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Synthesis of some novel-4-aryl-5-(carboxamido-N-pyridin-2'-yl)-6-methyl-2-Thioxos 1,3,5-trihydro-pyrimidines

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ABSTRACT

Starting material 3-oxo-N-Pyridin-2-yl butyramide have been synthesized by the reaction of 2-amino Pyridine and ethylacetoacetate. This is undergoes cyclization with thiourea & different aromatic aldehyde to yield desired pyrimidines **(3a-i)**. The compounds are expected to have antiviral activity. © 2011 Trade Science Inc. - INDIA

KEYWORDS

Pyrimidines

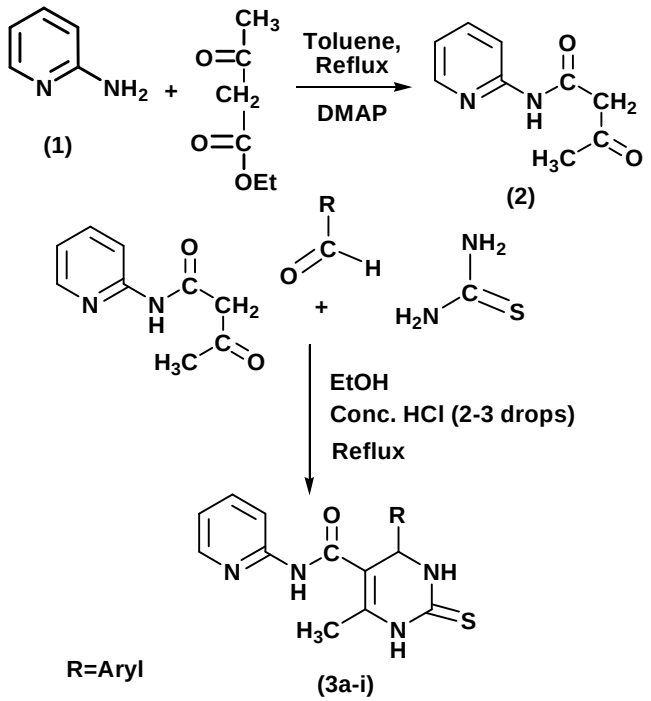
INTRODUCTION

Pyrimidine derivatives have wide variety of usages pyrimidine ring system is also present in Vitamin-B_2 & folic acid. Pyrimidine ring system having a mercapto group occupy a unique position in medicinal chemistry[1]. These types of derivative play a vital role in biological process[2-4] as well as synthetic drug[5].

Various Pyrimidine derivatives have claimed to possess a wide range of biological activity Viz. antitubercular[6], antitumor[7], antihypertensive[8] and anti-HIV[9] etc. Lead by these considerations it appeared of interest to synthesize some Novel Pyrimidines.

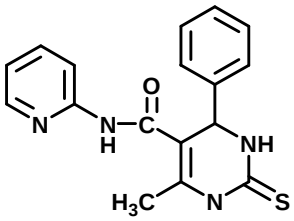
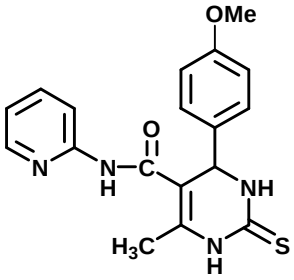
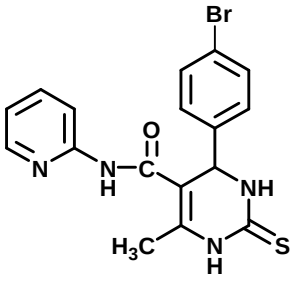
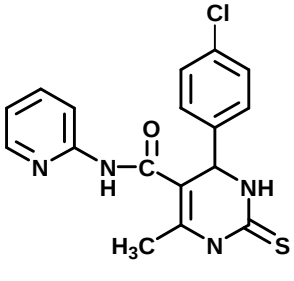
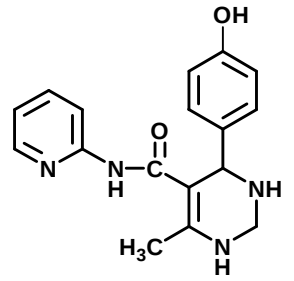
This title compounds **(3a-i)** and it's analogs were prepared by method outlined in Scheme 1. The starting material 3-oxo-N-Pyridin-2-yl-butyramide **(2)** was prepared by the reaction of 2-amino-Pyridine **(1)** & ethylacetoacetate in present of catalytic amount strong nucleophilic agent N,N-Dimethylamino pyridine (DMAP) to get in good yield. The starting material **(2)** undergoes Biginelli reaction with different aromatic aldehyde and thiourea to yield desired Pyrimidine **(3a-i)**.

