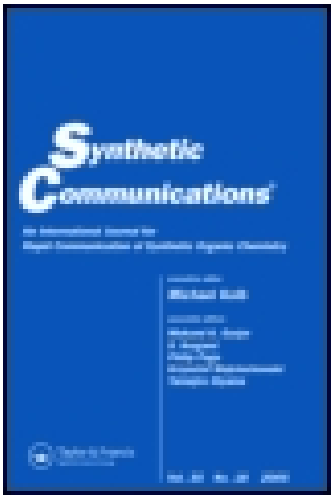


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Novel and Efficient Synthesis of Pyrimidine Derivatives

Maruti G. Ghagare [a], Dilip R. Birari [a], Deepak P. Shelar [a], Raghunath B. Toche [a] & Madhukar N. Jachak [a]

[a] Organic Chemistry Research Centre, Department of Chemistry, KTHM College, Nashik, India

Published online: 06 May 2010.

To cite this article: Maruti G. Ghagare, Dilip R. Birari, Deepak P. Shelar, Raghunath B. Toche & Madhukar N. Jachak (2010) Novel and Efficient Synthesis of Pyrimidine Derivatives, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 40:11, 1580-1587, DOI: 10.1080/00397910903108521

To link to this article: http://dx.doi.org/10.1080/00397910903108521

Synthetic Communications®, 40: 1580–1587, 2010

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910903108521

Taylor & Francis
Taylor & Francis Group

NOVEL AND EFFICIENT SYNTHESIS OF PYRIMIDINE DERIVATIVES

Maruti G. Ghagare, Dilip R. Birari, Deepak P. Shelar, Raghunath B. Toche, and Madhukar N. Jachak

Organic Chemistry Research Centre, Department of Chemistry, KTHM College, Nashik, India

A new series of 1-alkyl-2-oxo-1,2-dihydro-pyrimidine-5-carboxalic acid amides is described. The reaction of N-((E)-3-(dimethylamino)-2-formylacryloyl) formamidine, an intermediate obtained by Vilsmeier–Haack formylation of acetonitrile with various mono-substituted ureas, provides such compounds in good yields.

Keywords: Monosubstituted ureas; nucleophilic vinylic substitution; pyrimidine derivatives; synthesis

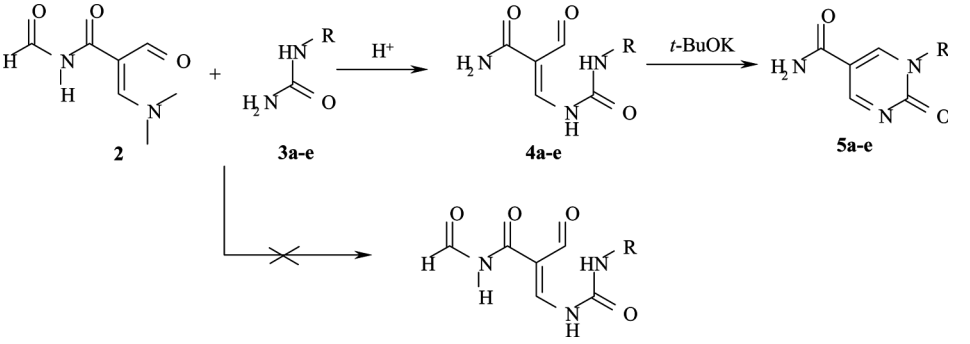
The reported methods for pyrimidine involves reaction of a 1,3-dicarbonyl component with a reagent bearing an N-C-N fragment such as urea,[1] amidine,[2] or guanidine.[3] The use of formamide or an orthoester in combination with ammonia[4] as a potential surrogate N-C-N reagent in the synthesis of pyrimidines has also been reported. A variety of β-dicarbonyl compounds,[5] tris-(formylamino)methanes,[6] and 3-methyl-5-nitro-3*H*-pyrimidin-4-ones[7] have been used as synthons for 1,3-dicarbonyl compounds in the synthesis.

