Design, synthesis and biological characterization of S-linked hydrazones by natural acid catalyst

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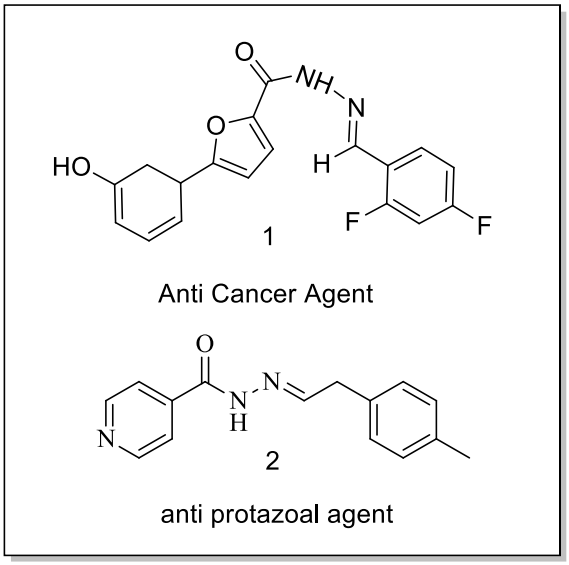
Abstract

Hydrazones have been classified as previliged heterocyclic moieties which displayed a broad spectrum of pharmacological and biological properties. This article reports the synthesis of S-linked hydrazone derivatives and anti bacterial properties of these derivatives.

Introduction

A class of chemical compounds known as hydrazones has the general formula: $R_1R_2C=N–NR_3R_4$. Hydrazones are special chemical molecules descended from the Schiff-base group. Hydrazones are used for a variety of things, including medications, the production of polymers and adhesives, industries, and many other things (Thiyagarajan & Gunanathan, 2020). Heterocyclic ring structures with multiple atoms have been found to use acid hydrazides as intermediates, offering potential applications in medicine, herbicides, antimalarials, antibacterial products, anticonvulsants, anti-inflammatory treatments, antidepressants, anticancer, and pigments (DeMarinis et al., 1975).



Hydrazones, or hydrazides, are chemical compounds with azomethine groups connected to carbonyl groups, used in various pharmaceutical formulations. They are formed when a NNH2 group replaces oxygen in a ketone and an aldehyde. The azomethine -NHN=CH-proton family is crucial for creating new pharmaceuticals. Since hydrazones serve as linkers for mineral complexes, organotrophs, and the production of organic molecules, they are crucial substances in medication design.

Additionally, commonly used chemotherapeutic drugs like nitrofurazone,

furazolidone, and nitrofurantoin have been found to contain the distinctive hydrazide-hydrazone group or fragment,in which the oxazolidine or imidazolidine ring contains both the carbonyl group and the nitrogen atom. Also, it is well recognized that the creation of extremely crystalline hydrazone derivatives is a highly efficient method for the identification, separation, and distillation of carbonyl compounds (Denmark, Chang, Houk, & Liu, 2015).

MATERIALS AND METHODS

Infra-red spectrum of the manufactured complexes was noticed on the Burker FT-Infrared spectrometer. Nuclear magnetic resonance was obtained on the Burker FT-Infrared spectrometer typical AV-400 at 400 Mega Hertz. M.p of manufactured complexes was present in glass vessels by used the Gallenkamp equipment. The manufactured complex was distilled by column chromatography as well as recrystallization process using ethanol as well as dichloro-benzoic acid as reagents. Thin layer chromatography take place on precoated Si gel using 60 F254 plates by analytical grade solvent such as CH_3OH, DCM.

Synthesis of hydrazide derivative

2,7-dihydro-6,7 dimethylthieno [3,2c] pyridin-5(4H)-yl) acetohydrazide was synthesized by treating the 2-(2-chlorophenyl)-2,7-dihydrothienylmethyl [3,2-c]Acetate of pyridin-5(4H)-yl) (0.1g, 0.0003107 mol) with hydrazine monohydrate (0.5g, 0.0154 mol) under reflux for 8 hours. The product underwent filtering when the reaction was complete. The recrystallization of the crude result with ethanol purified it.

General protocol for synthesis of substituted aryl hydrazones

The prepared hydrazide (0.1g, 0.00031) analogue has been reacted with various aldehydes under reflux for 4 hours in the presence of lemon extract used as catalyst. Filtration was used to isolate the product and recrystallization with ethanol to afford pure product.

Biological Evaluation

Antibacterial activity

Multidrug-resistant bacterial and fungal pathogens pose a global healthcare threat, necessitating ongoing research for novel antimicrobial drugs, despite their positive treatment outcomes (Zhang et al., 2021). Aryl hydrazones, a challenging synthone for chemists, are used to fight bacteria (Ragavendran et al., 2007).

Inhibitory Minimum Concentration (MIC)

The rising bacterial resistance to antibiotics necessitates the development of more effective therapies, primarily due to the inappropriate antibiotic dosage used in treating infections (Devasahayam, Scheld, & Hoffman, 2010). New evaluations revealed microbiological parameters of long-known antibiotics, including MIC (milligrams per liter). A smaller MIC number indicates less medication needed

and more effective in preventing organism development (Turnidge, Kahlmeter, & Kronvall, 2006). The MIC values of each chemical were determined using a Resazurin microtiter-plate analyzer.

