Monatshefte für Chemie 135, 1529–1538 (2004)
DOI 10.1007/s00706-004-0192-8

**Monatshefte für Chemie**
**Chemical Monthly**
Printed in Austria

# A Convenient Route for the Synthesis of 4-Aryl- and 4-Aminopyrimidines

**Madhukar N. Jachak***, **Chanda D. Tantak, Raghunath B. Toche,** and **Naresh S. Badgujar**

Post Graduate Department of Chemistry, K.R.T. Arts, B.H. Commerce & A.M. Science College, Nashik, 422002, India

Received January 7, 2004; accepted (revised) February 2, 2004
Published online September 24, 2004 

**Summary.** A series of ureidopropenenitriles were synthesised by *Knoevenagel* condensation of *Ar*$COCH_2CN$ and $HC(OEt)_3$ in presence of ureas in a one pot reaction. These ureidopropenenitriles were cyclised to 4-aryl-5-cyano-3-substituted pyrimidines (in acid) or to 4-amino-5-benzoylpyrimidines (in base) in 60–70% yields. The amine pyrimidine derivatives were further converted to substituted uracils by hydrolysis with isopentyl nitrite in *DMF*. Alkylation of uracils furnished 1,3-dimethyluracil derivatives with *DMS* in alkali. All new compounds were characterised by spectral and analytical methods.

**Keywords.** Parasubstituted benzoylacetonitrile; 4-Arylpyrimidone; 5-Aroyluracils; 4-Aminopyrimidone; 1,3-Dimethyluracils.

## Introduction

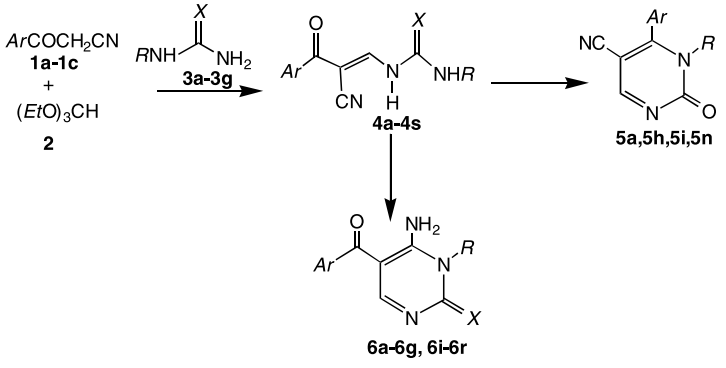
Several 4-arylpyrimidine derivatives have recently emerged as the integral backbone of calcium channel blockers, antihypertensive agents, and antagonists [1–5]. Furthermore several marine alkaloids containing a pyrimidine nucleus display interesting antifungal activity [6, 7]. *H. Junek* and *MNJ* have reported the synthesis of cytosine derivatives using cyanoacetaldehyde, *DMF*-acetal, and ureas [8]. In an earlier communication the synthesis of 5-benzoylcytosine derivatives starting with ureidopropenenitriles has been reported [9]. As a part of ongoing interest in this area we now report the synthesis of ureidopropenenitriles **4**, 4-arylpyrimidines **5**, and 4-aminopyrimidines **6**.

## Results and Discussion

In a previous communication [9] we have reported the one-pot synthesis of ureidopropenenitriles **4** using benzoylacetonitrile, triethyl orthoformate, and urea or

* Corresponding author. E-mail: mn_jachak@hotmail.com

substituted ureas. Herein we report the synthesis of **4** using substituted benzoylacetonitriles **1a–1c** and their transformation to pyrimidine derivatives **5**, **6**, **7**, and **8**. Thus, the mixture of substituted benzoylacetonitriles **1** triethyl orthoformate and urea or substituted ureas **3** on heating at 70°C furnishes **4** in high yields. All ureidopropenenitriles were characterized by spectral and analytical methods. These ureidopropenenitriles **4** could be cyclised to pyrimidine derivatives **5** or **6** in acid or on basic medium. Thus, **4a**, **4h**, **4i**, and **4n** when refluxed in acetic acid yielded 4-arylpyrimidine derivatives **5** in good yields. On refluxing **4** in ethanol/sodium ethoxide furnished the 4-aminopyrimidine derivatives **6**, with the exception of **4h** and **4s**. In the $^1$H NMR spectrum of compounds **6** it was observed that the N–H proton of the $NH_2$ group at position **4** gave two different signals at $\delta = 8.80$ and 9.90 ppm. This may be due to H-bonding with the carbonyl oxygen of aroyl at position **5** (Scheme 1). Compounds **6** on heating in *DMF* in the presence of isopentyl nitrite at 65°C furnished uracil derivatives **7** in 80–90% yields (Scheme 2).




| **1** | *Ar* |
|---|---|
| **a** | 4-Cl*Ph* |
| **b** | 4-Br*Ph* |
| **c** | 4-Me*Ph* |