In connection with our previous work,[8–10] we decided to study the reaction of substituted ureas with **2** as an attractive procedure for pyrimidines. In the synthesis of compounds **4a**–**e** (Scheme 1, Table 1), the first step of the reaction always proceeds via nucleophilic vinylic substitution (S_NV) of the activated dimethylamino methylene derivative. We first allowed **2** to react with 1.0 equiv of urea/*N*-substituted ureas **3a**–**e** in acidic medium at 50–60 °C for 4–5 h, and we were pleased to find that such reaction conditions afforded open chain compounds **4a**–**e** in 78–83% yield. During this condensation, it was observed that the N-formyl group in **2** undergoes hydrolysis to amido function to yield **4a**–**e**.

The ^{1}H NMR spectrum of **4a** revealed it to be 2-formyl-3-ureido-acrylamide. In the ^{1}H NMR spectrum of **4a,** the aldehyde proton resonated at δ 9.35, a doublet resonated at δ 11.46 corresponding to NH proton near to olefinic CH, and another doublet resonated at δ 8.20, representing the olefinic proton. The two NH_2 groups

Received January 18, 2009.

Address correspondence to Madhukar N. Jachak, Organic Chemistry Research Centre, Department of Chemistry, KTHM College, Gangapur Road, Nashik 422001, M.S., India. E-mail: mn_jachak@hotmail.com



Scheme 1. Reaction of compound **2** with substituted ureas.

appeared as four broad singlets at δ 8.15, 7.77, 7.52, and 7.28. In the ^{13}C NMR spectrum, a peak at δ 191.5 corresponding to aldehyde carbon was observed. Peaks at δ 167.0 and 157.8 represent two amide carbonyl carbons. The olefinic carbon resonated at δ 152.1, and the remaining carbon appeared at δ 107.8. The mass spectrum of **4** displayed the molecular ion (M^+) peak at 157 m/z, which is consistent with the molecular weight of **4a**. The structures of the other products **4b**–**e** were established on the basis of spectral analysis. (see Experimental data.)

In our attempts to cyclize **4a**–**e**, we discovered that treatment of a mixture of **4a**–**e** and triethylamine in acetonitrile at 60–70 °C produced **5a**–**e** in only 45–52% yield. Because the yields of the resulting pyrimidines **5a**–**e** were very low (Table 2), we decided to substitute triethyl amine with *t*-BuOk in methanol as an alternate base. Under these reaction conditions, **4a**–**e** were cyclized to substituted pyrimidines **5a**–**e** in 89–95% yield. No further improvements in yields were seen by changing other reaction conditions for the cyclization. The ^1H NMR spectrum of **5a** showed a singlet at δ 8.66 representing two olefinic protons, a broad singlet at δ 12.32 corresponding to ring NH proton, and the two broad singlets at δ 7.80 and 7.36 for the amide protons of NH_2. The ^{13}C NMR spectrum of **5a** showed five distinct signals in agreement with the proposed structure. The mass spectrum of **5a** displayed the molecular ion (M^+) peak at 139 m/z, which is consistent with the molecular weight of **5a**. All pyrimidine derivatives **5a**–**e** were characterized by spectral analysis. (see Experimental data.)

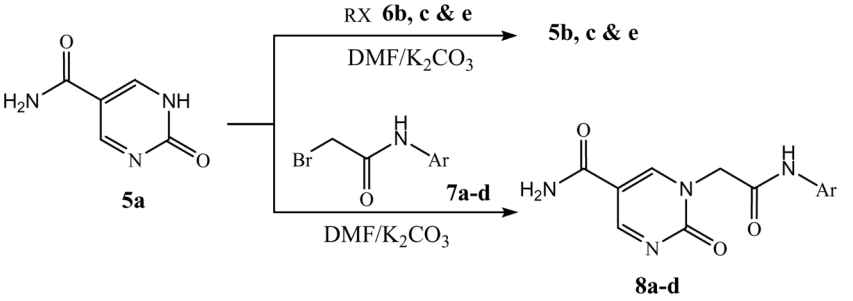
Alternatively, compounds **5b**, **c**, and **e** were prepared from **5a** by alkylation using dimethylformamide (DMF)/K_2CO_3 at room temperature (Scheme 2).