Statistical analysis

Microsoft Excel 2010 was used for the statistical analysis, which was done in triplicate for all the experimental activities. The result has been presented as mean± SD.

Figure 1: General Pathway for synthesis of Hydrazones

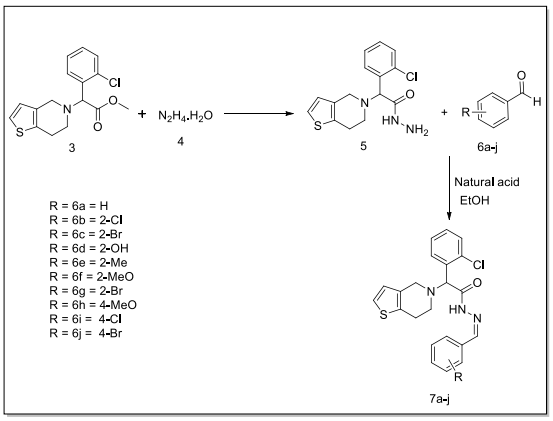
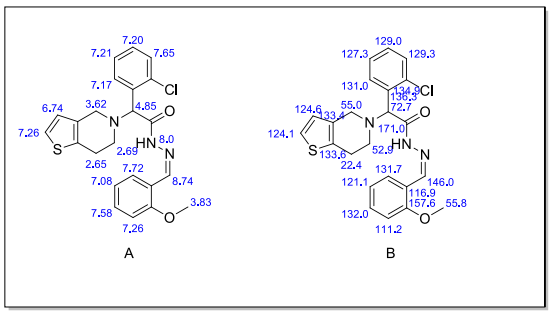


Figure 2: HNMR and CNMR analysis of compound **7f**



Results and Discussion

Synthesis of Hydrazones

The hydrazones 7a-j has been synthesized using novel methodology including use of lemon extract as natural acid. A series of new derivatives has been prepared with good antibacterial activity.

Antibacterial activity

Antibacterial infections have traditionally been treated with hydrazone. For a long time, bacterial infections have been treated using medications based on S-heterocyclic aryl hydrazide (Ajiboye, Ajiboye, Marzouki, & Onwudiwe, 2022). Aryl hydrazide replaced with hydrazone is produced, and its biological use is evaluated (Thebti et al., 2019). Bacillus subtilis and Escherichia coli have been used as test subjects for the synthetic hydrazone derivatives **7a-j** antibacterial activity. Table 1 lists the minimal inhibitory concentration (MIC) and zone of inhibition (ZI) values. In addition to ciprofloxacin being utilized as a positive control, typical medications included ampicillin and ibuprofen (Turnidge et al., 2006).

Table 1: *Antibacterial activity results of compounds* ***7a-j***

Compound	*Bacillus subtilis*		*Escherichia coli*	
	ZI (mm)	MIC (mg/mL)	ZI (mm)	MIC (mg/mL)
7a	19.21 ±0.45	2.3 ± 0.00	20.1 ± 1.3	2.9 ± 0.34
7b	18.11 ±0.21	3.1 ± 0.01	12.1 ±1.1	2.1 ± 1.1
7c	32.1 ± 0. 11	4.1 ± 0.00	12.1 ± 2.1	1.1 ± 0.11
7d	12.1 ± 2.1	0.7 ± 0.25	11.2 ± 1.1	1.0 ± 0.43
7e	19 ± 0.12	2.9 ± 0.00	10.1 ± 1.3	0.5 ± 0.9
7f	33 ± 0.12	3.3 ± 0.00	11.1 ± 1.1	1.3 ± 0.81
7g	22.1 ± 0. 11	4.1 ± 0.00	19.1 ± 2.1	1.4 ± 0.23
7h	17.1 ± 2.2	0.2 ± 0.25	14.3 ± 1.4	1.6 ± 0.87
7i	17.6 ± 0.12	2.1 ± 0.00	10.1 ± 0.9	0.9 ± 1.1
7j	31.2 ± 0.12	3.2 ± 0.00	10.1 ± 0.8	1.1 ± 0.81
Ampicillin Iburofen Ciprofloxacin	18 ± 1.0 15 ± 0.9 29.3 ± 1.0	9.0 ± 1.1 14.0 ± 1.0 0.3 ± 0.0	12 ± 0.6 11 ± 0.5 31.1 ± 1.2	16 ± 1.1 21 ± 1.4 2.2 ± 0.1

Conclusion

Aryl hydrazones are chemically adaptable substances with numerous biological properties, including antimicrobial, antiviral, anti-cancer, anti-fungal, anti-malarial, and anti-tumor properties. They are used in various industries, including medicine, polymer production, and industries. Acid hydrazides and their derivatives are effective in synthesizing heterocyclic rings with various properties. They have been used in various applications, including medicines, herbicides, and anticancer. They can be cyclized or cycloadditioned with various reagents to produce a wide range of compounds. They are crucial for their manufacture due to their ability to scavenge ferric ions, making them useful in clinical medicinal applications.

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