixture of **5** (1.82 g, 10 mmol) and the appropriate reagent *viz.* Br₂, PhSH, NaCN, HS(CH₂)₂OH (10 mmol) was taken in ethanol and stirred at 50-60° for 8-10 hrs. After removing the solvent, the impure residue was purified by column chromatography using ethyl acetate-hexane as eluents.

5-Bromo-5-(2-bromoethyl)-1,3-dimethyl-pyrimidine-2,4,6-trione (19):

This compound was obtained as yellowish oil; 60%; ir (KBr): CO 1666, 1697 cm⁻¹; ¹H nmr (CDCl₃): δ 3.20 (t, 2H, CH₂, J=8.0 Hz), 3.40 (s, 6H, N-CH₃), 3.45 (t, 2H, CH₂, J=8.0 Hz); ¹³C nmr (normal/DEPT-135): δ 26.7 (-ve, CH₂), 29.5 (+ve, N-CH₃), 30.1 (+ve, N-CH₃), 37.6 (-ve, CH₂), 79.0 (C-5), 149 (C-2), 165.5 (C-4), 168.7 (C-6); ms: m/z 343 (M⁺+1).

Anal. Calcd. for C₈H₁₀Br₂N₂O₃: C, 28.10; H, 2.95; N, 8.19. Found: C, 28.25; H, 3.01; N, 8.11.

1,3-Dimethyl-5-(2-phenylsulfanyl-ethyl)-1H-pyrimidine-2,4,6-trione (20).

This compound was obtained as white solid (ethanol); 55%; mp 175°; ir (KBr): CO 1645 cm⁻¹; ¹H nmr (CDCl₃): δ 3.24 (s, 3H, N-CH₃), 3.29 (s, 3H, N-CH₃), 3.30 (t, 2H, CH₂, J=6.3 Hz), 4.16 (t, 2H, S-CH₂, J=5.8 Hz), 5.01 (s, 1H, C-5H), 7.27-7.39 (m, 5H, Ph); ¹³C nmr (normal/DEPT-135): δ 27.8 (+ve, N-CH₃), 28.9 (+ve, N-CH₃), 32.6 (-ve, CH₂), 68.6 (-ve, S-CH₂), 78.3 (+ve, C-5H), 127.4 (+ve, ArCH), 129.3 (+ve, ArCH), 130.9 (+ve, ArCH), 134.0 (ArC), 160.0 (C-2), 163.1 (C-4, C-6); ms: m/z 293 (M⁺+1).

Anal. Calcd. for C₁₄H₁₆N₂O₃S: C, 57.52; H, 5.52; N, 9.58; S, 10.97. Found: C, 57.29; H, 5.32; N, 9.28; S, 10.82.

3-(1,3-Dimethyl-2,4,6-trioxo-hexahydro-pyrimidin-5-yl)-propionitrile (21).

This compound was obtained as yellowish oil; 52%; ir (KBr): CO 1660, CN 2250 cm⁻¹; ¹H nmr (CDCl₃): δ 2.28 (t, 2H, CH₂, J=6.0 Hz), 3.33 (s, 3H, N-CH₃), 3.37 (s, 3H, N-CH₃), 3.42 (t, 2H, CH₂, J=6.4 Hz), 5.11 (s, 1H, C-5H); ¹³C nmr (normal/DEPT-135): δ 24.0 (-ve, CH₂), 27.8 (+ve, N-CH₃), 28.7 (+ve, N-CH₃), 32.2 (-ve, CH₂), 78.1 (+ve, C-5), 160.4 (C-2), 163.4 (C-4, C-6); ms: m/z 210 (M⁺+1).

Anal. Calcd. for C₉H₁₁N₃O₃: C, 51.67; H, 5.30; N, 20.09. Found: C, 51.82; H, 5.39; N, 19.95.

5-[2-(2-Hydroxy-ethylsulfanyl)-ethyl]-1,3-dimethyl-pyrimidine-2,4,6-trione (22).

This compound was obtained as yellowish oil; 55%; ir (KBr): CO 1680 cm⁻¹; ¹H nmr (CDCl₃): δ 2.87 (t, 2H, CH₂, J=4.8 Hz), 3.31 (s, 3H, N-CH₃), 3.40 (s, 3H, N-CH₃), 3.68 (t, 2H, CH₂, J=4.8 Hz), 3.91 (t, 2H, S-CH₂, J=5.4 Hz), 4.34 (t, 2H, CH₂, J=5.4 Hz), 5.11 (s, 1H, C-5H); ¹³C nmr (normal/DEPT-135): δ 24.6 (-ve, CH₂), 27.3 (+ve, N-CH₃), 28.9 (+ve, N-CH₃), 41.5 (-ve, S-CH₂), 60.2 (-ve, S-CH₂), 69.3 (-ve, O-CH₂), 78.3 (+ve, C-5H), 169.8 (C-2), 163.2 (C-4, C-6); ms: m/z 261 (M⁺+1).

Anal. Calcd. for C₁₀H₁₆N₂O₄S: C, 46.14; H, 6.20; N, 10.76, S, 12.32. Found: C, 46.20; H, 6.35; N, 10.58, S, 12.20.

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