Table 1. Synthesis of **4a**–**e** and **5a**–**e**

3, **4**, **5**	R
a	-H
b	$-C_2H_5$
c	$-CH_2C_6H_5$
d	$-C_6H_5$
e	$-CH_2CH_2C_6H_5$

Table 2. Yield optimization of pyrimidine derivatives

5	R	TEA/CH_3CN (%)	*t*-BuOk/MeOH (%)
a	-H	45	89
b	$-C_2H_5$	47	92
c	$-CH_2C_6H_5$	52	95
d	$-C_6H_5$	50	90
e	$-CH_2CH_2C_6H_5$	47	93



Scheme 2. Synthesis of **5b**, **c**, **e** and **8a**–**d**.

However, attempts for arylation of **5a** with bromobenzene under similar reaction conditions were unsuccessful. Compound **5a** was further studied for *N*-alkylation reactions with substituted anilides **7a**–**d**. Thus, the condensation of 2-oxo-1,2-dihydro-pyrimidine-5-carboxalic acid amide **5a** with 1 equiv of anilide derivatives **7a**–**d** in DMF using K_2CO_3 proceeded smoothly at room temperature to obtain the corresponding *N*-substituted pyrimidines **8a**–**d** in 87–91% yield (Scheme 2, Table 3).

In conclusion, we have established a simple and scalable synthesis of pyrimidine derivatives using *N*-((*E*)-3-(dimethylamino)-2-formylacryloyl) formamidine as a convenient precursor. The simplicity and excellent yields make this method one of the most attractive approaches to the pyrimidine synthesis.

EXPERIMENTAL

Melting points were determined on a Buchi melting-point apparatus, model B-545, and are uncorrected. The ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a Varian XL-300 spectrometer. Chemical shifts are reported in

Table 3. Synthesis of compounds **8a**–**d**

7, 8	Ar
a	2,4-*di*-ClC_6H_3
b	4-Cl-3-$F_3CC_6H_3$
c	4-ClC_6H_4
d	4-FC_6H_4

parts per million (ppm) relative to tetramethylsilane (TMS), and multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). The solvent for NMR spectra was dimethylsulfoxide (DMSO-d_6) unless otherwise stated. Infrared (IR) spectra were taken on Thermo Electron Corporation Nicolet 380 Fourier transform (FT)–IR instrument in potassium bromide pellets unless otherwise stated. Mass spectrum was recorded on a Shimadzu GC-MS QP 2010A mass spectrometer with an ionization potential of 70 eV. Elemental analyses were performed on a Hosli CH-Analyzer and are within ±0.4 of the theoretical percentage. All reactions were monitored by thin-layer chromatography (TLC), carried out on 0.2-mm silica gel 60 F-254 (Merck) plates using ultraviolet (UV) light (254 and 366 nm) for detection. Common reagent-grade chemicals are either commercially available (and were used without further purification) or prepared by standard literature procedures.

General Procedure for the Synthesis of 4a–e

Concentrated hydrochloric acid (1.7 ml) was added to an equimolar solution of **2** (1.7 g, 10 mmol) and urea (0.6 g, 10 mmol) or *N*-substituted urea in ethanol (25 ml), and the mixture was heated to 50–60 °C for 4–5 h (TLC monitoring). After cooling, the precipitate was collected by filtration and recrystallized from ethanol to afford 1.25 g of **4a** as a yellow solid.

Selected Data

2-Formyl-3-ureido-acrylamide (4a). Yield: 80%; mp 194–197 °C; IR (KBr): 3365, 3164, 1728, 1670, 1574, 1446, 1419, 1322, 1259, 1210, 1023 cm^{-1}; ^1H NMR (300 MHz, DMSO): $\delta = 11.46$ (d, $J = 12$ Hz,1H, -NH), 9.35 (s, 1H, -CHO), 8.20 (d, $J = 12$ Hz, 1H, -CH), 8.15 (bs, 1H, -NH), 7.77 (bs, 1H, -NH), 7.52 (bs, 1H, -NH), 7.28 (bs, 1H, -NH); ^{13}C NMR (75 MHz, DMSO): $\delta = 191.5$, 167.0, 157.8, 152.1, 107.8; MS (ESI): $m/z = 157$ [M + H]. Anal. calcd. for $C_5H_7N_3O_3$: C, 38.22; H, 4.49; N, 26.75%. Found: C, 38.05; H, 4.20; N, 26.49%.