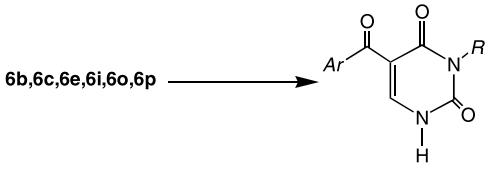
| **3** | *R* | *X* |
|---|---|---|
| **a** | H | O |
| **b** | *Me* | O |
| **c** | *Et* | O |
| **d** | *Ph* | O |

| **3** | *R* | *X* |
|---|---|---|
| **e** | Allyl | O |
| **f** | *Bz* | O |
| **g** | *Me* | S |

| **4,5,6** | *Ar* | *R* | *X* |
|---|---|---|---|
| **a** | 4-Cl*Ph* | H | O |
| **b** | 4-Cl*Ph* | *Me* | O |
| **c** | 4-Cl*Ph* | *Et* | O |
| **d** | 4-Cl*Ph* | *Ph* | O |
| **e** | 4-Cl*Ph* | Allyl | O |
| **f** | 4-Cl*Ph* | *Bz* | O |
| **g** | 4-Cl*Ph* | *Me* | S |
| **h** | 4-Br*Ph* | H | O |
| **i** | 4-Br*Ph* | *Me* | O |
| **j** | 4-Br*Ph* | *Et* | O |

| **4,5,6** | *Ar* | *R* | *X* |
|---|---|---|---|
| **k** | 4-Br*Ph* | *Bz* | O |
| **l** | 4-Br*Ph* | *Me* | S |
| **m** | 4-Br*Ph* | Allyl | O |
| **n** | 4-Me*Ph* | H | O |
| **o** | 4-Me*Ph* | *Me* | O |
| **p** | 4-Me*Ph* | *Et* | O |
| **q** | 4-Me*Ph* | *Ph* | O |
| **r** | 4-Me*Ph* | Allyl | O |
| **s** | 4-Me*Ph* | *Me* | S |

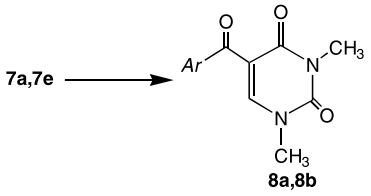
**Scheme 1**




**7a-7f**

| 7 | *Ar* | *R* | 7 | *Ar* | *R* |
|---|---|---|---|---|---|
| **a** | 4-Cl*Ph* | *Me* | **d** | 4-Br*Ph* | *Me* |
| **b** | 4-Cl*Ph* | *Et* | **e** | 4-Me*Ph* | *Me* |
| **c** | 4-Cl*Ph* | Allyl | **f** | 4-Me*Ph* | *Et* |

**Scheme 2**




**8a,8b**

| 8 | *Ar* |
|---|---|
| **a** | 4-Cl*Ph* |
| **b** | 4-Me*Ph* |

**Scheme 3**

It was noted from literature that compounds containing an alkyl or sugar moiety on the pyridine nitrogen display anticancer activity [10], hence we attempted alkylation of **7**. Thus, methylation of **7** with *DMS* in alkali furnished the 1,3-dimethyl uracil derivatives **8** (Scheme 3). However, attempts to derivatise with sugar residues were unsuccessful. All new compounds **5**, **6**, **7**, and **8** were characterized by IR, $^1$H NMR and elemental analysis.

## Experimental

Melting points (uncorrected): *Gallenkamp* Melting Point Apparatus; IR Spectra (KBr-compression mould): Schimadzu IR-408; $^1$H NMR spectra: Varian XL-300 (300 MHz), *DMSO*-$d_6$, $CDCl_3$, *TMS*; elemental analysis: HOSLI CH-Analyser; the results were in agreement with calculated values.

### *General Procedure for the Synthesis of 2-Aroyl-3-ureido- or -thioureidopropenenitriles **4a–4s***

A mixture of 0.01 mol of **1**, 2.22 g of **2** (0.015 mol) and 0.012 mol of urea, substituted urea, or thiourea **3a–3x** was heated at 60–70°C in an oil bath for 30 min (TLC check). The resulting solid was stirred in 30 $cm^3$ of petroleum ether, filtered, dried, and recrystallised.

### *2-(4-Chlorobenzoyl)-3-ureidopropenenitrile* (**4a**, $C_{11}H_8ClN_3O_2$)

Yield 2.11 g (84%), mp 202–203°C (*DMF* ethanol); IR: $\bar{\nu} = 3400, 2240, 1750, 1700\,cm^{-1}$; $^1$H NMR: $\delta = 6.75$ (bs, $NH_2$), 7.49–7.62 (m, Ar–H), 7.84 (d, $J = 12.5$ Hz, =CH), 8.28 (d, $J = 12.5$ Hz, NH) ppm.

*2-(4-Chlorobenzoyl)-3-methylureidopropenenitrile* (**4b**, $C_{12}H_{10}ClN_3O_2$)

Yield 1.41 g (53%), mp 184–185°C (ethanol); IR: $\bar{\nu} = 3450, 3250, 2250, 1750, 1710\,cm^{-1}$; $^1H$ NMR: $\delta = 2.68$ (d, $J = 5$ Hz, $CH_3$), 7.18 (bs, NH), 7.60–7.81 (m, Ar–H), 7.80 (d, $J = 12.5$ Hz, =CH), 11.31 (d, $J = 12.5$ Hz, NH) ppm.

*2-(Chlorobenzoyl)-3-ethylureidopropenenitrile* (**4c**, $C_{13}H_{12}ClN_3O_2$)

Yield 2.41 g (86%), mp 213–214°C (methanol); IR: $\bar{\nu} = 3330, 2240, 1740, 1640\,cm^{-1}$; $^1H$ NMR: $\delta = 1.05$ (t, $J = 7.5$ Hz, $CH_3$), 3.25 (q, $J = 7.5$ Hz, $CH_2$), 7.34 (d, $J = 7.5$ Hz, NH), 7.61–7.72 (m, Ar–H), 8.35 (d, $J = 12.5$ Hz, =CH), 11.65 (d, $J = 12.5$ Hz, NH) ppm.