The purity & structures of Pyrimidines products **(3a-i)** was established on the basis of their spectral (IR & ^{1}H NMR) data and TLC. The IR & ^{1}H NMR data are summarized in TABLE 1.



Scheme 1

TABLE 1 : Physical & spectral data of 4-Aryl-5-(Carboxamido-N-Pyridin-2[1]-yl)-6-methyl-2-thioxo-1,3,5-Trihydro pyrimidines (3a-i)

Sr. No.	R	Product	NMR Data	IR Data	M.P. °C	Yield %
3a	C_6H_5	 3a	^{1}H NMR (300 MH$_z$, DMSO-d$_6$) : δ 2.10 (S, 3H-CH$_3$), 5.41 (S, 1H, -CH), 7.08-8.28 (m,9H,Ar-H), 9.50 (S, 1H-CO-NH), 10.08 (S, 1H,NH), 10.15 (S, 1H, NH)	3265,3177 (-NH-Stretching), 1678 (-C=O-stretching), 1650 (-C-N-stretching, pyrimidine)	253°C	75.0%
3b	4-OCH$_3$-C_6H_4	 3b	^{1}H NMR (300 MH$_z$, DMSO-d$_6$) : δ 2.11 (S, 3H-CH$_3$), 3.71 (S, 3H, -OCH$_3$), 5.40 (S, 1H,-CH), 6.91-8.28 (m, 8H, Ar-H), 9.4 (S,1H,CO-NH), 9.99 (S, 1H-NH), 10.21 (S, 1H,NH)	3250, 3189 (-NH stretching Sec. amine, 1673 (C=O-stretching, amide). 1653 (C-Nstretching, Pyrimidine).	243°C	72.0%
3c	4-Br-C_6H_4	 3c	^{1}H NMR (300 MH$_z$, DMSO-d$_6$) : δ 2.09 (S, 3H, -CH3), 5.41 (S, 1H,CH), 7.04-8.28 (m,8H,Ar-H), 9.50 (S, 1H-CO-NH), 10.10 (S, 1H,NH), 10.15 (S, 1H,NH)	3250, 3165 (-NH stretching, sec. amine, 1680 (C=O-stretching, amide). 1652 (C-N stretching, Pyrimidine).	238°C	65.0%
3d	4-Cl-C_6H_4	 3d	^{1}H NMR (300 MH$_z$, DMSO-d$_6$) : δ 2.10 (S, 3H, -CH$_3$), 5.41 (S, 1H,-CH), 7.04-8.28 (m,8H, Ar-H), 9.50 (S, 1H,CO-NH), 10.10 (S, 1H,NH), 10.15 (S, 1H,-NH)	3260,3180 (-NH Stretching, sec. amine, 1680 (-C=O-stretching, amide), 1652 (C-N-stretching, pyrimidine)	245°C	78.0%
3e	4-OH-C_6H_4	 3e	^{1}H NMR (300 MH$_z$, DMSO-d$_6$) : δ 2.11 (S, 3H, CH$_3$), 5.45 (S,1H-CH), 6.95-8.28 (m,8H, Ar-H), 9.45 (S, 1H, OH), 9.52 (S, 1H,CO-NH), 10.10 (S, 1H, NH), 10.16 (S, 1H, NH)	3252, 3189 (-NH stretching sec. amine, 3302 (-OH stretching, Ar-OH), 1688 (-C=O-stretching amide), 1653 (C-N stretching, pyrimidine)	254°C	70.0%

