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One pot Synthesis of Synthesis of substituted pyrido [1,2-a] pyrimidine-3,9-dicarbonitrile

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Abstract:

A mixture of 8-(3-bromo-4,5-dimethoxyphenyl)-4-imino-2-(methylthio)-6-(4-nitrophenyl)-4H-pyrido[1,2-a] pyrimidine-3,9-dicarbonitrile and 2-chloroaniline in presence of anhydrous potassium carbonate (1-2 pinch) in DMF as solvent and reflux for about 6 to 7 hours to get 8-(3-bromo-4,5-dimethoxyphenyl)-2-((2-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, ^{1}HNMR and Mass spectral studies.

Keywords:

Bis methyl thio methylene malononitrile, anhydrous Potassium Carbonate, DMF, 2-chloroaniline

Introduction:

A literature survey has revealed the diversified biological and pharmacological significance of several nitrogen and Sulphur heterocycles. This aspect has been drawing the attention of many researchers towards exploiting the biological importance of various heterocyclic compounds and to establish the relationship between their biological, pharmacological potency and structural features. A rapid progress in the work on fused quinazolinones and thienopyridines has given rise to a number of compounds exhibiting potent pharmacological actions.

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 activity[1]. Similarly, the fused heterocyclic compound containing pyrido pyrimidine and its derivatives possesses better antibacterial activity against Gram positive & Gram negative species[2]. From many years researchers have been highly interested in the chemistry of heterocyclic compound and its derivatives with their excepted biological activity[3-6].

A.B.A. El-Gazzar et al[7] was reported the one spot synthesis of pyrido[2,3-d] pyrimidine-2-thiones by the reaction of appropriate aldehyde, malononitrile and 6-aminothiouracil. Alternatively, he was also reported the same compound by the reaction of arylidine malononitrile with 6-amino thiouracil. Sangeeta Bhargava et al[8] reported the synthesis of novel pyido pyrimidine derivatives and their microbial investigation She was prepared a series of pyrido pyrimidine

derivatives by the condensation reaction of 2-amino-3-cyano-4,6-disubstituted pyridine with the different reagent like formamide, urea, thiourea respectively and all these synthesized compounds were reported as a antibacterial & antifungal agent. The heterocyclic compound containing cyanopyridine & cyanopyrane derivatives possesses versatile biological activity like antimicrobial[9], antitubercular[10], antiflammatory[11], antitumor[12], antiviral[13] & antifungal[14]

D.H. Vyas, Et al[5] have reported the synthesis of an antimicrobial activity of some new cyanopyridine & cyanopyrane. They were prepared cyanopyridine by the reaction of substituted chalcones with the malononitrile in the presence of ammonium acetate to offer 2-amino-3-cyanopyridine. 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, ^{1}H 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.

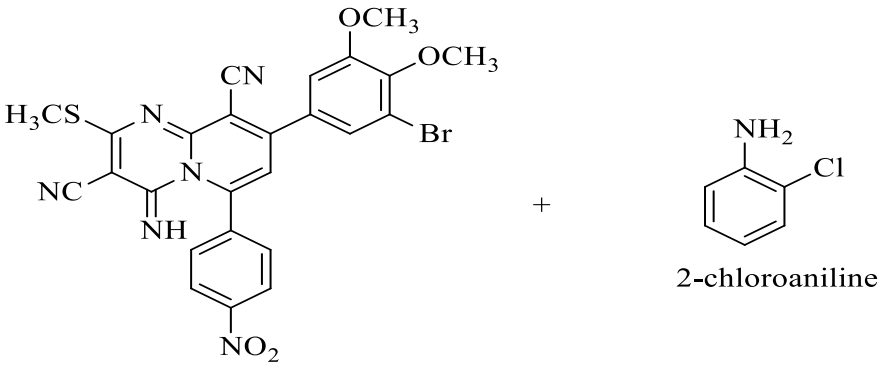
Materials and Methods :

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

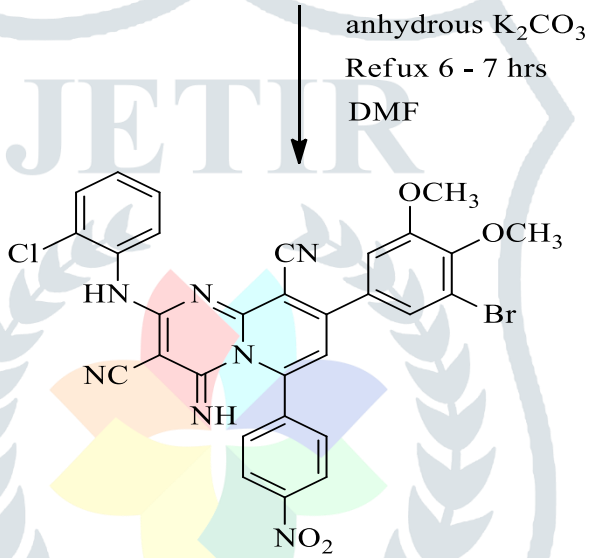
In the present work, we report synthesis of 8-(3-bromo-4,5-dimethoxyphenyl)-2-((2-chlorophenyl) amino)-4-imino-6-(4-nitrophenyl)-4H-pyrido[1,2-a] pyrimidine-3, 9-dicarbonitrile by refluxing mixture of 1 mole of 8-(3-bromo-4,5-dimethoxyphenyl)-4-imino-2-(methylthio)-6-(4-nitrophenyl)-4H-pyrido[1,2-a] pyrimidine-3,9-dicarbonitrile with 2-chloro aniline in presence of anhydrous K_2CO_3 & DMF as a solvent for about 6-7 hrs.

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 :



8-(3-bromo-4,5-dimethoxyphenyl)-4-imino-2-(methylthio)-6-(4-nitrophenyl)-4*H*-pyrido[1,2-*a*]pyrimidine-3,9-dicarbonitrile



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

Yield: 70 %, M.P : 266 ^{0}C, **IR:(KBr/cm^{-1}) :** 3440 (=NH), 3385 (-NH), 1622 (C=N), 1511 & 1340 (-NO_2, asymmetric and symmetric stretching),

EI-MS: (m/z:RA%) : 657 (M+1), **Elemental analysis :** $C_{30}H_{19}BrClN_7O_4$ Calculated: (%) C 54.85, H 2.92, Br 12.16, Cl 5.40, N 14.93, O 9.74 Found (%) : C 54.82, H 2.90, Br 12.11, Cl 5.38, N 14.90, O 9.72

Results and Discussion :

Literature survey reveals that, many work was published on pyrimido pyrimidine heterocycles compound, Heterocycles containing pyrimido pyridine derivatives exhibited remarkable anti-inflamatory, antiallergic, antitumor and antihypertensive activity. In the present work. We report the synthesis of 8-(3-bromo-4,5-dimethoxyphenyl)-2-((2-chlorophenyl) amino)-4-imino-6-(4-nitrophenyl)-4H-pyrido[1,2-a] pyrimidine-3,9-dicarbonitrile by refluxing mixture of 1 mole of 8-(3-bromo-4,5-dimethoxyphenyl)-4-imino-2-(methylthio)-6-(4-nitrophenyl)-4H-pyrido [1,2-a] pyrimidine-3,9-dicarbonitrile with 2-chloro aniline in presence of anhydrous K_2CO_3 & DMF as a solvent for about 6-7 hrs.

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.

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