*2-(4-Chlorobenzoyl)-3-phenylureidopropenenitrile* (**4d**, $C_{17}H_{12}ClN_3O_2$)

Yield 2.60 g (80%), mp 225–226°C (*DMF*); IR: $\bar{\nu} = 3500, 3100, 2250, 1740, 1695\,cm^{-1}$; $^1H$ NMR: $\delta = 7.15$ (s, NH), 7.31–7.55 (m, Ar–H), 7.65–7.80 (m, Ar–H), 7.95 (d, $J = 12.5$ Hz, =CH), 11.92 (d, $J = 12.5$ Hz, NH) ppm.

*3-Allylureido-2-(4-chlorobenzoyl)propenenitrile* (**4e**, $C_{14}H_{12}ClN_3O_2$)

Yield 2.61 g (89%), mp 195–196°C (ethanol); IR: $\bar{\nu} = 3400, 2250, 1750, 1660\,cm^{-1}$; $^1H$ NMR: $\delta = 3.82$ (d, $J = 6$ Hz, $CH_2$), 5.18 (dd, $J = 10.6$, 6.0 Hz, $=CH_2$), 5.85 (m, =CH), 7.45 (t, $J = 12$ Hz, NH), 7.68–7.82 (m, Ar–H), 8.38 (d, $J = 12.5$ Hz, =CH), 11.62 (d, $J = 12.5$ Hz, NH) ppm.

*3-Benzylureido-2-(4-chlorobenzoyl)propenenitrile* (**4f**, $C_{18}H_{14}ClN_3O_2$)

Yield 2.65 g (78%), mp 204–205°C (*DMF*:ethanol); IR: $\bar{\nu} = 3320, 2230, 1740, 1655\,cm^{-1}$; $^1H$ NMR: $\delta = 4.42$ (d, $J = 8$ Hz, $CH_2$), 7.21–7.45 (m, Ar–H), 7.65–7.82 (m, Ar–H), 8.35 (d, $J = 12.5$ Hz, =CH), 8.90 (t, $J = 8$ Hz, NH) 11.75 (d, $J = 12.5$ Hz, NH) ppm.

*2-(4-Chlorobenzoyl)-3-methylthioureidopropenenitrile* (**4g**, $C_{12}H_{10}ClN_3OS$)

Yield 1.80 g (64%), mp 205–206°C (ethanol); IR: $\bar{\nu} = 3370, 3250, 3220, 2240, 1640\,cm^{-1}$; $^1H$ NMR: $\delta = 3.04$ (s, $CH_3$), 7.60–7.73 (m, Ar–H), 7.96 (d, $J = 12.5$ Hz, =CH), 8.92 (bs, NH), 11.43 (d, $J = 12.5$ Hz, NH) ppm.

*2-(4-Bromobenzoyl)-3-ureidopropenenitrile* (**4h**, $C_{11}H_8BrN_3O_2$)

Yield 2.05 g (70%), mp 198–199°C (ethanol); IR: $\bar{\nu} = 3450, 3300, 2250, 1710, 1670\,cm^{-1}$; $^1H$ NMR: $\delta = 6.73$ (bs, $NH_2$), 7.41–8.01 (m, Ar–H), 8.32 (d, $J = 12.5$ Hz, =CH), 11.55 (d, $J = 12.5$ Hz, NH) ppm.

*2-(4-Bromobenzoyl)-3-methylureidopropenenitrile* (**4i**, $C_{12}H_{10}BrN_3O_2$)

Yield 2.15 g (70%), mp 198–199°C (ethanol); IR: $\bar{\nu} = 3450, 3330, 2250, 1750, 1710\,cm^{-1}$; $^1H$ NMR: $\delta = 2.73$ (s, $CH_3$), 7.15 (bs, NH, exchangeable with $D_2O$), 7.67–7.71 (m, Ar–H), 8.29 (d, $J = 12.5$ Hz, =CH), 11.70 (d, $J = 12.5$ Hz, NH, exchangeable with $D_2O$) ppm.

*2-(4-Bromobenzoyl)-3-ethylureidopropenenitrile* (**4j**, $C_{13}H_{12}BrN_3O_2$)

Yield 2.15 g (67%), mp 180–181°C (ethanol); IR: $\bar{\nu} = 3350, 3250, 2210, 1750, 1650\,cm^{-1}$; $^1H$ NMR: $\delta = 1.04$ (t, $J = 7.5$ Hz, $CH_3$), 3.22 (q, $J = 7.5$ Hz, $CH_2$), 7.14 (s, NH), 7.59–7.74 (m, Ar–H), 8.26 (d, $J = 12.5$ Hz, =CH), 11.84 (d, $J = 12.5$ Hz, NH, exchangeable with $D_2O$) ppm.

*3-Benzylureido-2-(4-bromobenzoyl)propenenitrile* (**4k**, $C_{18}H_{14}BrN_3O_2$)

Yield 2.46 g (76%), mp 195–196°C (*DMF*); IR: $\bar{\nu} = 3320, 2230, 1740, 1655\,cm^{-1}$; $^1H$ NMR: $\delta = 4.31$ (d, $J = 8$ Hz, $CH_2$), 7.50–7.55 (m, Ar–H), 7.56–7.65 (m, Ar–H), 7.85 (s, NH, exchangeable with $D_2O$), 8.44 (d, $J = 12.5$ Hz, =CH), 11.59 (d, $J = 12.5$ Hz, NH, exchangeable with $D_2O$) ppm.