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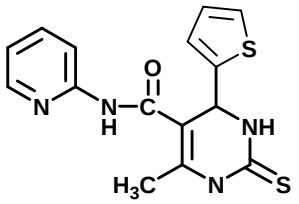
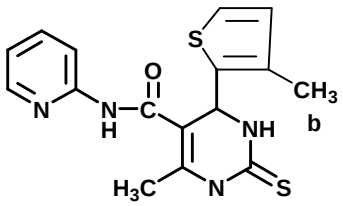
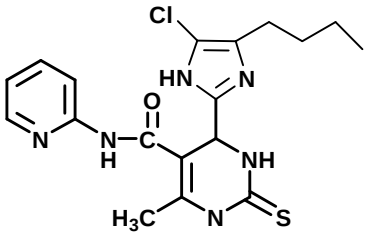
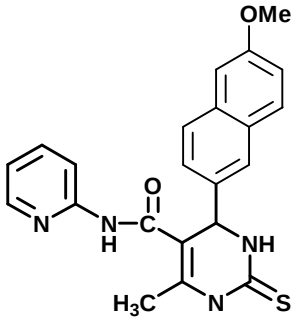
Sr. No.	R	Product	NMR Data	IR Data	M.P. °C	Yield %
3f	C_4H_3S	 3f	^{1}H NMR (300 MH$_z$, DMSO-d$_6$) : δ 2.10 (S,3H, CH_3),5.80 (S,1H,CH), 6.70-8.28 (m,7H,Ar-H), 9.51 (S, 1H,CO-NH), 10.13 (S, 1H,NH), 10.17 (S,1H,NH)	3265,3191 (-NH stretching, sec. amine, 1675 (-C=O-stretching, amide), 1650 (C-N-stretching, pyrimidine)	240°C	62.0%
3g	3-CH_3-C_4H_2	 a 3g	^{1}H NMR (300 MH$_z$, DMSO-d$_6$) : δ 2.10 (S, 3H, -CH_3a), 2.17 (S, 3H,CH_3b), 5.80 (S, 1H,CH), 6.75-8.25 (m, 6H,Ar-H), 9.51 (S, 1H, CO-NH), 10.13 (S, 1H, NH), 10.17 (S,1H,NH)	3230, 3180 (-NH-Stretching, Sec. Amine), 1677 (C=O-Stretching, amide), 1650 (C-N stretching, pyrimidine).	248°C	67.0%
3h	5-Cl-4-C_4H_9-C_3HN_2	 3h	^{1}H NMR (300 MH$_z$, DMSO-d$_6$) : δ 1.12 (t,3H,CH_3), 1.61 (q,2H-CH_2b), 1.93 (m, 2H-CH_2b), 2.12 (S,3H-CH_3), 2.58 (t-2H, CH_d), 4.65 (S, 1H-CH), 7.1-8.28 (m-4H, Ar-H), 9.50 (S,1H-CO-NH), 10.1 (S, 1H,NH), 10.15 (S,1H,-NH)	3270,3185 (-NH stretching sec. amine, 1678(-C=O-stretching, Amide),1652 (C-N, Stretching, Pyrimidine)	226°C	71.0%
3i	6-OCH_3-$C_{10}H_6$	 3i	^{1}H NMR (300 MH$_z$, DMSO-d$_6$) : δ 2.10 (S,3H,CH_3), 5.40 (S,1H,CH), 7.01-8.25 (m,10H, Ar-H), 9.50 (S, 1H,-CO-NH), 10.0 (S, 1H,NH), 10.11 (S,-1H,-NH)	3250, 3160 (-NH stretching, sec. amine, 1680 (-C=O-stretching, amide), 1653 (C-N-stretching, pyrimidine).	232°C	79.0%

