



SYNTHESIS OF 8-(3-BROMO-4,5-DIMETHOXY PHENYL)-2-((4-CHLORO PHENYL) AMINO)-4-IMINO-6-(4-NITROPHENYL)-4H-PYRIDO [1,2-a] PYRIMIDINE-3,9-DICARBONITRILE

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ABSTRACT

A mixture of 8-(3-bromo-4,5-dimethoxyphenyl)-6-(nitrophenyl-4-imino-2-(methylsulfanyl)-4H-pyrido [1,2-a] pyrimidine-3,9-dicarbonitrile and 4-Chloroaniline was refluxed in presence of K₂CO₃ in DMF as solvent for 6 to 7 hours to get 8-(3-bromo-4,5-dimethoxyphenyl)-2-((4-chlorophenyl) amino)-4-imino-6-(4-nitrophenyl)-4H-pyrido [1,2-a] pyrimidine-3,9-dicarbonitrile. The structures for the synthesized compounds are assigned on the basis of IR, ¹HNMR and Mass spectral studies.

KEYWORDS

4-Chloroaniline, Anhydrous Potassium Carbonate, DMF

INTRODUCTION

Pyridopyrimidine derivatives are a privileged bicyclic ring system. Due to its potent and significant biological activities, it has great pharmaceutical importance; synthesis of these compounds is considerable interest. Fused pyridopyrimidine derivatives if present in compounds involved in research aimed at evaluating new products that possess interesting biological activities. The fused pyridopyrimidine derivatives play an important role in biochemical processes because the side groups of the most typical and essential constituents of living cells DNA and RNA are based on aromatic heterocycles.

Recently, pyrido pyrimidine derivatives used as inhibitors of stable toxin a (STa) for their ability to inhibit cyclic nucleotide synthesis in the presence of stable toxin a of Escherichia coli.19 This encouraged us to become involved in a program directed to the development of syntheses of various new pyridopyrimidines and fused pyridopyrimidines.

Heterocyclic compounds constitute the largest, most varied family of organic compounds and are very widely distributed in nature. They play a vital role in the metabolism of all the living cells. The study of heterocycles is of great interest both from the theoretical as well as practical stand point. A heterocyclic compound is one which possesses acyclic structure at least two different kinds of atoms in the ring. The most common types contain largely carbon atom, nitrogen, oxygen and sulphur but many other elements, including even bromine, chlorine can

also be present. The heterocyclic containing the less common atoms have been subject to much investigation in recent years.

Heterocyclic chemistry and medicinal chemistry share a venerable common history. Many of the founders of heterocyclic systems had an intense interest not only in molecules from nature but also in the effects of synthetic compounds on living systems.

The current interest in the creation of large, searchable libraries of organic compounds has captured the imagination of organic chemists and the drug discovery community. In numerous laboratories, the efforts are focused on the introduction of chemical diversity, which have been recently reviewed and pharmacologically interesting compounds have been identified from libraries of widely different compositions¹⁻⁵.

Today, the chief sources of agents for the cure, the improvement or the prevention of diseases are the heterocyclic compounds, natural or synthetic. Such agents have their origin in a number of ways (a) from naturally occurring materials of both plant and animal origin, and (b) from the isolation of organic compounds synthesized in laboratory whose structures are closely related to those of naturally occurring compounds.

The heterocyclic compound containing Nitrogen, Oxygen, Sulphur possesses best pharmacological activity. Compound like pyridine, Pyrimidine, triazine exhibited interesting pharmacological properties among them some fused heterocyclic compound containing pyridine possess remarkable antitubercular activity⁶. Similarly, the fused heterocyclic compound containing pyrido pyrimidine and its derivatives possesses better antibacterial activity against Gram positive & Gram negative species⁷. From many years researchers have been highly interested in the chemistry of heterocyclic compound and its derivatives with their expected biological activity⁸⁻¹¹. The heterocyclic compound containing cyanopyridine & cyanopyrane derivatives possesses versatile biological activity like antimicrobial¹², antitubercular¹³, anti-inflammatory¹⁴, antitumor¹⁵, antiviral¹⁶ & antifungal¹⁷

In view of the literature survey, the present work we thought worthwhile to synthesize the bicyclic heterocyclic compound which containing pyrido pyrimidine nucleus & its 2-substituted derivatives.