3-(3-Ethyl-ureido)-2-formyl-acrylamide (4b). White solid; 1.57 g, yield: 85%; mp 218–220 °C; IR (KBr): 3381, 3254, 3064, 2969, 1723, 1548, 1452, 1392, 1345, 1316, 1234, 1103 cm^{-1}; ^1H NMR (300 MHz, DMSO): $\delta = 11.61$ (d, $J = 12$ Hz, 1H, -NH), 9.23 (s, 1H, -CHO), 8.38 (t, $J = 5.1$ Hz, 1H, -NH), 8.24 (d, $J = 12$ Hz, 1H, -CH), 8.18 (bs, 1H, -NH), 7.54 (bs, 1H, -NH), 3.21 (m, 2H, $-CH_2$), 2.51(t, $J = 1.65$ Hz, 3H, $-CH_3$); ^{13}C NMR (75 MHz, DMSO): $\delta = 191.4$, 167.2, 157.6, 151.3, 107.6, 34.6, 14.6; MS (ESI): $m/z = 185$ [M + H]. Anal. calcd. for $C_7H_{11}N_3O_3$: C, 45.40; H, 5.99; N, 22.69%. Found: C, 45.11; H, 6.35; N, 23.00%.

3-(3-Benzyl-ureido)-2-formyl-acrylamide (4c). White solid; 1.92 g, yield: 78%; mp 190–192 °C; IR (KBr): 3392, 3278, 3145, 2721, 1681, 1542, 1497, 1469, 1447, 1401, 1308, 1222 cm^{-1}; ^1H NMR (300 MHz, DMSO): $\delta = 11.71$ (d, $J = 12$ Hz, 1H, -NH), 9.24 (s, 1H, -CHO), 8.88 (t, $J = 5.7$ Hz, 1H, -NH), 8.26 (d, $J = 12$ Hz, 1H, -CH), 8.17 (bs, 1H, -NH), 7.56 (bs, 1H, -NH), 7.37 (m, 5H, -ArH), 4.37 (d, $J = 5.4$ Hz, 2H, $-CH_2$); ^{13}C NMR (75 MHz, DMSO): $\delta = 191.6$, 167.1, 157.6, 151.7, 138.4, 128.3, 127.2, 127.0, 107.9, 43.3; MS (ESI): $m/z = 247$ [M + H]. Anal. calcd. for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30; N, 16.99%. Found: C, 57.95; H, 5.55; N, 17.35%.

2-Formyl-3-(3-phenyl-ureido)-acrylamide (4d). Yellow solid; 1.84 g, yield: 79%; mp 214–216 °C; IR (KBr): 3455, 3290, 3081, 3024, 2741, 1741, 1670, 1619, 1544, 1447, 1380, 1289, 1243 cm^{-1}; ^1H NMR (300 MHz, DMSO): $\delta = 11.89$ (d, $J = 11.7$ Hz, 1H, -NH), 10.62 (bs, 1H, -NH), 9.31 (s, 1H, -CHO), 8.34 (d, $J = 11.7$ Hz, 1H, -CH), 8.19 (d, $J = 3$ Hz, 1H, -NH), 7.66 (d, $J = 3$ Hz, 1H, -NH), 7.54 (m, 5H, ArH); ^{13}C NMR (75 MHz, DMSO): $\delta = 191.5$, 167.0, 156.5, 149.3, 142.2, 135.6, 132.4, 128.6, 125.3; MS (ESI): $m/z = 233$ [M + H]. Anal. calcd. for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.75; N, 18.02%. Found: C, 57.00; H, 4.53; N, 18.40%.

