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Design, synthesis and characterization of some novel Thiocarbamidopyrimidines

Siddharth A. Waghmare and Swapnil B. Sarkate *

Department of Chemistry, Ghulam Nabi Azad Arts, Commerce and Science College Barshitakli Dist. Akola 444401 (M.S.), India.

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Abstract

Interaction of 2 chloro pyrimidines with various substituted thioureas such as thiourea, N- phenylthiourea, 1,3 Dimethylthiourea, N- allylthiourea and ethyl thiourea were carried in presence of isopropanol as a medium. The product isolated in these reactions were characterized on the basis of elemental analysis, chemical characteristics and spectral studies.

Keywords: 2-chloropyrimidines; Substituted thioureas; Isopropanol; Sodium Bicarbonate; Ethyl alcohol.

1. Introduction

Pyrimidines are vital potent intermediates for synthesizing different heterocyclic compound as well as for their various biological activities. The compounds with the pyrimidines backbone have been described to possess different biological activites[1,2]such as anti-inflammatory[3]anti- cancer[4]anti HIV[5] anti-tumour[6]and so many application in various field.

Pyrimidines had proved subject of great consideration due to numerous reasons. Their ease of synthesis, simplest intermediate in synthetic chemistry, potent biological activities[7,8] and pharmacological activities[2-5].

Literature survey shine back overall many and various scope of pyrimidines as they gave various type of reaction with various types of reagent. Reactivity of pyrimidines changes with change in the medium viz. acidic, basic, and neutral. Acidic and basic medium reactions are investigate the synthesis of different biological potent heterocyclic compound. The reactions of halo pyrimidines in neutral medium proceed with orbital interaction of halo group with the nitrogen in thioureas and gives formation of substituted thiocarbamides pyrimidines[9-13]. Substituted thiocarbamides shows antibacterial[14], antiviral activities[15] as well as some are broadly used commercial pesticides mainly herbicides[16,17].

Taking all these things in consideration, it was planned to carry out the interaction of pyrimidines with various type of substituted thiourea.

As a part of present research work it has been planned to design and synthesize novel series Synthesize of 2-(3-substitutedthiocarbamido) pyrimidines (III-a-e) in this laboratory with the easiest and cheaper method by interaction of 2 chloro pyrimidines with various substituted thiourea. The present method utilized somewhat suitable, convenient, cheaper, more practical utility and only a single step direct method for the synthesis of (IIIa-e).

* Corresponding author: Swapnil B. Sarkate.

2. Material and method

2.1. Material

All the chemical used were of loba chemie (AR grade).

2.2. Method

In the present experiment for the synthesis of different substituted thiocarbamidopyrimidines is conventional refluxing under electronic water bath for different hours for different experiment.

2.3. Experimental

All the chemicals used for the synthesis were purified. After refluxing the purity of the compounds were checked by TLC (aluminium TLC) with thin layer thickness of 200 um. The melting points of all synthesize compounds will be recorded using hot paraffin bath. The carbon and hydrogen analysis were carried out on Carlo-Ebra-1106 analyser Nitrogen estimation were carried out with colmon-N-analyzer-29. IR spectra were recorded with Bruker spectrometer in the range 4000-400 cm^{-1}. PMR spectra were recorded on VARIAN 400 MHz spectrometer with TMS as internal standard using $CDCL_3$ and DMSO Solvent.

2.3.1. Experiment No. 1

Synthesize of 2-(3-thiocarbamido) pyrimidines (III-a)

A reaction between 0.01M 2-Chloropyrimidines **(I)** 1.1553gm and 0.01M thiourea **(IIa)** 0.76gm was refluxed over water bath in isopropanol (30ml) medium for 5 hours. During refluxion new product was found to be gradually separated out, which on basification with dilute sodium bicarbonate afforded yellow crystals was formed. It was recrystallized with aqueous ethanol then dry and weight it.

Yield- 85% M.P.184^{0}C.

2.3.2. Experiment No.2

Synthesis of 2-(3- phenylthiocarbamido) pyrimidines (III-b)

A reaction between 0.01M 2-Chloropyrimidines **(I)** 1.1453gm and 0.01M N-phenyl thiourea **(IIb)** 1.522gm was refluxed over water bath in isopropanol (30ml) medium for 5 hours. During refluxion new product was found to be gradually separated out, which on basification with dilute sodium bicarbonate afforded black crystals was formed. It was recrystallized with aqueous ethanol then dry and weight it.

Yield-82 %, M.P.192^{0}C.

2.3.3. Experiment No.3

Synthesis of 2-(3-(1, 3-Dimethylthiocarbamido) pyrimidines (III-c)

A reaction between 0.01M 2-Chloropyrimidines **(I)** 1.1453gm and 0.01M 1,3-dimethyl thiourea **(IIc)** 1.0457gm was refluxed over water bath in isopropanol (30ml) medium for 5 hours. During refluxion new product was found to be gradually separated out, which on basification with dilute sodium bicarbonate afforded white yellowish crystals was formed. It was recrystallized with aqueous ethanol then dry and weight it.