EXPERIMENTAL

Melting points were determined on Buchi B-545 melting point apparatus and are uncorrected. IR spectrum was recorded in KBr on a Perkin Elmer spectrometer, ^{1}H NMR was recorded in DMSO-d$_6$ using 300 MHZ bruker spectrometer (Chemical shift in δppm) with TMS as internal standard. The TLC was performed on precoated silica gel sheets obtained from Merck & Co., Germany, which were visualizing using U.V. light and Iodine. The analytical Research Department of Ipca Labs. Ltd. (Kandivali, Mumbai) carried out all analytical work.

Preparation of 3-Oxo-N-Pyridin-2-yl-butyramide (2)

A mixture of 2-amino pyridine (50gm, 0.531 mole), ethylacetoacetate (76gm, 0.584 mole) and N,N-Dimethylaminopyridine (5gm) in toluene (500ml) was heated under reflux condition for 15 hrs. Collect ethanol azeotropically by dean stark apparatus. The reaction was monitoring by TLC (solvent system: Ethyl acetate 100%) after completion of reaction, distilled out half of the toluene under vacuum. Cool the reaction mass at 5-10°C for 2-3 hrs to precipitate out the solid. The solid crystalline material was filtered and washes with cold toluene to give 2. Yield 86%, M.P 98°C.

IR(Cm^{-1}) : 3189 (N-H Str,), 3054 (C-H- Str. Ar-H), 2967, 2923 (C-H Str. Alkane), 1720, 1665 (C=O

Str.), 1615 (N-H, deformation).

Preparation of 4-(4-methoxy phenyl)-5-(carboxamido-N-pyridin-2'-yl)-6-methyl-2-thioxo-1,3,5-trihydro pyrimidine (3b)

A mixture of 3-oxo-N-pyridine-2-yl-butyramide (2gm, 0.011mole), Thiourea (0.74gm, 0.0123mole), p-methoxy Benzaldehyde (1.7gm, 0.0124 moles) and Conc. Hydrochloric acid (2-3 drops) was heated under reflux condition in ethanol (20ml) for 12 hrs. Reaction was monitoring by TLC (Solvent system: 20% methanol: 80% toluene). Reaction mass was kept in deep freezer for 10 hrs. Filter the yellow crystalline product. Yield 72%, M.P.243°C.The spectral data are outline in TABLE 1.

Similarly other compounds **(3a-i)** were prepared.

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REFERENCES

[1] S.C.Nigam, G.S.Saharia, H.R.Sharma; Ind.Chem. Soc., **60**, 583 **(1983)**.
[2] J.Baddilay, B.Lythgoe, A.R.Todd; J.Chem.Soc., 318 **(1944)**.
[3] G.W.Kenner, B.Lythgoe, A.R.Todd; J.Chem.Soc., 652 **(1944)**.
[4] J.Baddilay, G.W.Kenner, B.Lythgoe, A.R.Todd; J.Chem.Soc., 657 **(1944)**.
[5] A.P.Contolella, J.W.Nelson, H.G.Kolloff; J.Am. Chem.Soc., **65**, 209 **(1943)**.
[6] M.K.Jain, B.R.Shuh, N.K.Undavia, P.B.Trivedi; Chem.Abstr., **121**, 35513P **(1994)**.
[7] C.C.Heidelberger et al.; Scheiner Nature, **179**, 663 **(1957)**.
[8] R.K.Rushell et al., J.Med.Chem., **31**, 1986 **(1988)**.
[9] P.Steilbuck, R.Baltzyl, M.M.Hood; J.Org.Chem., **28**, 1963 **(1983)**.
[10] M.Okabe et al.; J.Org.Chem., **56**, 4393 **(1991)**.