2-Formyl-3-(3-phenethyl-ureido)-acrylamide (4e). Yellow solid; 2.16 g, yield: 83%; mp 180–182 °C; IR (KBr): 3374, 3282, 3061, 3026, 2969, 1730, 1627, 1548, 1449, 1367, 1318, 1235 cm^{-1}; ^1H NMR (300 MHz, DMSO): $\delta = 11.55$ (d, $J = 12.3$ Hz, 1H, -NH), 9.20 (s, 1H, -CHO), 8.44 (t, $J = 5.4$ Hz, 1H, -NH), 8.20 (d, $J = 12.3$ Hz, 1H, -CH), 8.14 (d, $J = 3.0$ Hz, 1H, -NH), 7.52(d, $J = 3.0$ Hz, 1H, -NH), 7.31 (m, 5H, -ArH), 3.43 (q, $J = 7.2$ Hz, 2H, $-CH_2$), 2.79 (t, $J = 7.2$ Hz, $-CH_2$); ^{13}C NMR (75 MHz, DMSO): $\delta = 191.5$, 167.1, 157.5, 151.5, 138.9, 128.5, 128.2, 126.1, 107.7, 41.0, 35.0; MS (ESI): $m/z = 261$ [M +H]. Anal. calcd. for $C_{13}H_{15}N_3O_3$: C, 59.76; H, 5.79; N, 16.08%. Found: C, 58.92; H, 6.10; N, 16.24%.

General Procedure for the Synthesis of 5a–e

A mixture of **4a–e** (1.5 g, 10 mmol) and *t*-BuOK (1.12 g, 10 mmol) in methanol (50 ml) was heated to 55–60 °C for 4–5 h (TLC monitoring). The solvent was removed in vacuo at 50 °C. The residue was suspended in water (30 ml), pH was adjusted to 4–5 with acetic acid, and the solid was collected by filtration to give 1.23 g of **5a** as a brown solid.

Selected Data

2-Oxo-1,2-dihydro-pyrimidine-5-carboxalic acid amide (5a). Yield: 89%; mp 297–300 °C; IR (KBr): 3360, 3196, 3053, 2959, 2918, 2815, 1671, 1618, 1550, 1430, 1383, 1359, 1227 cm^{-1}; ^1H NMR (300 MHz, DMSO): $\delta = 12.32$ (bs, 1H, -NH), 8.66 (s, 2H, -CH), 7.80 (bs, 1H, -NH), 7.36 (bs, 1H, -NH); ^{13}C NMR (75 MHz, DMSO): $\delta = 163.7$, 155.7, 153.5, 135.0, 110.5; MS (ESI): $m/z = 139$ [M + H]. Anal. calcd. for $C_5H_5N_3O_2$: C, 43.17; H, 3.62; N, 30.21%. Found: C, 43.38; H, 3.35; N, 29.88%.

1-Ethyl-2-oxo-1,2-dihydro-pyrimidine-5-carboxalic acid amide (5b). Yellow solid; 1.53 g, yield: 92%; mp 176–178 °C; IR (KBr): 3368, 3213, 2985, 2214, 1704, 1650, 1602, 1524, 1449, 1391, 1265 cm^{-1}; ^1H NMR (300 MHz, DMSO): $\delta = 8.92$ (d, $J = 3$ Hz 1H, -CH), 8.72 (d, $J = 3$ Hz 1H, -CH), 7.83 (bs, 1H, -NH), 7.41 (bs, 1H, -NH), 3.94 (q, $J = 7.1$ Hz 2H, $-CH_2$), 1.28 (t, $J = 6.9$ Hz 3H, $-CH_3$); ^{13}C NMR (75 MHz, DMSO): $\delta = 164.0$, 163.5, 154.7, 150.9, 111.0, 46.4, 13.8; MS (ESI): $m/z =$ 167 [M + H]. Anal. calcd. for $C_7H_9N_3O_2$: C, 50.30; H, 5.43; N, 25.14%. Found: C, 50.75; H, 5.15; N, 24.89%.