Yield-84 % M.P.208^{0}C.

2.3.4. Experiment No. 4

Synthesis of 2-(3-allylthiocarbamido) pyrimidines (III-d)

A reaction between 0.01M 2-Chloropyrimidines **(I)** 1.1453gm and 0.01M N-allyl thiourea **(IId)** 1.1619gm was refluxed over water bath in isopropanol (30ml) medium for 5 hours. During refluxion new product was found to be gradually separated out, which on basification with dilute sodium bicarbonate afforded black crystals was formed. It was recrystallized with aqueous ethanol then dry and weight it.

Yield- 80% M.P.190^{0}C.

2.3.5. Experiment No.5

Synthesis of 2-(3- ethylthiocarbamido) pyrimidines (III-e)

A reaction of 0.01M 2-Chloropyrimidines **(I)** 1.1453gm and 0.01M ethyl thiourea **(IIe)** 1.0418gm was refluxed over water bath in isopropanol (30ml) medium for 5 hours. During refluxion new product was found to be gradually separated out, which on basification with dilute sodium bicarbonate afforded green crystals was formed. It was recrystallized with aqueous ethanol then dry and weight it.

Yield- 85% M.P. 145^{0}C.

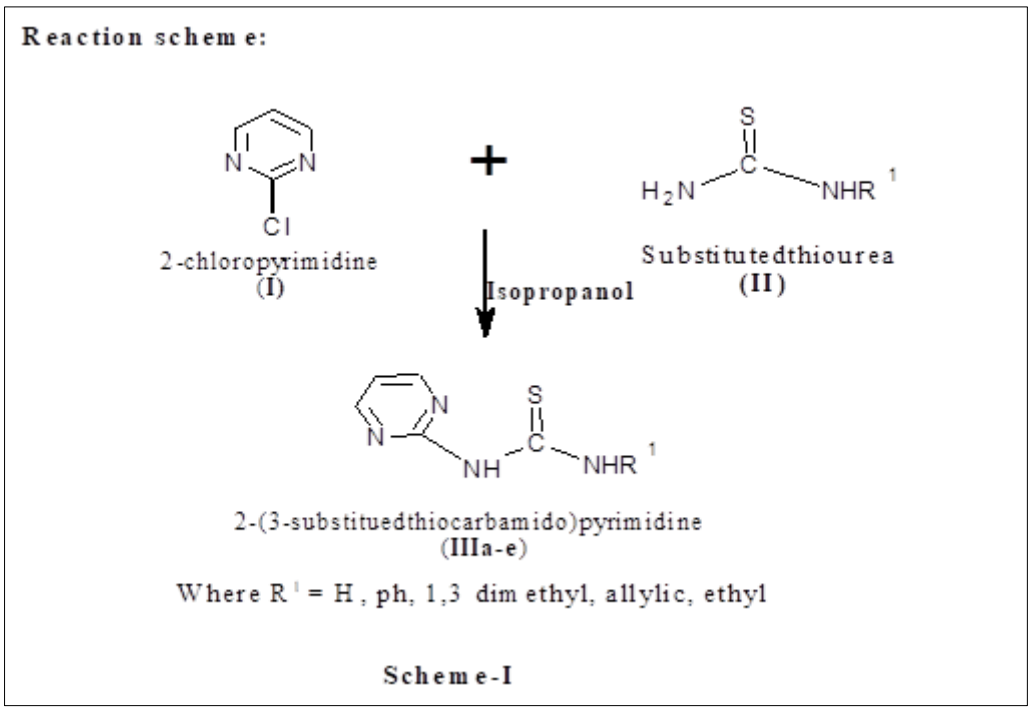

Figure 1 General reaction scheme of synthesis of various thiocarbamidopyrimidines

3. Result and discussion

Spectral characterization results for all the synthesized compounds are given below:

3.1. Spectral Characterization-

3.1.1. Synthesize of 2-(3-thiocarbamido) pyrimidines (III-a)

Colour-Yellow solid, **Molecular formula**- $C_5H_6N_4S$, **Yield** 85%, **M.P**. 184^{0}C, **% Composition found (calculated)** C-38.95 , H-3.92 , N-36.34, S-20.80 , **FTIR (Kbr) vcm**- 3384.22 N-H stretching, 3051.47 (C-H Ar Stretching), 1598.58 (N-H Bending), 1903.37 (C-H Ar Bending,) 1038 (C-N Stretching), 1173.99 (C=S Stretching), 971.68, 789.48 (=C-H bending); **1H NMR (400MHz $CDCL_3$ δ ppm)**, 8.8 ppm (1H, d, CH), 7.6 ppm (1H, CH, triplet), 7.2 ppm (1H, NH, singlet), 3.4 ppm (2H, singlet NH_2). **Mass** m/z 154.03, 112.78 base peak, 134.

