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ONE POT SYNTHESIS OF SYNTHESIS OF 8-(3-BROMO-4,5-DIMETHOXYPHENYL)-6-(NITROPHENYL-4-IMINO-2-(METHYLSULFANYL)-4*H*-PYRIDO[1,2-*A*]PYRIMIDINE-3,9-DICARBONITRILE

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ABSTRACT

A mixture of 2-amino-4-(3-bromo-4,5-dimethoxyphenyl)-6-(4-nitrophenyl) pyridine-3-carbonitrile and bis-methyl thio methylene malononitrile (BMMM) in presence of anhydrous Potassium Carbonate (1-2 pinch) in DMF as solvent and reflux for about 6-hours to get nucleus pyrido pyrimidine (72%). 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.

INTRODUCTION

The heterocyclic compound containing Nitrogen, Oxygen, Sulpher possess 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.

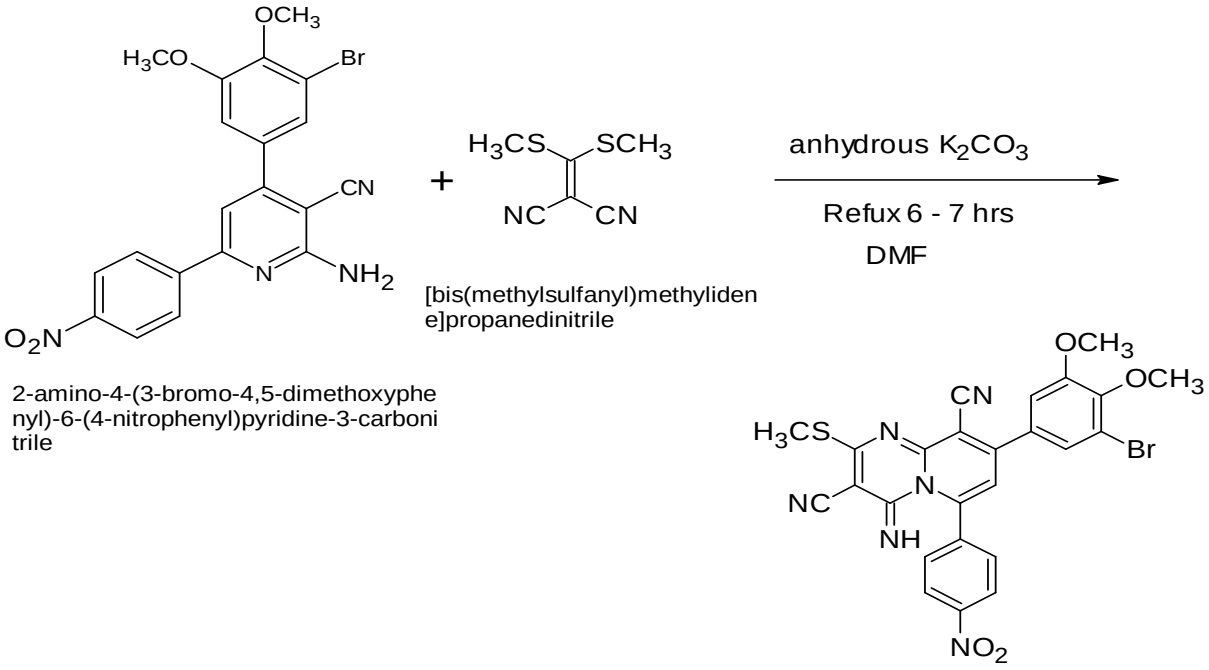
MATERIALS AND METHODS

Synthesis of Synthesis of 8-(3-bromo-4,5-dimethoxyphenyl)-6-(nitrophenyl-4-imino-2-(methylsulfanyl)-4*H*-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)-4*H*-pyrido[1,2-*a*] pyrimidine-3,9-dicarbonitrile by mixture of A mixture of 1 gm (0.0017m moles) of 2-amino-4-(3-bromo-4,5-dimethoxyphenyl)-6-(4-nitrophenyl) pyridine-3-carbonitrile with reagent 0.29 gm (0.0017m moles) [bis (methyl sulfanyl) methylidene] propane dinitrile was refluxed in in presence of 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



2-amino-4-(3-bromo-4,5-dimethoxyphenyl)-6-(4-nitrophenyl)pyridine-3-carbonitrile

[bis(methylsulfanyl)methylidene]propanedinitrile

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

Yield: 72 %, M.P : 260 ^{0}C, **IR:(KBr/cm^{-1}) :** 3441 (=NH), 3380 (-NH), 1620 (C=N), 1515 & 1338 (-NO_2, asymmetric and symmetric stretching), **EI-MS: (m/z:RA%) :** 577 (M+1), **Elemental analysis :** $C_{25}H_{17}BrN_6O_4S$ Calculated: (%) C 52.00, H 2.97, N 14.55, O 11.08, S 5.55 Found (%) : C 51.90, H 2.95, N 14.50, O 11.03, S 5.50.

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 pyrido pyrimidine and it's 2-anilino derivatives. Nucleus pyrido pyrimidine i.e. 8-(3-bromo-4, 5-dimethoxyphenyl)-6-nitrophenyl-4-imino-2-(methylsulfanyl)-4*H*-pyrido[1,2-*a*] pyrimidine-3,9-dicarbonitrile was synthesised by the reaction of 2-amino-4-(3-bromo-4,5-dimethoxyphenyl)-6-(4-nitrophenyl) pyridine-3-carbonitrile pyridine with Bis-(methyl thio) methylene malononitrile in presence of anhydrous K_2CO_3 in DMF. Compound i.e. pyrido pyrimidine having methyl thio group at 2 position which is act as best leaving group. It has been replaced by selected nucleophile like substituted aniline group. Hence the reaction of pyrimido pyrimidine with selected nucleophile like substituted aniline group in presence of anhydrous K_2CO_3 in DMF to offered 2-anilino derivatives of pyrido pyrimidine nucleus, respectively.

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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