1-Benzyl-2-oxo-1,2-dihydro-pyrimidine-5-carboxalic acid amide (5c). Colorless solid; 2.17 g, yield: 95%; mp 224–226 °C; IR (KBr): 3325, 3161, 2793, 2164, 1949, 1673, 1520, 1494, 1445, 1455, 1411, 1375, 1220, 1135 cm^{-1}; ^1H NMR

(300 MHz, DMSO): $\delta = 8.99$ (d, $J = 3$ Hz, 1H, -CH), 8.88 (d, $J = 3$ Hz, 1H, -CH), 7.90 (bs, 1H, -NH), 7.47 (bs, 1H, -NH), 7.36 (m, 5H, -ArH), 5.11 (s, 2H, $-CH_2$); ^{13}C NMR (75 MHz, DMSO): $\delta = 164.4$, 163.4, 154.8, 151.3, 135.6, 128.5, 127.9, 127.8, 111.3, 53.8; MS (ESI): $m/z = 229$ [M + H]. Anal. calcd. for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.84; N, 18.33%. Found: C, 62.35; H, 4.50; N, 18.59%.

2-Oxo-1-phenyl-1,2-dihydro-pyrimidine-5-carboxylic acid amide (5d). Colorless solid; 1.93 g, yield: 90%; mp 256–259 °C; IR (KBr): 3303, 3142, 3057, 1892, 1685, 1515, 1454, 1435, 1372, 1284, 1178, 1133 cm^{-1}; ^{1}H NMR (300 MHz, DMSO): $\delta = 9.05$ (d, $J = 3.3$ Hz, 1H, -CH), 8.68 (d, $J = 3.3$ Hz, 1H, -CH), 7.84 (bs, 1H, -NH), 7.58 (m, 5H, -ArH), 7.45 (bs, 1H, -NH). ^{13}C NMR (75 MHz, DMSO): $\delta = 165.0$, 162.5, 155.0, 143.7, 134.5, 131.6, 129.0, 124.8, 111.7; MS (ESI): $m/z = 215$ [M + H]. Anal. calcd. for $C_{11}H_9N_3O_2$: C, 61.39; H, 4.22; N, 19.52%. Found: C, 61.70; H, 4.51; N, 19.78%.

2-Oxo-1-phenethyl-1,2-dihydro-pyrimidine-5-carboxylic acid amide (5e). Colorless solid; 2.25 g, yield: 93%; mp 224–226 °C; IR (KBr): 3369, 3157, 3029, 2167, 1674, 1514, 1452, 1416, 1381, 1325, 1267, 1191 cm^{-1}; ^{1}H NMR (300 MHz, DMSO): $\delta = 8.92$ (d, $J = 3.0$ Hz, 1H, -CH), 8.55 (d, $J = 3.0$ Hz, 1H, -CH), 7.77 (bs, 1H, -NH), 7.37 (bs, 1H, -NH), 7.30 (m, 5H, -ArH), 4.13 (t, $J = 7.3$ Hz, 2H, $-CH_2$), 3.02 (t, $J = 7.3$ Hz, 2H, $-CH_2$); ^{13}C NMR (75 MHz, DMSO): $\delta = 164.1$, 163.4, 154.8, 151.4, 137.4, 128.7, 128.7, 128.4, 128.4, 126.5, 110.8, 52.5, 33.7; MS (ESI): $m/z = 243$ [M + H]. Anal. calcd. for $C_{13}H_{13}N_3O_2$: C, 64.19; H, 5.39; N, 17.27%. Found: C, 64.52; H, 5.64; N, 17.45%.

General Procedure for the Synthesis of 8a–d

A mixture of **5a** (0.5 g, 3.5 mmol), K_2CO_3(0.48 g, 3.5 mmol), and **7a** (0.99 g, 3.5 mmol) in DMF (5 ml) was stirred at 40–45 °C for 8–10 h (TLC monitoring). Reaction mass was then quenched in ice-cold water; the precipitated solid was collected by filtration, washed with water, and recrystallized from ethanol to afford **8a** (1.04 g, 86%).