3.1.2. Synthesis of 2-(3- phenylthiocarbamido) pyrimidines (III-b)

Colour-Black solid, **Molecular formula** $C_{11}H_{10}N_4S$, **Yield** 82%, M.P. 192^{0}C, **% Composition found (calculated)**, C-57.37, H-4.38, N-24.33, S-13.92, **FTIR (Kbr) vcm**- 3443.87 (N-H stretching), 3192.44 (C-H Ar Stretching), 1492.79 (C=C Ar Stretching), 1182.73 (C=S Stretching), 1492.79 (C-H bending), **1H NMR (400MHz $CDCL_3$ δ ppm),** 8.6(1H, doublet, CH), 8.4(1H, triplet, CH), 7.2(1H, singlet, NH), 7.0(1H, singlet, NH), 7.6(2H, doublet, CH_2), 7.4(2H, doublet, CH_2), 6.7 (1H, doublet CH). **Mass** m/z 230.21, 172.02 base peak, 136.01.

3.1.3. Synthesis of 2-(3-(1, 3-Dimethylthiocarbamido) pyrimidines (III-c)

Colour-White solid, **Molecular formula** $C_7H_{10}N_4S$, **Yield** 90%, **M.P**. 208^{0}C, **% Composition found (calculated**), C-46.13, H-5.53, N-30.74, S-17.59, **FTIR (Kbr) vcm**- 3343.87 (N-H stretching), 3065.47 (C-H Ar Stretching), 1620.90 (N-H Bending), 1910.68, (C-H Ar Bending,) 1318.41 (C-N Stretching), 1196.44 (C=S Stretching), 992.27, 823.81, 697.36 (=C-H bending); **1H NMR (400MHz CDCL$_3$ δ ppm)**, 7.2(1H, doublet, CH), 6.58 (1H, CH triplet) 2.47 (3H, singlet, CH_3), 1.5 (3H, singlet CH_3), 4.0 (1H, singlet, NH), 3.4 (1H, singlet, NH). **Mass** m/z 180.90, base peak 131.91, 158, 168.90.

3.1.4. Synthesis of 2-(3-allylthiocarbamido) pyrimidines (III-d)

Colour- Blackish blue solid, **Molecular formula** $C_9H_{12}N_4S$, **Yield** 80%, **M. P.** 190^{0}C **% Composition found (calculated)** C-49.46, H.-5.19 , N-28.84 , S-16.51 , **FTIR (Kbr) vcm**- 3182.79, 3236, 3384.57 N-H stretching, 3056.95 (C-H Ar Stretching), 1543.13 (N-H Bending), 1910.96, 1967.54 (C-H Ar Bending), 1182.36 (C=S Stretching), 948.25, 684.10 (=C-H bending); **1H NMR (400MHz CDCL$_3$ δ ppm),** 8.8 (2H, doublet, CH),7.6 (1H, triplet, CH), 7.2(1H, singlet, NH), 3.4 (1H, singlet, 3.8 (2H) doublet, 5.2 (1H, quartet, CH), 5.0(1H, triplet, CH), 5.0(1H, triplet, CH). **Mass** m/z 195.01, 181.01, 154.87, 143.

3.1.5. Synthesis of 2-(3- ethylthiocarbamido) pyrimidines (III-e)

Colour- Green solid, **Molecular formula** $C_7H_{10}N_4S$, **Yield** 83%, **M.P.** 144^{0}C, **% Composition found (calculated)**, C-46.13, H-5.53, N-30.74, S-17.59, **FTIR (Kbr) vcm**- 3190.15 (N-H stretching), 3056.95 (C-H Ar Stretching), 1554.17 (N-H Bending), 1910.96, 1967.54, (C-H Ar Bending,) 1318.41 (C-N Stretching), 1174.85 (C=S Stretching), 976.05, 737.33.81, (=C-H bending); **1H NMR (400MHz CDCL$_3$ δ ppm)**, 8.6 (1H, doublet CH), 8.5(1H, singlet, CH) 7.1(1H, singlet, NH), 3.4(1H, singlet, NH), 3.2 (2H, quartet CH_2), 1.34(3H, triplet, CH_3). **Mass m/z** 182.06, 168.89, 104.87, 110.90.

4. Conclusion

In the present work is cheaper and less time consuming method for synthesis of organic compound (IIIa-e). In all the synthesized compounds give the maximum yield of product (III a-e). Synthesis of various type of thiocarbamidopyrimidines structure supported by spectral and analytical data.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

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