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Isolation of Lansoprazole intermediate impurity resulting in yield improvement

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ABSTRACT

The aim of work is to isolate Lansoprazole intermediate impurity resulting into its yield improvement. Lansoprazole is a proton pump inhibitor, generally used in treatment of peptic ulcer. Lansoprazole is synthesized in seven stages. Meta-nitro impurity i.e. (2, 3-dimethyl-5-nitropyridine-N-Oxide) occurs at stage II which is isolated by a very conventional method and elemental analysis is performed by Proton NMR and IR.

Key words: Impurity, Lansoprazole, Isolation.

INTRODUCTION

Pharmaceutical Industry is under growing pressure of environmental issues which includes major losses of revenue in form of waste material of solvents, solids and residues. Impurities in pharmaceuticals are unwanted chemicals that occur with active pharmaceutical ingredients (APIs) which influence efficacy and safety of pharmaceutical products [5].

Current research paper explains the isolation of meta-nitro impurity from second crop of Lansoprazole nitro stage leading to yield improvement. Generally for every 100kg batch of Lansoprazole nitro compound, 35kg second crop is obtained from left out mother liquor. The obtained second crop is of 75% purity which is waste material but by simple isolation 15-16kg of para-nitro can be recovered with purity 99% which leads to its yield improvement [1-4].

EXPERIMENTAL SECTION

Purity of compound was monitored on silica gel 60 F_{254} purchased from Merck and solvents were procured from Aldrich Chemical Co. Ltd. Elemental analysis was performed using IR spectra, and Proton NMR.

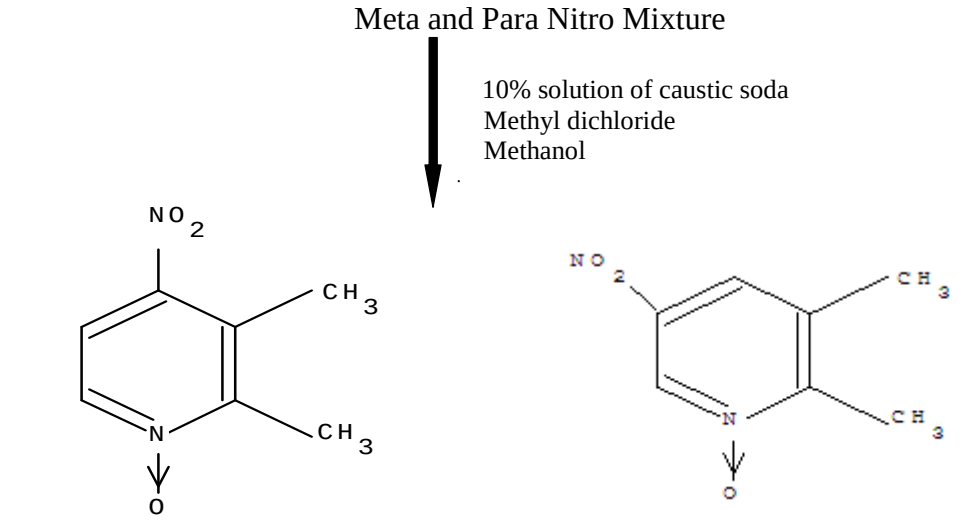
General procedure for Isolation of Meta Nitro Impurity i.e. 2, 3-dimethyl-5-nitro pyridine-N-oxide:

100gm of Lansoprazole nitro IInd crop was charged in 1lit water and stirred for 30mins. The reaction mass was heated to 40°C, maintained for 15-30mins, cooled to room temperature and filtered. Solid obtained on buckner was Meta-nitro impurity which was purified by hot and cool method using methanol as a solvent. Clear Filtrate was charged in the reactor, 50% solution of NaOH was added to obtain pH 10. 200ml of Methylene dichloride was added to it and stirred for 30mins further allowed to settle for 30mins. Two layers obtained were separated. The aqueous layer was washed twice with methylene dichloride of 200ml each. The pH of organic layer was checked and organic layer was washed with water till neutral pH was attained. Methylene dichloride was recovered atmospherically and then degassed under vacuum with methanol. 100ml of methanol was charged, cooled and chilled to 10°C, maintained for 2hrs, further filtered and dried to obtain solid [Purified Lansoprazole para-nitro compound].

Dry weight of solid: 50gm
Melting point: 90-92°C
Assay [By H.P.L.C.]: 99.03%

RESULTS AND DISCUSSION

Isolation of Meta Nitro Compound from Para Nitro Compound:



Nitro Compound
2, 3-dimethyl-4-nitropyridine-N-Oxide

Meta Nitro [impurity]
2, 3-dimethyl-5-nitropyridine-N-Oxide

Elemental Analysis was carried with IR [Fig. 1-2] and Proton NMR [Fig. 3-4]. H.P.L.C. analysis was also carried out [6] method to check the retention time [Fig. 5-9].

CONCLUSION

Isolated compound can be used for next stage resulting in yield improvement of Lansoprazole.

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