Selected Data

1-[(2,4-Dichloro-phenylcarbamoyl)-methyl]-2-oxo-1,2-dihydro-pyrimidine-5-carboxylic acid amide (8a). Off-white solid; yield: 86%; mp 240–245 °C (decom.); IR (KBr): 3280, 1677, 1620, 1583, 1520, 1476, 1386, 1326, 1290, 1255, 1195 cm^{-1}; ^{1}H NMR (300 MHz, DMSO): $\delta = 10.12$ (bs, 1H, -NH), 9.01 (d, $J = 3.0$ Hz 1H, -CH), 8.74 (d, $J = 3.0$ Hz 1H, -CH), 7.90 (bs, 1H, -NH), 7.79 (m, 3H, -ArH), 7.55 (bs, 1H, -NH), 4.95 (s, 2H, $-CH_2$); ^{13}C NMR (75 MHz, DMSO): $\delta = 165.5$, 164.7, 163.4, 154.9, 152.9, 133.4, 129.4, 128.9, 127.5, 126.7, 126.6, 111.0, 53.3; MS (ESI): $m/z = 341$ [M + H]. Anal. calcd. for $C_{13}H_{10}Cl_2N_4O_3$: C, 45.77; H, 2.95; N, 16.42%. Found: C, 45.45; H, 2.72; N, 17.16%.

1-[(4-Chloro-3-trifluoromethyl-phenylcarbamoyl)-methyl]-2-oxo-1,2-dihydro-pyrimidine-5-arboxylic acid amide (8b). Yellow solid; 1.11 g, yield: 83%; mp 285–287 °C (decom.); IR (KBr): 3400, 3190, 3071, 1657, 1604, 1564,

1522, 1489, 1429, 1391, 1321 cm^{-1}; ^1H NMR (300 MHz, DMSO): $\delta = 10.89$ (bs, 1H, -NH), 9.04 (d, $J = 3.3$ Hz, 1H, -CH), 8.75 (d, $J = 3.3$ Hz, 1H, -CH), 7.94 (bs, 1H, -NH), 7.78 (m, 3H, -ArH), 7.49 (bs, 1H, -NH), 4.82 (s, 2H, $-CH_2$); ^{13}C NMR (75 MHz, DMSO): $\delta = 165.3$, 164.7, 163.3, 154.8, 152.8, 137.7, 132.1, 132.0, 128.5, 124.2, 123.7, 117.4, 111.0, 53.5; MS (ESI): $m/z = 374$ [M + H]. Anal. calcd. for $C_{14}H_{10}ClF_3N_4O_3$: C, 44.88; H, 2.69; N, 14.95%. Found: C, 45.15; H, 3.00; N, 15.20%.

1-[(4-Chloro-phenylcarbamoyl)-methyl]-2-oxo-1,2-dihydro-pyrimidine-5-carboxylic acid amide (8c). Brown solid; 0.96 g, yield: 87%; mp 215–220 °C (decom.); IR (KBr): 3291, 2927, 1666, 1599, 1524, 1492, 1401, 1304, 1250, 1092, 1013 cm^{-1}; ^1H NMR (300 MHz, DMSO): $\delta = 10.57$ (bs, 1H, -NH), 9.03 (d, $J = 3.3$ Hz, 1H, -CH), 8.74 (d, $J = 3.3$ Hz, 1H, -CH), 7.93 (bs, 1H, -NH), 7.63 (m, 4H, -ArH), 7.59 (bs, 1H, -NH), 4.80 (s, 2H, $-CH_2$); ^{13}C NMR (75 MHz, DMSO): $\delta = 164.7$, 163.4, 162.2, 154.9, 152.9, 137.3, 128.7, 127.1, 120.5, 111.0, 53.6; MS (ESI): $m/z = 306$ [M + H]. Anal. calcd. for $C_{13}H_{11}ClN_4O_3$: C, 50.91; H, 3.62; N, 18.27%. Found: C, 51.28; H, 3.88; N, 18.49%.