*2-(4-Bromobenzoyl)-3-methylthioureidopropenenitrile* (**4l**, $C_{12}H_{10}BrN_3OS$)

Yield 2.43 g (75%), mp 180–181°C (ethanol); IR: $\bar{\nu} = 3450, 3330, 2250, 1750, 1710\,cm^{-1}$; $^1H$ NMR: $\delta = 3.04$ (d, $J = 5$ Hz, $CH_3$), 7.45 (d, $J = 5$ Hz, NH), 7.60–7.76 (m, Ar–H), 8.80 (d, $J = 12.5$ Hz, =CH), 11.25 (d, $J = 12.5$ Hz, NH) ppm.

*3-Allylureido-2-(4-bromobenzoyl)propenenitrile* (**4m**, $C_{14}H_{12}BrN_3O_2$)

Yield 2.24 g (65%), mp 190–191°C (ethanol); IR: $\bar{\nu} = 3300, 3200, 2200, 1740, 1650\,cm^{-1}$; $^1H$ NMR: $\delta = 3.81$ (d, $J = 6$ Hz, $CH_2$), 5.52 (dd, $J = 10.6$, 6.0 Hz, $=CH_2$), 5.81 (m, =CH), 7.43 (bs, NH, exchangeable with $D_2O$), 7.45–7.89 (m, Ar–H), 8.23 (d, $J = 12.5$ Hz, =CH), 11.70 (d, $J = 12.5$ Hz, NH, exchangeable with $D_2O$) ppm.

*2-(4-Methylbenzoyl)-3-ureidopropenenitrile* (**4n**, $C_{11}H_{11}N_3O_2$)

Yield 1.81 g (78%), mp 204–205°C (*DMF* ethanol); IR: $\bar{\nu} = 3397, 3294, 2212, 1738, 1705, 1630\,cm^{-1}$; $^1H$ NMR: $\delta = 2.36$ (s, $CH_3$), 6.77 (bs, $NH_2$), 7.35–7.52 (m, Ar–H), 8.30 (d, $J = 12.6$ Hz, =CH), 11.60 (d, $J = 12.6$ Hz, NH) ppm.

*2-(4-Methylbenzoyl)-3-methylureidopropenenitrile* (**4o**, $C_{13}H_{13}N_3O_2$)

Yield 2.00 g (82%), mp 204–205°C (ethanol); IR: $\bar{\nu} = 3374, 3138, 2217, 1693, 1620\,cm^{-1}$; $^1H$ NMR: $\delta = 2.41, 2.52$ (2s, $2CH_3$), 7.41–7.75 (m, Ar–H), 7.93 (bs, NH), 8.20 (d, $J = 12.5$ Hz, =CH), 12.92 (bs, NH) ppm.

*3-Ethylureido-2-(4-methylbenzoyl)propenenitrile* (**4p**, $C_{14}H_{15}N_3O_2$)

Yield 2.11 g (81%), mp 144–145°C (methanol); IR: $\bar{\nu} = 3400, 3300, 2245, 1740, 1650\,cm^{-1}$; $^1H$ NMR: $\delta = 1.10$ (t, $J = 7.5$ Hz, $CH_3$), 2.42 (s, $CH_3$), 3.62 (d, $J = 7.5$ Hz, $CH_2$), 7.08 (bs, NH), 7.29–7.82 (m, Ar–H), 8.23 (d, $J = 12.5$ Hz, =CH), 11.89 (d, $J = 12.5$ Hz, NH) ppm.

*2-(4-Methylbenzoyl)-3-phenylureidopropenenitrile* (**4q**, $C_{18}H_{15}N_3O_2$)

Yield 2.80 g (92%), mp 232–233°C (*DMF*); IR: $\bar{\nu} = 3400, 3300, 2445, 1740, 1650\,cm^{-1}$; $^1H$ NMR: $\delta = 2.44$ (s, $CH_3$), 7.08 (bs, NH), 7.07–7.52 (m, Ar–H), 7.62–7.83 (m, Ar–H), 9.95 (d, $J = 12.5$ Hz, =CH), 12.02 (d, $J = 12.5$ Hz, NH) ppm.

*3-Allylureido-2-(4-methylbenzoyl)propenenitrile* (**4r**, $C_{15}H_{15}N_3O_2$)

Yield 2.00 g (74%), mp 140–141°C (aqueous ethanol); IR: $\bar{\nu} = 3300, 3200, 2200, 1740, 1650\,cm^{-1}$; $^1H$ NMR: $\delta = 2.42$ (s, $CH_3$), 3.83 (d, $J = 6$ Hz, $CH_2$), 5.28 (dd, $J = 10.6$, 6.0 Hz, $=CH_2$), 5.78 (m, =CH), 7.43 (bs, NH), 7.65–7.89 (m, Ar–H), 8.47 (d, $J = 12.5$ Hz, =CH), 11.89 (d, $J = 12.5$ Hz, NH) ppm.

