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Synthesis, Charaterization and Bioactivities of Fused Pyrimidobenzothiazol-4-one

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Abstract: *Heterocyclic compounds are an important class of basic building blocks, being used by chemists to create compounds of biological or medical relevance. Various heterocyclic building blocks are used in medicinal research, agriculture, and medication discoveries. Considering the significance of heterocyclic ring-containing molecules, 2-amino-6-cyanobenzothiazole is combined with ethylacetoacetate in the presence of polyphosphoric acid to form 8-cyano-2-methyl-4H-pyrimido[2,1-b]benzothiazol-4-one. The structure of the produced chemical is characterised using H1NMR, IR, and mass spectrometry and The synthesized compound successfully showed Biochemical activity against E.Coli, as well as antifungal efficacy against Bacillus subtilis species.*

Keywords: 2-amino-6-cyanobenzothiazole, 8-cyano-2-methyl-4H-pyrimido[2,1-b]-benzothiazol-4one, ethylacetoacetate[1-4].

I. INTRODUCTION

Since the development of Salvarsan for the treatment of Syphilis by German bacteriologist Paul Ehrlich and his student Sahachiro Hata in 1910, heterocycles have been one of the most important fields of research in organic chemistry. It was the first synthetic chemotherapeutic agent. In 1929, Alexander Fleming discovered Penicillin, the world's first antibiotic, from Penicillium notatum. At the same period, the first sulfa medication was synthesised, and Streptomycin (an antituberculosis agent), Tetracycline, and other antibiotics with high antibacterial effectiveness were discovered one after the other. The existence of heterocycles in all of these chemical molecules sparked intense attention in biology, pharmacology, and other fields. Sulfur and nitrogen-containing heterocyclic compounds have piqued the curiosity of researchers, and their unusual structures have led to a variety of uses in several fields. Pyrimidobenzothiazoles are nitrogen and sulfur-containing compounds that have been shown to have a wide range of properties such as GABA receptor binding, antiviral, antitumor, anti-inflammatory, and so on. Over the last several decades, there has been a surge of interest in the characteristics and transformations of these heterocycles. We produced and tested for bioactivity 8-cyano-2-methyl-4H-pyrimido[2,1-b]-benzothiazol-4one, a pyrimidobenzothiazole derivative. The purity of the produced chemical was determined using thin layer chromatography with various polar and nonpolar solvent mixes. The infrared spectrum was recorded on a SHIMADZU-8400S FTIR in KBr, and the 1H NMR spectra were recorded on an AV500 FT spectrometer in a DMSO/CDCl3 combination using TMS as an internal reference, without shifting the melting point[5,6].

II. SCOPE AND PURPOSE

For more than a century, the nitrogen and sulfur containing heterocycles have constituted one of the emerging branches of chemical sciences in the fields of pharmacology, pathology, anticancer, anti-inflammatory, and others. We have synthesised nitrogen and sulphur containing heterocycles of biological and pharmacological importance incorporating diverse structural features in light of the structural changes caused by the presence of heteroatoms and the relationship of structures with biological / pharmacological activities. The current exploration of these nitrogen and sulfur-containing heterocycles aims for possible medicinal relevance, particularly with thiazole and pyrimidine heterosystems known as Pyrimidobenzothiazoles. These structural characteristics allow them to display a variety of pharmacological and biological activities, the intensity of which is mostly determined by the structural specificity and the degree of contact between a drug and receptor sites present in biological systems[6-8].

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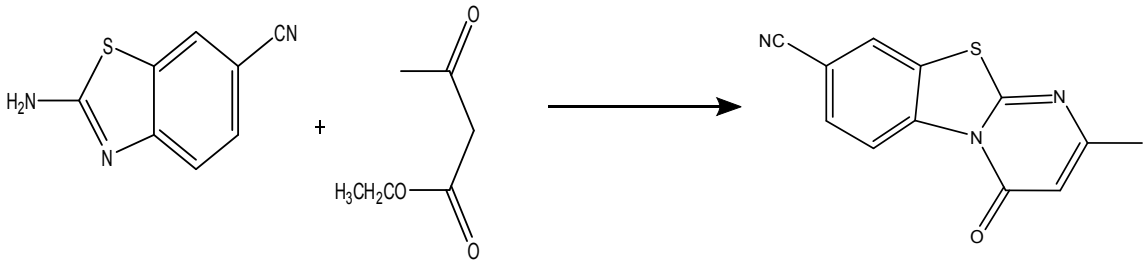
III. CHEMISTRY

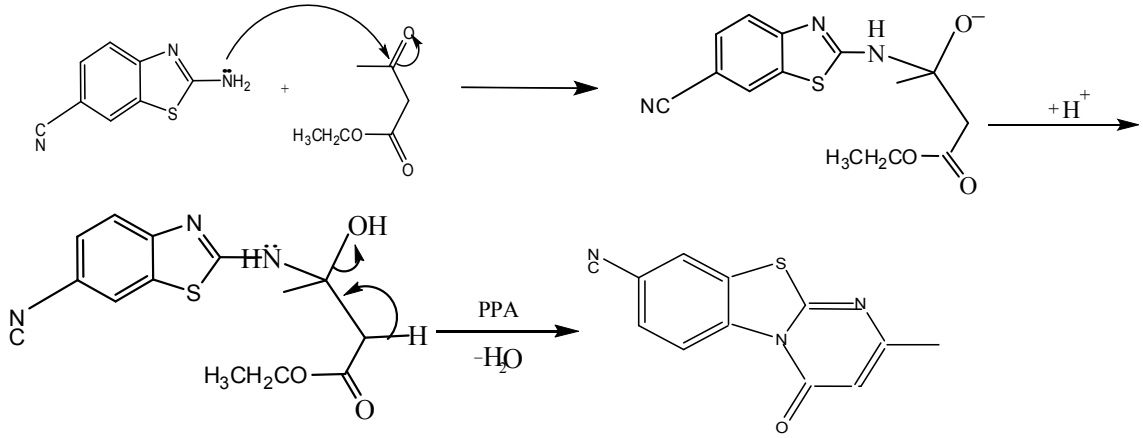
3.1-Synthesis of 8-CYANO-2-METHYL-4H-PYRIMIDO[2,1-B] BENZO- THIAZOL-4-ONE

We used a straightforward and convenient regioselective one-pot synthesis of 2-amino-6-cyanobenzothiazole with ethylacetoacetate in the presence of polyphosphoric acid to produce 8-cyano-2-methyl-4H-pyrimido[2,1-b]benzothiazol-4-one.



