



## **A NOVEL SYNTHESIS OF SUBSTITUTED PYRIMIDINO-3-SUBSTITUTED THIOCARBAMIDES**

**D. T. TAYADE<sup>\*</sup>, D. A. PUND<sup>a</sup>, R. A. BHAGWATKAR and S. U. PATIL**

Department of Chemistry, S. R. R. L. Science College, MORSHI - 444 905 (M.S.) INDIA

<sup>a</sup>Department of Chemistry, Javaharlal Darda Inst. of Engg. and Technology, LOHARA, Dist. Yevatmal (M.S.) INDIA

### **ABSTRACT**

Pyrimidines, thiocarbamides and various analogue of pyrimidino containing nucleus have their own importance in medicinal, pharmaceutical, agricultural and biochemical sciences. So, it was thought interesting to synthesize 2-amino-4-hydroxy-6-methylpyrimidine by interacting guanidine with acetoacetic ester and its reaction with various isothiocyanates in acetone-ethanol medium. 1-(4-Hydroxy-6-methylpyrimidino)-3-substitutedthiocarbamide was isolated as final product with greater yield and purity.

**Key words:** Guanidine, Substituted thiocarbamide, Acetoacetic ester, Isothiocyanates, Pyrimidines.

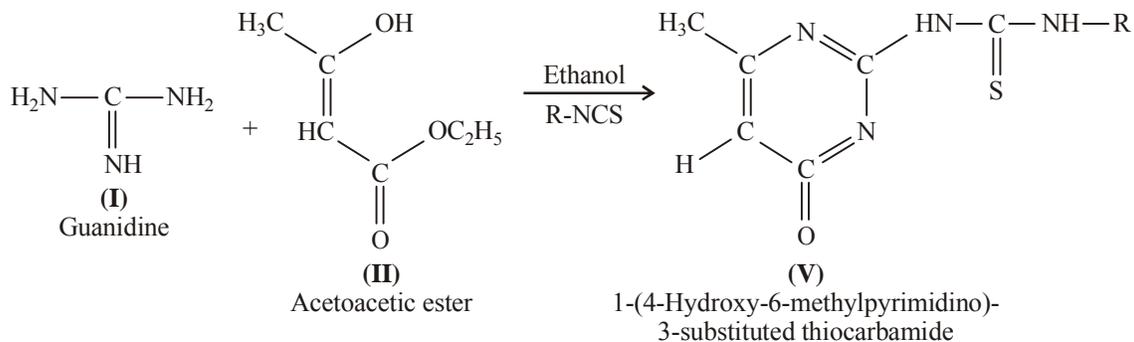
### **INTRODUCTION**

The literature survey reveals that pyrimidino and thiocarbamido nucleus containing heterocycles possesses pharmaceutical, medicinal, agricultural, industrial and biotechnological significance<sup>1-5</sup>. Hence, it was thought interesting to synthesize such drug, which possesses pyrimidino as well as thiocarbamido nucleus in the same molecule. Recently in this laboratory, 2-amino-4-hydroxy-6-methylpyrimidine was successfully condensed with various isothiocyanates in acetone, ethanol and dioxane media to obtain 1-(4-hydroxy-6-methylpyrimidino)-3-substituted thiocarbamides<sup>6</sup>. But, when this reaction mixture was condensed in acetone-ethanol mediums in 1 : 1 molar ratio, the yield and purity increases and the time span also decreases.

The structure determination of compound was carried out by chemical characteristics and elemental and spectral analysis.

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\* Author for correspondence; E-mail: bhagwatkar83@gmail.com

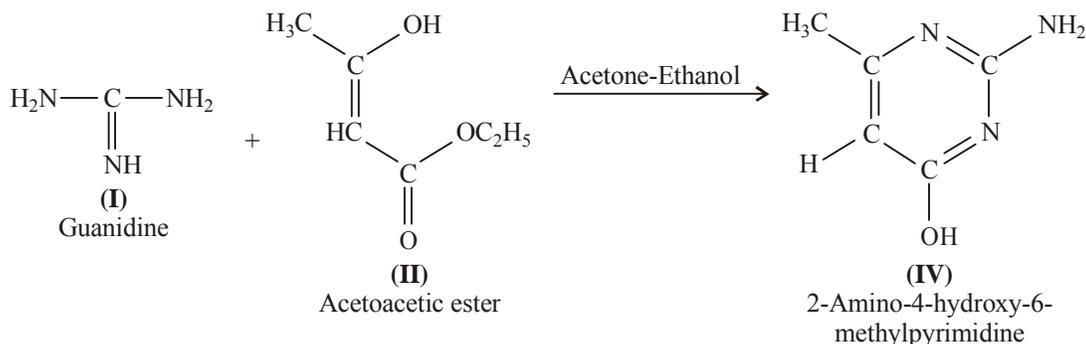


## EXPERIMENTAL

All the chemicals used were of Analar grade (India make). Alkyl/arylisothiocyanates were prepared according to literature method<sup>7</sup>. Melting points of all synthesized compounds were determined in open capillary and uncorrected. IR spectra were recorded on Perkin-Elmer spectrophotometer in the range 4000-400  $\text{cm}^{-1}$  in KBr pellets. PMR spectra were recorded with TMS as internal standard using  $\text{CDCl}_3$  and  $\text{DMSO}-d_6$ . The purity of the compounds was checked on silica gel-G plates by TLC.

