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32

# Synthesis, spectral studies and antimicrobial activity of 4-(2'-n-butyl-4'-chloro-1'-H-imidazol-5'-yl)-6-aryl-1, 6-dihydro-2-mercapto pyrimidines

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**ABSTRACT:**

The study focuses on the synthesis, spectral studies and antimicrobial activity of 4-(2'-n-butyl-4'-chloro-1'-H-imidazol-5'-yl)-6-aryl-1,6-dihydro-2-mercapto pyrimidine derivatives against Gram +ve bacteria, Gram –ve bacteria and fungi. The products have been characterized by IR, $^{1}$H NMR, Mass Spectra and TLC.

**KEYWORDS:** Thiourea, Mercaptopyrimidines, Antimicrobial activity, Spectral Study

## 1. Introduction

Pyrimidines are found to be versatile scaffolds and a selective N-heterocyclic moieties which have been significantly evolved recently due to their promising applications in the various fields like life science, industrial chemistry and pharmaceutical industries. Pyrimidines and derivatives of pyrimidine like uracil I, thymine II and cytosine III occurs naturally in a wide range, expressing a better therapeutic importance due to different biological activities.

Pyrimidine molecules are responsible for the building blocks of Deoxyribonucleic acid and Ribonucleic acid. A wide range of therapeutic activities have been observed in pyrimidines found in some natural products (R. Williams and J. Cline, 1936) such as vitamins and nucleic acid with a good remarkable biological importance. Various conjugates of nucleic acid like fluorouracil is used for treatment of cancer belongs to pyrimidine class.

The Pyrimidines have been exhibited a broad class of different therapeutic activities out of which some activities are; Antidiabetic (A. Naranyan, et. al., 1997), Fungicidal (N. Robert, et. al. 1996), Insecticidal (M. Ghorob and S. Hamid, 1994), Analgesics (O. Fuji, et. al., 1995), Tranquilizer (R. Russell, et. al., 1988), Antihypertensive (A. Khalafalah, et. al., 1993), Anticancer and antiviral activity (C. Wyiss, et. al., 2003), etc. A series of novel pyrimidine derivatives (2a-2j) i.e. 4-(2'-n-Butyl-4'-chloro-1'-H-imidazol-5'-yl)-6-aryl-1, 6-dihydro-2-mercapto pyrimidines have been synthesized by the condensation reaction of 3-(2'-n-butyl-4'-chloro-1'-H-imidazol-5'- yl)-1-aryl-prop-2-ene-1-ones and thio-urea in Alc. KOH solution. The products (2a-2j) were assigned by IR, $^{1}$H NMR, mass spectral data, TLC. The physical data & antimicrobial activity is represented in Table 1.

**2. Antimicrobial Activity**

The antimicrobial activity was determined by cup plate method at a concentration of 50 µg/ml using DMF as a solvent. The activity was taken by Gram positive bacteria B.megaterium, S. aureus, Gram negative bacteria Escherichia coli, and S. Taphimarium and antifungal activity against Aspergillus niger. The zone of inhibition was measured in mm. The antibacterial activity was compared with the known standard drugs, viz, Ampicillin, Chloramphenicol, Norfloxacin and antifungal activity was compared with known standard drug viz. Fluconazole. The zone of inhibition that displayed by standard drugs are recorded in Table 2.

**3. Experimental Techniques**

All the melting points were measured by open glass capillary method. IR absorption spectra (in cm-1) were recorded on SHIMADZU-FT-IR-8400 spectrophotometer, frequency range:

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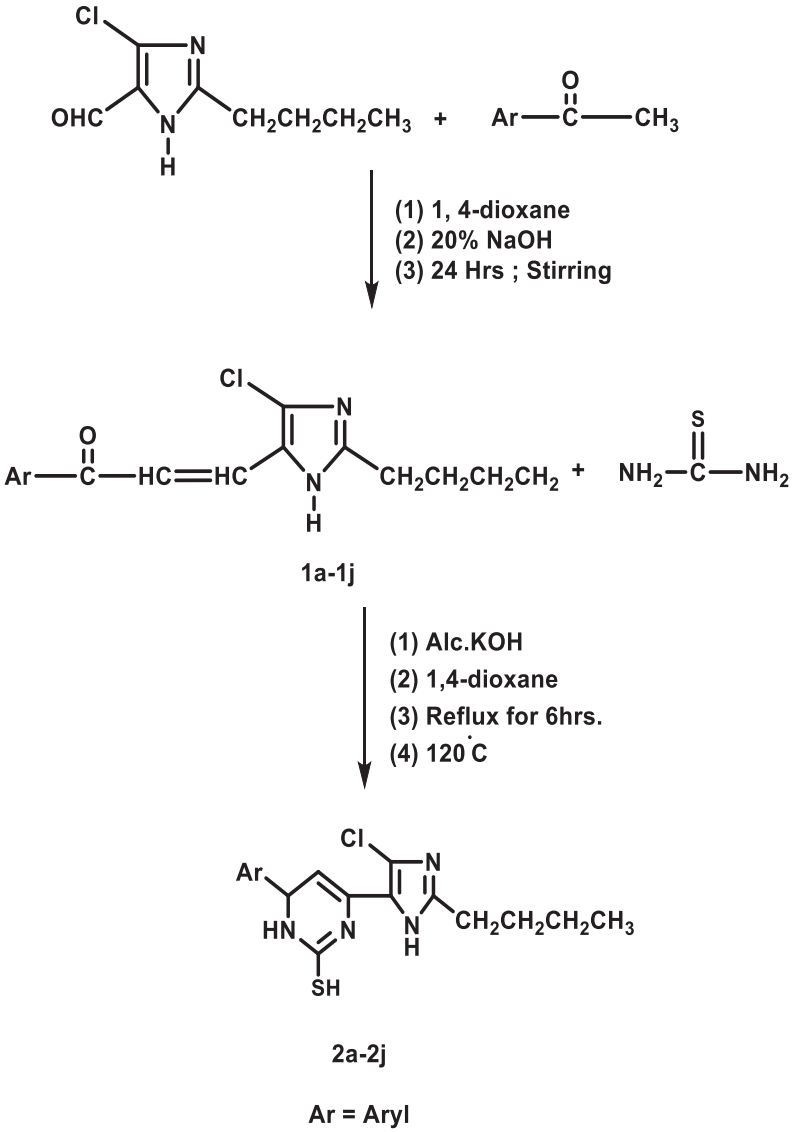
4000-400cm-1 using KBr disc pallet method, $^{1}$H NMR on 400 MHz Bruker Avance-III spectrometer using DMSO-d6 as a solvent and TMS as instrument standard and mass spectra on SHIMADZU-GC-MS QP-2010 Ultra. The purity of the compounds were routinely checked by TLC using silica gel-G.

**4. Reaction Scheme**



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***4.1 Synthesis of 3-(2'-n-butyl-4'-chloro-1'-H-imidazol-5'-yl)-1-(4''-methoxy phenyl)-prop-2-ene-1-one (1i).***

A mixture of 2-(n-butyl)-4-chloro-5-carboxaldo-1H-imidazole (1.87gm, 0.01M); 4-Methoxy acetophenone (1.50gm, 0.01M); 1, 4-dioxane (20ml) and 20% NaOH (20ml) was stirred for 24 hours at room temperature. Completion of reaction was checked with TLC. The reaction mixture was poured into crushed ice, filtered and dried. The product was crystallized in 1, 4-dioxane.

Yield: 77%; M.P.: 87°C; (Required: C: 64.05; H: 6.01; N: 8.79%; $C_{17}H_{19}ClN_2O_2$; Found: C: 64.05; H: 6.01; N: 8.70%).

IR (KBr): 2968 (C-H str. asym); 2864 (C-H str. sym); 1459 (C-H str. Def) 3060 (C-H str. aromatic); 1558 (C=C ring skeletal); 1166 (C-H i.p. (def)); 751 (C-H-str.def); 1600 (C-N str.); 1515 (C=N str.); 3415 (N-H str); 1600 (N-H bending); 1653 (C=O str.); 1459 (CH=CH); 728 (C-Cl); 1250 (C-O-C str.).