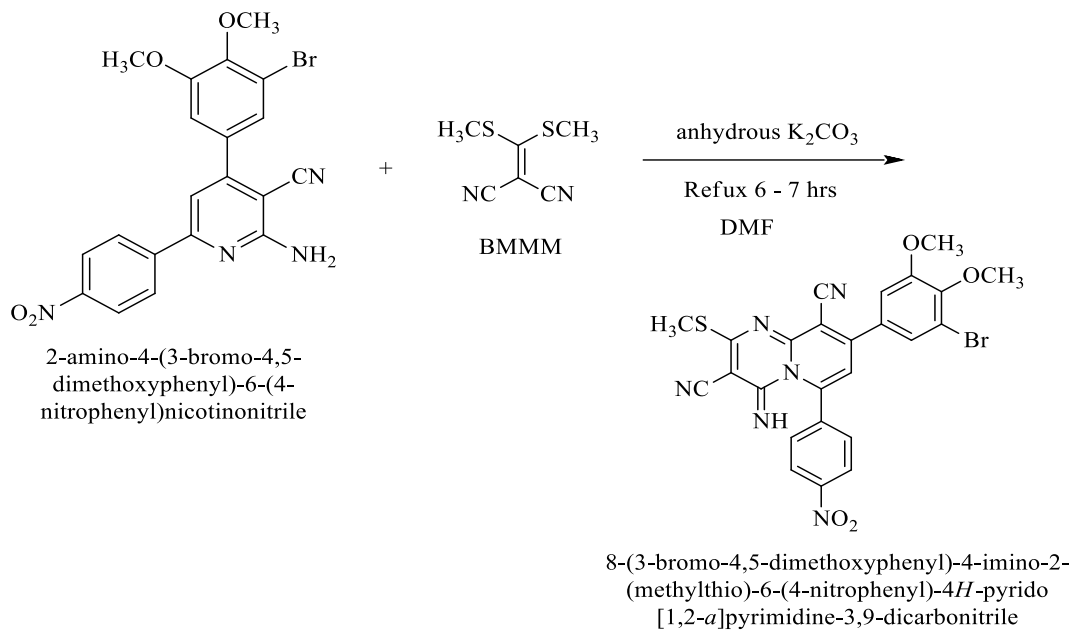
EXPERIMENTAL SECTION

All melting points were determined in open capillary tube and were uncorrected. IR spectra were recorded with potassium bromide pellets technique, ¹H NMR spectra were recorded on AVANCE 300 MHz Spectrometer in DMSO using TMS as internal standard. Mass spectra were recorded on a FT VG-7070 H Mass Spectrometer using EI technique at 70 eV. All the reactions were monitored by thin layer chromatography.

MATERIAL AND METHODS

1) Synthesis of 8-(3-bromo-4,5-dimethoxyphenyl)-6-(nitrophenyl-4-imino-2-(methylsulfanyl)-4H-pyrido[1,2-a]pyrimidine-3,9-dicarbonitrile (Starting material)

A mixture of 2-amino-4-(3-bromo-4,5-dimethoxyphenyl)-6-(4-nitrophenyl)nicotinonitrile and bis-methyl thio methylene malononitrile (BMMM) refluxed in presence of anhydrous Potassium Carbonate(1-2 pinch) in DMF as solvent and refluxed for about 6-hours to get 8-(3-bromo-4,5-dimethoxyphenyl)-6-(nitrophenyl-4-imino-2-(methylsulfanyl)-4H-pyrido[1,2-a]pyrimidine-3,9-dicarbonitrile.