*2-(4-Methylbenzoyl)-3-methylthioureidopropenenitrile* (**4s**, $C_{13}H_{13}N_3OS$)

Yield 2.00 g (77%), mp 204–205°C (ethanol); IR: $\bar{\nu} = 3450, 3330, 2250, 1750, 1710\,cm^{-1}$; $^1H$ NMR: $\delta = 2.44$ (s, $CH_3$), 3.10 (d, $J = 6\,Hz$, $CH_3$), 7.41 (bs, NH), 7.59–7.62 (m, Ar–H), 7.86 (d, $J = 12.5\,Hz$, =CH), 12.44 (d, $J = 12.5\,Hz$, NH) ppm.

*General Procedure for the Synthesis of 5-Cyanopyrimidine Derivatives* **5a**, **5h**, **5i**, **5n**

A solution of 0.01 mol of **4** in 30 $cm^3$ of glacial acetic acid was refluxed for 24 h (TLC check). After removal of acetic acid under reduced pressure, the solid residue was washed with acetonitrile, and recrystallized.

*4-(4-Chlorophenyl)-2[1H]-pyrimidine-5-carbonitrile* (**5a**, $C_{11}H_6ClN_3O$)

Yield 0.60 g (48%), mp 276–277°C (ethanol); IR: $\bar{\nu} = 3100, 2240, 1700, 1660, 1620, 1600\,cm^{-1}$; $^1H$ NMR: $\delta = 7.65$–$7.88$ (m, Ar–H), 8.90 (s, =CH), 13.07 (bs, NH), ppm.

*4-(4-Bromophenyl)-2[1H]-pyrimidine-5-carbonitrile* (**5h**, $C_{11}H_6BrN_3O$)

Yield 1.33 g (48%), mp 270–271°C (acetonitrile); IR: $\bar{\nu} = 2250, 1700, 1670, 1640, 1610\,cm^{-1}$; $^1H$ NMR: $\delta = 7.45$–$7.79$ (m, Ar–H), 8.91 (s, =CH), 9.34 (bs, NH), ppm.

*4-(4-Bromophenyl)-3-methyl-2[1H]-pyrimidine-5-carbonitrile* (**5i**, $C_{12}H_8BrN_3O$)

Yield 1.55 g (60%), mp 194–195°C (acetonitrile); IR: $\bar{\nu} = 2210, 1690, 1660\,cm^{-1}$; $^1H$ NMR: $\delta = 3.20$ (s, $CH_3$) 7.58–7.86 (m, Ar–H), 8.91 (s, =CH), ppm.

*4-(4-Methylphenyl)-2[1H]-pyrimidine-5-carbonitrile* (**5n**, $C_{12}H_9N_3O$)

Yield 0.5 g (47%), mp 249–251°C (acetonitrile); IR: $\bar{\nu} = 3200, 2225, 1787, 1665, 1662\,cm^{-1}$; $^1H$ NMR: $\delta = 2.41$ (s, $CH_3$) 7.39–7.40 (m, Ar–H), 8.40 (s, =CH), 10.02 (s, NH), ppm.

*General Procedure for the Synthesis of 4-Amino-5-benzoyl-2(1H)-pyrimidine Derivatives* **6a**–**6g**, **6i**–**6r**

To a solution of 0.01 mol of **4**, 0.23 g of sodium ethoxide (freshly cut Na in 10 $cm^3$ of dry ethanol) in 40 $cm^3$ of dry ethanol was refluxed for 1 h. The solvent was removed under reduced pressure and the residue was dissolved in 100 $cm^3$ of cold $H_2O$ and acidified with 2 *N* HCl. The obtained solid was recrystallized.

*4-Amino-5-(4-chlorobenzoyl)-2[1H]-pyrimidone* (**6a**, $C_{11}H_8ClN_3O_2$)

Yield 1.00 g (40%), mp 359–361°C (methanol); IR: $\bar{\nu} = 3450, 1720, 1670\,cm^{-1}$; $^1H$ NMR: $\delta = 7.93$ (bs, NH), 7.56–7.63 (m, Ar–H), 7.88 (s, =CH), 8.23 (s, NH) ppm.

*4-Amino-5-(4-chlorobenzoyl)-3-methyl-2[1H]-pyrimidone* (**6b**, $C_{12}H_{10}ClN_3O_2$)

Yield 1.50 g (56%), mp 232–233°C (*DMF* ethanol); IR: $\bar{\nu} = 3400, 1670\,cm^{-1}$; $^1H$ NMR: $\delta = 3.37$ (s, $CH_3$), 7.50–7.56 (m, Ar–H), 8.21 (s, =CH), 8.65 (s, NH), 9.81 (s, NH) ppm.

*4-Amino-3-ethyl-5-(4-chlorobenzoyl)-2[1H]-pyrimidone* (**6c**, $C_{13}H_{12}ClN_3O_2$)

Yield 0.50 g (18%), mp 260–261°C (ethanol); IR: $\bar{\nu} = 3400$, 1670, 1600 $cm^{-1}$; $^1H$ NMR: $\delta = 1.17$ (t, $J = 7.5$ Hz, $CH_3$), 3.91 (q, $J = 7.5$ Hz, $CH_2$), 7.48–7.64 (m, Ar–H), 8.19 (s, =CH), 8.77 (s, NH, exchangeable with $D_2O$), 9.91 (s, NH) ppm.