$^1$H NMR: 0.9 (t, 3H, -C$\underline{H}_3$); 1.2-1.3 (m, 2H, -C$\underline{H}_2$-CH$_3$); 1.5-1.6 (m, 2H, -C$\underline{H}_2$-CH$_2$-CH$_3$); 2.6 (t, 2H, -C$\underline{H}_2$-CH$_2$-CH$_2$-CH$_3$); 12.8 (s, 1H, -N$\underline{H}$); 7.4 (d, 1H, -CH=C$\underline{H}$-) 7.6 (d, 1H, -C$\underline{H}$=CH-); 7.1 (d, 2H, Ar-$\underline{H}$); 8.0 (d, 2H, Ar-$\underline{H}$); 3.8 (s, 3H, -OC$\underline{H}_3$).

m/z: 318, 283, 268, 253, 240, 225, 211, 200, 184, 167, 145, 135, 115, 107, 92, 77, 64, 43, 41, 40.

Similarly, other compounds (1a-1j) were synthesized. Chalcones physical data and antimicrobial activities are published in another journal.

***4.2 Synthesis of 4-(2'-n-Butyl-4'-chloro-1'-H-imidazol-5'-yl)-6-(4''-methoxy phenyl)-1, 6-dihydro-2-mercapto pyrimidine (2i).***

A mixture of 3-(2'-n-Butyl-4'-chloro-1'-H-imidazol-5'-yl)-1-(4''-methoxy phenyl)-prop-2-ene-1-one (3.19gm, 0.01M); 1, 4-dioxane (20ml); Alcoholic KOH (0.15gm, 0.02M) and thiourea (1.5gm, 0.02M) was taken in a RBF. The reaction mixture was refluxed in oil bath for 6 hours at 120° C. On successful completion of the above reaction, the solution was

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poured into ice cold water. The products were formed, filtered and dried. Completion of reaction was checked with TLC. Crystallization of products was carried out in 1, 4-dioxane.

Yield: 77%; M.P.: 219˚C; (Required: C: 57.36; H: 5.62; N: 14.87%; $C_{18}H_{21}ClN_4OS$; Found: C: 57.32; H: 5.60; N: 14.80%).

IR (KBr): 2927 (C-H str. Asym.); 2857 (C-H str. Sym.); 1422 (C-H str. def.); 3035 (C-H str.); 1509 (C=C ring skeletal); 1231 (C-H i.p. def.); 695 (C-H o.o.p. str. def.); 1438 (C-N str.); 1656 (C=N str.); 3454 (N-H str.); 1545 (N-H bending); 695 (C-Cl); 827 (-SH str.); 1231 (C-O-C str.).

1H NMR: 0.8 (t, 3H, -C<u>H</u>$_3$); 1.2-1.3 (m, 2H, -C<u>H</u>$_2$-CH$_3$); 1.6 (m, 2H, -C<u>H</u>$_2$-CH$_2$-CH$_3$); 2.6 (t, 2H, -C<u>H</u>$_2$-CH$_2$-CH$_2$-CH$_3$); 12.8 (s, 1H, -N<u>H</u>); 3.8 (s, 3H, -OC<u>H</u>$_3$); 2.0 (s, 1H, N<u>H</u>-); 7.4 (d, 1H, Ar-<u>H</u>); 7.6 (d, 1H, Ar-<u>H</u>); 7.1 (d, 2H, Ar-<u>H</u>); 8.0 (d, 2H, Ar-<u>H</u>).

m/z: 361, 343, 329, 317, 303, 276, 262, 253, 226, 203, 196, 184, 177, 164, 157, 135, 107, 98, 84, 77, 57, 43, 41, 40, 31.

Similarly, other compounds (2a-2j) were synthesized. The physical data and antimicrobial activity of (2a-2j) represented in Table 1.