### Synthesis of 2-amino-4-hydroxy-6-methyl pyrimidine (IV)

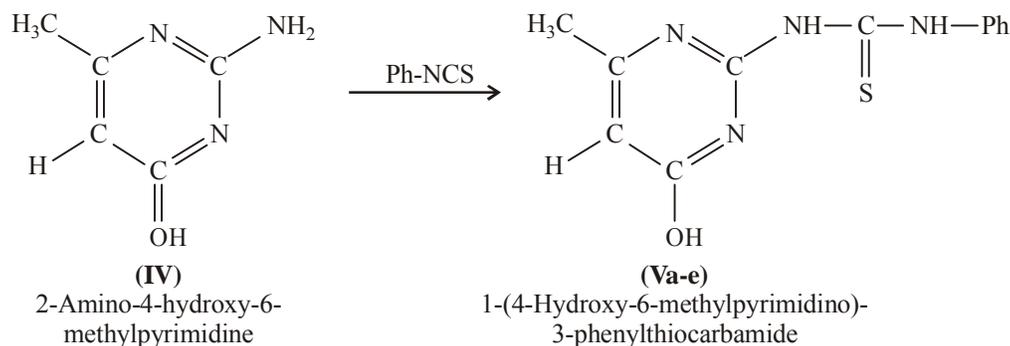
The interaction of guanidine and acetoacetic ester had been carried out on water bath in acetone-ethanol medium for eight hours. The separated solid was filtered. It was crystallized by precipitation method. (By precipitating it with acetic acid from its alkaline solution).



### Synthesis of 1-(4-hydroxy-6-methylpyrimidino)-3-phenylthiocarbamide (Va)

The interaction of 2-amino-4-hydroxy-6-methyl pyrimidine with phenylisothiocyanate has been carried out in acetone-ethanol medium in 1 : 1 molar proportion on the a

boiling water bath for four hours. A brownish white solid has been isolated. It was filtered, washed several times with water and crystallized with ethanol.



Similarly, 1-(4-hydroxy-6-methylpyrimidino)-3-p-chloro-phenyl-thiocarbamide (**Vb**), 1-(4-hydroxy-6-methylpyrimidino)-3-p-tolyl-thiocarbamide (**Vc**), 1-(4-hydroxy-6-methylpyrimidino)-3-methyl-thiocarbamide (**Vd**) and 1-(4-hydroxy-6-methylpyrimidino)-3-t-butyl-thiocarbamide (**Ve**) were synthesized by interacting 2-amino-4-hydroxy-6-methylpyrimidine with p-chloro-phenylisothiocyanate, p-tolylisothiocyanate, methylisothiocyanate and t-butylisothiocyanate in same reaction conditions. The products isolated are given in Table 1.

**Table 1**

| 1-(4-Hydroxy-6-methylpyrimidino)-3-substituted- thiocarbamide | Yield (%) | m.p. (°C) |
|---|-----------|-----------|
| p-Chlorophenyl  | 73        | 112       |
| p-Tolyl   | 68        | 178       |
| Methyl  | 87        | 129       |
| t-Butyl   | 56        | 101       |

Experimental data for **(IV)** (5.3 g, 82 %), m.p. 195°C. It is soluble in hot water, sodium hydroxide, hydrochloric acid sulphuric acid and nitric acid while it is insoluble in benzene, ether, chloroform and alcohol. When hot aqueous compound was treated with aqueous ferric chloride, red colouration was observed indicating the presence of a phenolic group. It formed picrate (m.p. 205°C). The product gave dye test indicating presence of aromatic amino group. Found C-46.28, H - 03.49, N - 32.92 (C<sub>5</sub>H<sub>7</sub>N<sub>3</sub>O) required C - 48.00,

H - 05.60, N - 33.60. IR  $\nu_{\max}/\text{cm}^{-1}$  (in KBr pallets) 1181.9 (C–O cyclic stretching), 1518.2 ( $> \text{C}=\text{N}$ ), 1652.5 (N–C=N) and 3118.3 (N–H); PMR ( $\delta$   $\text{CDCl}_3$  +  $\text{DMSO}_d_6$ ). 8.01-8.04 (Ar–OH), 7.23-7.55 (Ar–H), 5.45 (pyrimidino-H), 1.25 ( $-\text{CH}_3$ ) and 3.06 (DMSO).

Experimental data for (**Va**) (4.2 g, 79%), m.p. 168°C. It is a brownish white solid, soluble in hot acetone, benzene, hot ethanol and dioxane while it is insoluble in water and chloroform. When hot aqueous solution of the product was treated with ferric chloride, it gave red colouration, indicating the presence of a phenolic –OH group. Desulphuration was noticed, when the product was warmed with alkaline plumbite solution. It formed picrate (m.p. 183°C). Found C-54.87, H - 03.21, N - 20.04, S - 11.80 ( $\text{C}_{12}\text{H}_{12}\text{N}_4\text{SO}$ ) requires C - 55.38, H - 04.61, N - 21.53, S - 12.30. IR  $\nu_{\max}/\text{cm}^{-1}$  (in KBr pallets) 1178.2 ( $> \text{C}=\text{S}$ ), 1252.8 ( $> \text{C}-\text{O}$ ), 1579.6 (N–C=N), 1638.2 ( $> \text{C}=\text{N}$ ) and 3180.9 (N–H); PMR ( $\delta$   $\text{CDCl}_3$  +  $\text{DMSO}_d_6$ ). 10.80 (Ar–OH), 9.76 (N–H), 6.2-7.3 (Ar–H), 7.74 (pyrimidino-H), 2.19-2.59 ( $-\text{CH}_3$ ) and 4.57 (DMSO).

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