*4-Amino-5-(4-chlorobenzoyl)-3-phenyl-2[1H]-pyrimidone* (**6d**, $C_{17}H_{12}ClN_3O_2$)

Yield 0.60 g (18%), mp 259–261°C (ethanol); IR: $\bar{\nu} = 3200$, 1660 $cm^{-1}$; $^1H$ NMR: $\delta = 7.36$–7.61 (m, Ar–H), 7.58–7.69 (m, Ar–H) 8.06 (s, =CH), 11.00 (bs, $NH_2$) ppm.

*3-Allyl-4-amino-5-(4-chlorobenzoyl)-2[1H]-pyrimidone* (**6e**, $C_{14}H_{12}ClN_3O_2$)

Yield 1.50 g (52%), mp 245–247°C (*DMF* ethanol); IR: $\bar{\nu} = 3400$, 1670 $cm^{-1}$; $^1H$ NMR: $\delta = 4.62$ (d, $J = 6.0$ Hz, $CH_2$), 5.17 (dd, $J = 6.2$, 10.0 Hz, $CH_2$), 5.86 (m, =CH), 7.58–7.63 (m, Ar–H) 8.22 (s, =CH), 8.62 (s, NH), 9.92 (s, NH) ppm.

*4-Amino-3-benzyl-5-(4-chlorobenzoyl)-2[1H]-pyrimidone* (**6f**, $C_{18}H_{14}ClN_3O_2$)

Yield 1.80 g (53%), mp 276–278°C (*DMF*); IR: $\bar{\nu} = 3200$, 1670, 1610 $cm^{-1}$; $^1H$ NMR: $\delta = 5.24$ (s, $CH_2$), 7.21–7.30 (m, Ar–H), 8.27 (s, =CH), 8.70 (s, NH), 9.90 (s, NH) ppm.

*4-Amino-5-(4-chlorobenzoyl)-3-methyl-2[1H]-thiopyrimidone* (**6g**, $C_{12}H_{10}ClN_3OS$)

Yield 1.60 g (60%), mp 300–301°C (*DMF*); IR: $\bar{\nu} = 3283$, 3153, 1618 $cm^{-1}$; $^1H$ NMR: $\delta = 2.62$ (s, $CH_3$), 7.59–7.60 (m, Ar–H), 8.02 (s, =CH), 8.82 (s, NH), 9.80 (s, NH) ppm.

*4-Amino-5-(4-bromobenzoyl)-3-methyl-2[1H]-pyrimidone* (**6i**, $C_{12}H_{10}BrN_3O_2$)

Yield 1.69 g (55%), mp 279–281°C (ethanol); IR: $\bar{\nu} = 3400$, 3150, 3000, 1670, 1610 $cm^{-1}$; $^1H$ NMR: $\delta = 3.31$ (s, $CH_3$), 7.46–7.74 (m, Ar–H), 8.20 (s, =CH), 9.82 (s, NH), 11.25 (s, NH) ppm.

*4-Amino-5-(4-bromobenzoyl)-3-ethyl-2[1H]-pyrimidone* (**6j**, $C_{13}H_{12}BrN_3O_2$)

Yield 2.06 g (64%), mp 263–264°C (*DMF*); IR: $\bar{\nu} = 3400$, 3150, 1670, 1630 $cm^{-1}$; $^1H$ NMR: $\delta = 2.45$ (t, $J = 7.5$ Hz, $CH_3$), 5.29 (q, $J = 7.5$ Hz, $CH_2$), 8.80–9.06 (m, Ar–H), 9.02 (s, =CH), 10.15 (s, NH, exchangeable with $D_2O$), 11.26 (s, NH, Exchangeable with $D_2O$) ppm.

*4-Amino-3-benzyl-5-(4-bromobenzoyl)-2[1H]-pyrimidone* (**6k**, $C_{18}H_{14}BrN_3O_2$)

Yield 1.95 g (51%), mp 253–254°C (*DMF*); IR: $\bar{\nu} = 3310$, 3250, 1680, 1655, 1610 $cm^{-1}$; $^1H$ NMR: $\delta = 5.29$ (s, $CH_2$), 7.29–7.64 (m, Ar–H), 8.83 (s, NH, exchangeable with $D_2O$), 9.02 (s, 1H, =CH), 10.01 (s, NH, exchangeable with $D_2O$) ppm.

*4-Amino-5-(4-bromobenzoyl)-3-methyl-2[1H]-thiopyrimidone* (**6l**, $C_{12}H_{10}BrN_3OS$)

Yield 1.87 g (58%), mp 257–258°C (*DMF*); IR: $\bar{\nu} = 3300$–3100, 3000, 1660, 1630 $cm^{-1}$; $^1H$ NMR: $\delta = 3.31$(s, $CH_3$), 7.54–7.75 (m, Ar–H), 8.03 (s, =CH), 8.85 (s, NH), 9.95 (s, NH) ppm.

*3-Allyl-4-amino-5-(4-bromobenzoyl)-2[1H]-pyrimidone* (**6m**, $C_{14}H_{12}BrN_3O_2$)

Yield 1.70 g (51%), mp 250–252°C (*DMF* ethanol); IR: $\bar{\nu} = 3400$, 3200, 1670, 1610 $cm^{-1}$; $^1H$ NMR: $\delta = 3.77$ (d, $J = 6.0$ Hz, $CH_2$), 5.09 (dd, $J = 6.5$, 10.0 Hz, $CH_2$), 5.76 (m, =CH), 7.58–7.72

(m, Ar–H), 8.22 (s, =CH), 8.62 (s, NH, exchangeable with $D_2O$), 9.92 (s, NH, exchangeable with $D_2O$) ppm.