**Table 1** The physical data and antimicrobial activity of compounds (2a-2j). Zone of inhibition in mm.

| Sr. No. | Ar | Molecular Formula | M.P. (°C) | % Nitrogen yield | | Antibacterial activity | | | | Antifungal activity |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Gram +ve bacteria | | Gram –ve bacteria | | |
| | | | | Calcd. | Found | B. mega. | S. aureus | S. taphi. | E. coli. | A. niger |
| **2a** | $C_6H_5$- | $C_{17}H_{19}ClN_4S$ | 249 | 16.15 | 16.09 | 17 | 15 | 16 | 14 | 11 |

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|---|---|---|---|---|---|---|---|---|---|---|
| **2b** | 3-OH.$C_6H_4$- | $C_{17}H_{19}ClN_4OS$ | 194 | 15.44 | 15.39 | 19 | 18 | **20** | 17 | 13 |
| **2c** | 4-OH.$C_6H_4$- | $C_{17}H_{19}ClN_4OS$ | 292 | 15.44 | 15.41 | 12 | 15 | 18 | **21** | 15 |
| **2d** | 3-$NH_2$.$C_6H_4$- | $C_{17}H_{20}ClN_5S$ | >300 | 19.35 | 19.30 | 15 | 17 | **24** | 18 | 18 |
| **2e** | 4-Cl.$C_6H_4$- | $C_{17}H_{18}Cl_2N_4S$ | 190 | 14.69 | 14.62 | 17 | 14 | 19 | **24** | **20** |
| **2f** | 4-Br.$C_6H_4$- | $C_{17}H_{18}BrClN_4S$ | 221 | 13.16 | 13.09 | 19 | **23** | 17 | 16 | 16 |
| **2g** | 3-$NO_2$.$C_6H_4$- | $C_{17}H_{18}ClN_5O_2S$ | 282 | 17.87 | 17.81 | **24** | 18 | 15 | 19 | **23** |
| **2h** | 4-$NO_2$.$C_6H_4$- | $C_{17}H_{18}ClN_5O_2S$ | >300 | 17.87 | 17.78 | **23** | 17 | 19 | **23** | 19 |
| **2i** | 4-$OCH_3$.$C_6H_4$- | $C_{18}H_{21}ClN_4OS$ | 219 | 14.87 | 14.80 | 18 | 15 | **20** | 19 | **22** |
| **2j** | 3-$NH_2$,2-OH.$C_6H_3$- | $C_{17}H_{20}ClN_5OS$ | >300 | 18.53 | 18.49 | **20** | 14 | 19 | 18 | **24** |

**Table 2** Compounds showing comparable antimicrobial activity with known standard drugs.

| | **Compounds** | **Antibacterial activity** | | | | **Antifungal activity** |
|---|---|---|---|---|---|---|
| | | **Gram +ve Bacteria** | | **Gram -ve Bacteria** | | |
| | | ***B. mega.*** | ***S. aureus*** | ***S. taphi.*** | ***E. coli.*** | ***A. niger*** |
| | (2a-2j) | 2g | 2f | 2b | 2c | 2e |
| | | 2h | - | 2d | 2e | 2g |
| | | 2j | - | 2i | 2h | 2i |
| | | - | - | - | - | 2j |

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| **Activity of Standard Drugs:** | | | | | | |
| 1 | Ampicillin (50µg/ml) | 27 | 26 | 25 | 28 | - |
| 2 | Chloramphenicol (50µg/ml) | 29 | 28 | 27 | 25 | - |
| 3 | Norfloxacin (50µg/ml) | 32 | 30 | 24 | 27 | - |
| 4 | Fluconazole (50µg/ml) | - | - | - | - | 26 |

## 5. Conclusions

The study emphasis on the synthesis, spectral studies and antimicrobial activity of novel mercapto pyrimidine derivatives. The compounds- 2b, 2c, 2d, 2e, 2f, 2g, 2h, 2i, 2j have showed good remarkable antibacterial and antifungal activity with compared to known standard drugs e.g., Ampicillin, Chloramphenicol, Norfloxacin and Fluconazole at same concentration 50 µg/ml.

***Acknowledgement***

The authors are thankful to the Management and Principal, Shree M. and N. Virani Science College, Chemistry Department, Rajkot, for providing research facilities.

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