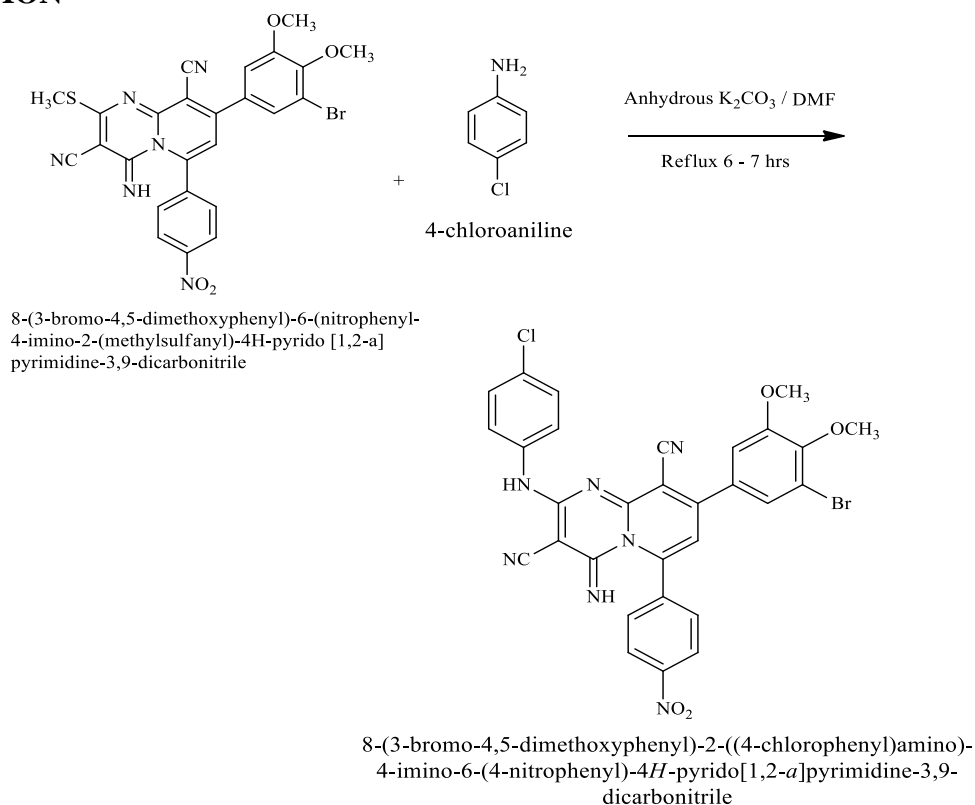


2) Synthesis of 8-(3-bromo-4,5-dimethoxyphenyl)-2-((4-chlorophenyl) amino)-4-imino-6-(4-nitrophenyl)-4H-pyrido [1,2-a] pyrimidine-3,9-dicarbonitrile

In the present work, we report synthesis of 8-(3-bromo-4,5-dimethoxyphenyl)-6-(nitrophenyl)-4-imino-2-(methylsulfanyl)-4H-pyrido [1,2-a] pyrimidine-3,9-dicarbonitrile. It is prepared by refluxing a mixture of 8-(3-bromo-4,5-dimethoxyphenyl)-6-(nitrophenyl)-4-imino-2-(methylsulfanyl)-4H-pyrido [1,2-a] pyrimidine-3,9-dicarbonitrile and 4-Chloro aniline in presence of K_2CO_3 & DMF as a solvent for about 6-7 hours, reaction mixture was monitored by TLC & cooled, then poured in ice cold water, solid get separated out known as 8-(3-bromo-4,5-dimethoxyphenyl)-2-((4-chlorophenyl)amino)-4-imino-6-(4-nitrophenyl)-4H-pyrido [1,2-a] pyrimidine-3,9-dicarbonitrile.

The Purity of compound was checked by TLC. The compound observed on TLC as single spot in benzene. Structures to these compounds are assigned on the basis of elemental analysis and spectral data.

REACTION



Yield: 66 %, M.P : 195 °C,

Spectral analysis :

IR:(KBr/cm⁻¹): 3440 (=NH), 3105 (Ar-H), 2920 (C-H), 2210 (-CN), 1620 (C=N), 1210 (C-O), 1520 & 1345 (-NO₂, asymmetric and symmetric stretching)

EI-MS: (m/z: RA%) : 656 (M+1), m/z: 655.04, 658.04, 656.04, 659.03, 660.04, 659.04, 657.04, 658.03, 656.03, 661.04

¹H-NMR: (DMSO) : δ 8.21 (d 2H Ar-H), δ 8.04 (d 2H Ar-H), δ 8.01 (s 1H Ar-H), δ 7.24 (d 2H Ar-H), δ 7.02 (s 1H Ar-H), δ 6.76 (s 1H Ar-H), δ 6.57 (d 2H Ar-H), δ 4.00 (s 1H NH), δ 8.50 (s 1H =NH), δ 3.82 (s 6H -OCH₃)

Elemental analysis: C₃₀H₁₉BrClN₇O₄ Calculated: (%) C, 54.85; H, 2.92; Br, 12.16; Cl, 5.40; N, 14.93; O, 9.74 Found (%) : C, 54.80; H, 2.90; Br, 12.12; Cl, 5.35; N, 14.90; O, 9.71

RESULTS AND DISCUSSION

Literature survey reveals that, many work was published on pyrimido pyrimidine heterocycles compound, Heterocycles containing pyrimido pyridine derivatives exhibited remarkable anti-inflammatory, antiallergic, antitumor and antihypertensive activity. In the present work. We report the synthesis of 8-(3-bromo-4,5-dimethoxyphenyl)-2-((4-chlorophenyl) amino)-4-imino-6-(4-nitrophenyl)-4H-pyrido [1,2-a] pyrimidine-3,9-dicarbonitrile

CONCLUSION

In conclusion a facile one pot synthesis has been developed for the title compounds using readily available starting materials. Thus, there is a network of reaction equilibria which all finally flow into an irreversible step yielding the product. In contrast to multi step synthesis, one pot reactions need minimal work and they have often quantitative yields.

ACKNOWLEDGEMENTS

The authors are thankful to the Principal, Degloor College, Degloor for providing laboratory facilities and the Director, Indian Institute of Chemical Technology, Hyderabad for providing spectra.

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Received on July 2, 2022.