*4-Amino-5-(4-methylbenzoyl)-2[1H]-pyrimidone* (**6n**, $C_{12}H_{11}N_3O_2$)

Yield 1.05 g (46%), mp 328–330°C (*DMF*); IR: $\bar{\nu} = 3350, 1720, 1670, 1610\,cm^{-1}$; $^1H$ NMR: $\delta = 3.30$ (t, $CH_3$), 7.33–7.81 (m, Ar–H), 8.22 (s, =CH), 8.63 (bs, NH), 9.86 (bs, NH) ppm.

*4-Amino-3-methyl-5-(4-methylbenzoyl)-2[1H]-pyrimidone* (**6o**, $C_{13}H_{13}N_3O_2$)

Yield 1.21 g (49%), mp 259–260°C (*DMF* ethanol); IR: $\bar{\nu} = 3410, 3110, 1670, 1610\,cm^{-1}$; $^1H$ NMR: $\delta = 2.37$ (s, $CH_3$), 3.27 (s, $CH_3$), 7.29–7.32 (m, Ar–H), 8.22 (s, =CH), 8.63 (bs, NH), 9.86 (bs, NH) ppm.

*4-Amino-3-ethyl-5-(4-methylbenzoyl)-2[1H]-pyrimidone* (**6p**, $C_{14}H_{15}N_3O_2$)

Yield 0.31 g (12%), mp 183–184°C (ethanol); IR: $\bar{\nu} = 3400, 3150, 1740, 1640\,cm^{-1}$; $^1H$ NMR: $\delta = 2.38$ (s, $CH_3$), 2.45 (t, $J = 7.5$ Hz, $CH_3$), 5.29 (q, $J = 7.5$ Hz, $CH_2$), 8.80–9.06 (m, Ar–H), 9.02 (s, =CH), 10.15 (s, NH, exchangeable with $D_2O$), 11.26 (s, NH, exchangeable with $D_2O$) ppm.

*4-Amino-5-(4-methylbenzoyl)-3-phenyl-2[1H]-pyrimidone* (**6q**, $C_{18}H_{15}N_3O_2$)

Yield 0.50 g (16%), mp 234–236°C (methanol); IR: $\bar{\nu} = 3300, 3110, 1650, 1630\,cm^{-1}$; $^1H$ NMR: $\delta = 2.38$ (s, $CH_3$), 7.12–7.38 (m, Ar–H), 7.40–7.84 (m, Ar–H), 7.99 (s, =CH), 11.20 (bs, NH), 11.81 (bs, NH) ppm.

*3-Allyl-4-amino-5-(4-methylbenzoyl)-2[1H]-pyrimidone* (**6r**, $C_{15}H_{15}N_3O_2$)

Yield 1.50 g (56%), mp 164–165°C (ethanol); IR: $\bar{\nu} = 3150, 1680\,cm^{-1}$; $^1H$ NMR: $\delta = 2.45$ (s, $CH_3$), 4.84 (d, $J = 6.0$ Hz, $CH_2$), 5.37 (dd, $J = 6.5, 10.0$ Hz, $CH_2$), 5.88 (m, =CH), 7.23–7.62 (m, Ar–H), 8.57 (s, =CH), 10.44 (bs, NH, exchangeable with $D_2O$), 11.20 (bs, NH, exchangeable with $D_2O$) ppm.

*General Procedure for the Synthesis of Uracil Derivatives* **7a–7f**

To a solution of 0.01 mol of **6** in 20 $cm^3$ of *DMF* 1.5 $cm^3$ of isopentyl nitrite in 7 $cm^3$ of *DMF* was added over a period of 10 min and the reaction mixture was stirred for 30 min at 60–65°C. After removal of solvent under reduced pressure the oily residue was triturated with acetonitrile to furnish a solid. It was collected, washed with cold acetonitrile, and recrystallized.

*5-(4-Chlorobenzoyl)-3-methyluracil* (**7a**, $C_{12}H_9ClN_2O_3$)

Yield 1.20 g (45%), mp 295–296°C (methanol); IR: $\bar{\nu} = 3350, 3200, 1720, 1660, 1645\,cm^{-1}$; $^1H$ NMR: $\delta = 3.35$ (s, $CH_3$), 7.45–7.88 (m, Ar–H), 7.91 (d, $J = 12.5$ Hz, =CH), 8.96 (bs, NH) ppm.

*5-(4-Chlorobenzoyl)-3-ethyluracil* (**7b**, $C_{13}H_{11}ClN_2O_3$)

Yield 1.46 g (52%), mp 270–271°C (methanol); IR: $\bar{\nu} = 3320, 1725, 1660, 1640\,cm^{-1}$; $^1H$ NMR: $\delta = 1.06$ (s, $CH_3$), 3.76 (q, $J = 7.5$ Hz, $CH_2$), 7.52–7.55 (m, Ar–H), 7.94 (d, $J = 12.5$ Hz, =CH), 11.90 (bs, NH) ppm.

*3-Allyl-5-(4-chlorobenzoyl)uracil* (**7c**, $C_{14}H_{11}ClN_2O_3$)

Yield 1.46 g (50%), mp 220–222°C (aqueous ethanol); IR: $\bar{\nu} = 3250$, 3200, 1725, 1680 $cm^{-1}$; $^1H$ NMR: $\delta = 4.54$ (d, $J = 5.2$ Hz, $CH_2$), 5.21 (dd, $J = 5.2$, 10.0 Hz, $CH_2$), 5.85 (m, =CH), 7.40–7.69 (m, Ar–H), 8.09 (d, $J = 12.5$ Hz, =CH), 10.98 (bs, NH), ppm.