3.2-Mechanism

We have deduced a mechanism for best suiting of this formation;



3.3-Experimental

2-amino-6-cyanobenzothiazole required for the synthesis of 8-hydroxy-2-methyl-4H-pyrimido-[2,1-b]benzothiazol-4-one have been purchased from the market, the name of the company is SPECTROCHEM PVT. LTD. MUMBAI (INDIA). All the errors or changes are subjected to the company.

We refluxed 01g (0.00392 moles) of 2-amino-6-cyanobenzothiazole with 6ml of ethylaceto- acetate for 48 hours in the presence of polyphosphoric acid (10g) to obtan the 8-hydroxy-2-methyl-4H-pyrimido[2,1-b]benzothiazol-4-one. TLC was used to rapidly analyse the response. We see distinct Rf-value discrepancies in TLC for various solvent fronts, thus TLC for this reaction works best in DCM (Dichloromethane),as soon as we noticed the bigger disparities in Rf-values, we terminated the reaction and the refluxing.

The reaction mixture was cooled and hence neutralised using Sodium Bicarbonate (NaHCO3). As the neutralisation process was completed, ethanol was distilled from the combination using a Water Rotor until precipitate was observed in the mixture. Following distillation, the residual solution was filtered to the crystals. These crystals were then re-crystallized in DCM, and the pure crystals were oven dried at up to 50 o C. To minimise water sensitivity, these crystals were preserved in butter paper. TLC was then done once more to ensure product formation. The melting point was determined to be 150-155o C, with a percentage yield of roughly 65 percent.

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IV. RESULTS

4.1 Solubility

S.No.	*Solvent*	*Compound*
01	Water	Insoluble
02	Chloroform	Soluble
03	DCM	Soluble
04	Butanol	Soluble
05	Ethanol	Soluble
06	Methanol	Soluble
07	Hexane	Insoluble

(Table-01)-Solubility of Synthesized compounds in various Solvents.

The solubility of the prepared chemical compound in various organic solvents was investigated. The following Table-01 shows Solubility of Synthesized compounds in various solvents;

4.2 Thin Layer Chromatography(TLC)

Chromatography is an essential technique for determining the production of an organic compound as well as the purity of such compounds, and the Retardation Factor (Rf) value of these chemicals is unique to each of them.

Chromatoplate preparation

Glass slides needed that were clean and dry, thenafter a thin layer of silica gel in water is applied to the slides at 1:2 ratio. The slurry was then put into the applicator's chamber, which was then secured and the thickness was adjusted at 0.5mm. After that, the plates were dried at 110ºC.

Preparation of the solvent system

The solvent mixture is made by taking one solvent or by properly combining several solvents in correct ratios.

Sample Application

The parent chemicals and their derivatives were observed in little drilled capillaries 2 cm from the slide's base.

Chromatogram Creation

Plates were developed using the ascending approach, and once the solvent front had reached a distance of 10-12 cm, they were removed and dried at room temperature.

Spot Detection

Iodine chambers were used to identify the spots.

Rf value calculation

The following formula was used to determine the Rf values:

$$RF = \frac{\text{Distance Travelled by the sample}}{\text{Distance Travelled by the solvent}}$$

The table (Table-02) below shows the Thin Layer Chromatography Data of the Synthesised Compounds;

COMPOUND	SOLVENT / SYSTEM	PROPORTION	Rf- VALUE
4H-pyrimido[2,1-b]- benzothiazol-4-one	DCM	100%	0.5

(Table-02)-Thin Layer Chromatography Data for the Synthesised Compounds.

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4.3 Spectral Data

8-cyano-2-methyl-4H-pyrimido[2,1-*b*]benzothiazol-4-one was confirmed mainly by spectroscopic studies. I have performed FTIR (model name of the FTIR instrument is SHIMADZU 8400s) to characterize my products and match them with the literature spectra of the synthesized compounds.

I have confirmed my product by determining the melting point of the sample and characterizing various peaks by spectrometric techniques. I have correlated my product FTIR spectrum with the literature spectrum of reactant and found the differences. Furthermore the compound was correlated with the literature available and confirmed the peaks.

On the FTIR bases the compound was confirmed by the presence of following peaks:

S. No	Group	Wave No.(cm^{-1})
1	C=O(Str.)	1645
2	Alkenic SP^2C-H(Str.)	3063
3	Alkenic C=C(Str.)	1492
4	Aromatic C=C(Str.)	1589

The presence of SP^2C-H (Str.) peak at 3063 cm^{-1} confirms the formation of c=c in the product. The reactant was lacking alkenic part. Furthermore the presence of SP^2 c=c peak at 1492 cm^{-1} confirms the formation of product.

Mass Spectrometry And ^{1}HNMR

The m/z peak at 280 (M^+) confirms the synthesis of the compound. Number of shielded and deshielded protons were confirmed with the literature available.

Author Contributions

This whole work belongs to me.

Conflicts Of Interest

There are no conflicts of interest to declare

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