1-[(4-Fluoro-phenylcarbamoyl)-methyl]-2-oxo-1,2-dihydro-pyrimidine-5-carboxylic acid amide (8d). White solid; 0.93 g, yield: 90%; mp 252–255 °C; IR (KBr): 3369, 3206, 3163, 3094, 2951, 1655, 1612, 1578, 1512, 1426, 1389 cm^{-1}; ^1H NMR (300 MHz, DMSO): $\delta = 10.49$ (bs, 1H, -NH), 9.02 (d, $J = 3.3$ Hz 1H, -CH), 8.73 (d, $J = 3.3$ Hz 1H, -CH), 7.92 (bs, 1H, -NH), 7.59 (m, 4H, -ArH), 7.47 (bs, 1H, -NH), 4.78 (s, 2H, $-CH_2$); ^{13}C NMR (75 MHz, DMSO): $\delta = 165.7$, 164.4, 162.9, 155.0, 149.3, 134.5, 129.7, 128.2, 118.1, 111.0, 53.5; MS (ESI): $m/z = 290$ [M + H]. Anal. calcd. for $C_{13}H_{11}FN_4O_3$: C, 53.80; H, 3.82; N, 19.30%. Found: C, 54.14; H, 3.60; N, 19.55%.

ACKNOWLEDGMENTS

The authors gratefully acknowledge financial support of this project by the University Grants Commission, New Delhi, India. We also thank Dr. V. B. Gaikwad for his valuable cooperation.

REFERENCES

1. Sherman, W. R.; Taylor, E. C. Diaminouracil hydrochloride. *Org. Synth.* **1963**, *4*, 247–248.
2. Kenner, G. W.; Lythgoe, B.; Todd, A. R.; Topham, A. Some reactions of amidines with derivatives of malonic acid. *J. Chem. Soc.* **1943**, 388–390.
3. VanAllan, J. A. 2,4-Diamino-6-hydroxypyrimidine. *Org. Synth.* **1963**, *4*, 245.
4. Bredereck, H.; Gompper, R.; Morlock, G. Eine neue pyrimidin-synthese. *Chem. Ber.* **1957**, *90*, 942–951.
5. Bredereck, H.; Gompper, R.; Herlinger, H. G. Darstellung, eigenschaften und umsetzungen des pyrimidins. *Chem. Ber.* **1958**, *91*, 2832–2848.
6. Bredereck, H.; Gompper, R.; Schuh, H. G.; Theilig, G. Neuere Methoden der praparativen organischen Chemie II, 16: Synthesen mit Saure-amiden, insbesondere mit formamide. *Angew. Chem.* **1959**, *71*, 753–774.

7. Nishiwaki, N.; Adachi, T.; Matsuo, K.; Wang, H.; Matsunaga, T.; Tohda, T.; Ariga, M. Two ring transformations of 3-methyl-5-nitropyrimidin-4(3*H*)-one for the construction of azaheterocycles. *J. Chem. Soc., Perkin Trans. 1* **2000**, *1*, 27–31.
8. Jachak, M.; Avhale, A.; Tantak, C.; Toche, R.; Reidlinger, C.; Stadlbauer, W. Friedlander condensation of 5-aminopyrazole-4-carbaldehydes with reactive α-methylene detones: Synthesis of pyrazolo[3,4-*b*]pyridines. *J. Heterocycl. Chem.* **2005**, *42*, 1311–1319.
9. Jachak, M.; Avhale, A.; Medhane, V.; Toche, R. A convenient route for the synthesis of pyrazolo[3,4-*b*]pyrimidine, pyrazolo[3,4-*b*][1,6]naphthyridine, and pyrazolo[3,4-*b*] quinoline derivatives. *J. Heterocycl. Chem.* **2006**, *43*, 1169–1175.
10. Jachak, M.; Avhale, A.; Toche, R.; Sabnis, R. Synthesis of pyrazolo-annelated heterocyclic ring compounds such as pyrazolo[3,4-*b*]pyridines and pyrazolo[4′,3′:5,6]-pyrido[2,3-*d*]pyrimidines. *J. Heterocycl. Chem.* **2007**, *44*, 343–347.