*5-(4-Bromobenzoyl)-3-methyluracil* (**7d**, $C_{12}H_9BrN_2O_3$)

Yield 1.85 g (60%), mp 285–286°C (methanol); IR: $\bar{\nu} = 3090$, 2900, 1730, 1668, 1630 $cm^{-1}$; $^1H$ NMR: $\delta = 3.65$ (s, $CH_3$), 7.61–7.80 (m, Ar–H), 7.92 (d, $J = 12.5$ Hz, =CH), 10.95 (bs, NH) ppm.

*3-Methyl-5-(4-methylbenzoyl)uracil* (**7e**, $C_{13}H_{12}N_2O_3$)

Yield 0.85 g (33%), mp 277–278°C (ethanol); IR: $\bar{\nu} = 3200$, 1725, 1670, 1640 $cm^{-1}$; $^1H$ NMR: $\delta = 2.50$, 3.31 (2s, $2CH_3$), 7.52–7.72 (m, Ar–H), 7.80 (d, $J = 12.6$ Hz, =CH), 11.89 (bs, NH) ppm.

*3-Ethyl-5-(4-methylbenzoyl)uracil* (**7f**, $C_{14}H_{14}N_2O_3$)

Yield 1.70 g (66%), mp 274–275°C (*DMF* ethanol); IR: $\bar{\nu} = 3150$, 1725, 1660, 1650 $cm^{-1}$; $^1H$ NMR: $\delta = 1.07$ (s, $CH_3$), 2.50 (s, $CH_3$), 3.76 (q, $J = 7.5$ Hz, $CH_2$), 7.52–7.72 (m, Ar–H), 7.94 (d, $J = 12$ Hz, =CH), 11.89 (bs, NH) ppm.

*General Procedure for the Synthesis of Uracil Derivatives* **8a** and **8b**

To a stirred solution of 0.001 mol of **7** in 5 $cm^3$ of aqu. NaOH 0.001 mol *DMS* was added dropwise at 45°C and the mixture was stirred for 30 min. Then the reaction mixture was poured into 30 $cm^3$ of ice cold $H_2O$. The separated solid was filtered, washed with cold $H_2O$, and recrystallized.

*5-(4-Chlorobenzoyl)-1,3-dimethyluracil* (**8a**, $C_{13}H_{11}ClN_2O_3$)

Yield 0.15 g (54%), mp 170–171°C (methanol); IR: $\bar{\nu} = 1730$, 1660, 1640, 1600 $cm^{-1}$; $^1H$ NMR: $\delta = 3.36$, 3.53 (2s, $2CH_3$), 7.51–7.70 (m, Ar–H), 7.80 (s, =CH) ppm.

*1,3-Dimethyl-5-(4-methylbenzoyl)uracil* (**8b**, $C_{14}H_{14}N_2O_3$)

Yield 0.16 g (62%), mp 224–226°C (methanol); IR: $\bar{\nu} = 1720$, 1670, 1600 $cm^{-1}$; $^1H$ NMR: $\delta = 2.50$ (s, $CH_3$), 3.36, 3.53 (2s, $2CH_3$), 7.40–7.69 (m, Ar–H), 7.96 (s, =CH) ppm.

## Acknowledgements

The authors thanks to Nashik District Maratha Vidya Prasark Samaj's, Nashik, and Principal, K.R.T. Arts B.H. Commerce & A.M. Science college, Nashik for academic leave and facilities. *RBT* and *CDT* thank UGC for financial support and Dr. *V. Balasubramaniyam* for useful discussion.

## References

[1] Grover G, Dzwonczyk S, McMullen D, Normadinam C, Sleph P, Moreland S, Cardovase J (1998) Pharmaco **26**: 289

[2] Cho H, Ueda M, Shima K, Mizuno A, Hayashimatasu M, Ohnaka Y, Takeuchi Y, Hamaguchi M, Aisaka K, Hidalca T, Kawai M, Takada M, Ishihara T, Funahashi K, Satah F, Morita M, Naguchi T (1989) J Med Chem **32**: 2399

[3] Rovnyak G, Atwal K, Hedberg A, Kimball S, Moreland S, Gougoutas B, Reilly B, Schwartz J, Malley M (1992) J Med Chem **35**: 3254
[4] Atwal K, Swanson B, Unger S, Floyd D, Moreland S, Hedberg A, Reilly B (1991) J Med Chem **34**: 806
[5] Atwal K, Rovnyak G, Kimball S, Floyd D, Moreland S, Swanson B, Gougoutas B, Schwartz J, Malley M, Smillie K (1990) J Med Chem **33**: 2629
[6] Agrawal N, Raghuwanshi S, Upadhyay D, Shukla P, Ram V (2000) Biorg Med Chem Lett **10**: 70
[7] Overman L, Rabinowitz M, Renhowe P (1995) J Am Chem Soc **117**: 2657
[8] Jachak M, Mittelbach M, Junek H (1993) Heterocycles **36**: 3281
[9] Jachak M, Toche R, Dalvi T, Sabnis R, Kappe T, Junek H (1998) OPPI **30**: 367
[10] Mishara A, Yadav A, Singh G, Singh G (2002) Ind J Chem **41B**: 430