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Synthesis, Characterization and Antimicrobial Screening of Oxazolopyridine Derivatives

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Abstract:

Modifications on the benzoxazole nucleus have resulted in a large number of compounds having diverse pharmacological activities. The synthesis, structures and biological activities of benzoxazole derivatives have long been focused of research interest in the field of medicine, due to potential activities exhibited by them. The biological profiles of these new generations of benzoxazole represent much progress with regards to older compounds. Looking into the medicinal importance of benzoxazole moiety, it will be worthwhile to synthesize certain newer derivatives of benzoxazole and screen them for their biological activities.

Keywords: Benzoxazole, Synthesis, Structure

INTRODUCTION

Synthetic organic chemistry is the art of building-up organic compounds from smaller entities. This science has found application in the production of organic compounds of commercial interest, in the construction of new, potentially bioactive molecules derived from rational design, in the challenge to synthesize very complex natural products, in finding new methods and strategies to render this science more efficient.

Diseases and disease agents that were once thought to be controlled by antibiotics are returning in new leagues resistant to these therapies. Poor sanitation conditions aided spread and small healthcare budgets prevented access to new effective but more expensive antibiotics. [1] Now the antimicrobial resistance is not new, but the number of resistant organisms, the geographic locations affected by drug resistance, and the breadth of resistance in single organisms are unprecedented and mounting.

Oxazole has cyclooxygenase-2 inhibitory property and tyrosinase inhibitory property. In this research it was to synthesize some new type of antimicrobial agent thus it was selected as oxalopyridine derivatives. [2,3] The selection of oxalopyridine derivatives as antimicrobial agent has to be for evaluation. Oxazole shows potential photophysical and photochemical activities, so they are used in semiconductor devices like electrophotographic photoreceptors and in non-linear optical materials.

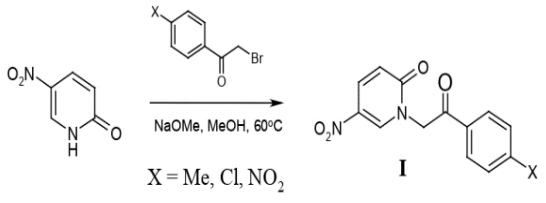
Experimental Work

Materials and methods

All the reagents and solvents used were of laboratory grade. The melting points of synthesized compounds were determined by open capillary method and were uncorrected. The purity and homogeneity of compounds were checked using TLC technique.

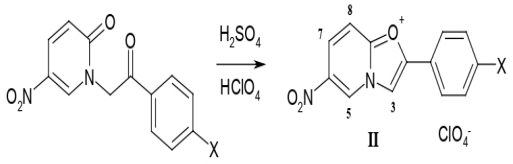
Phenacylation of 5-nitro-2-pyridone

The standard route to oxazolo[3,2-a]pyridinium salts is the cyclization of N-phenacyl-2-pyridones, which in turn could be obtained either by hydrolysis of 2-halo-N-phenacylpyridinium salts or by phenacylation of 2-pyridones. Suitable precursors of 6-nitrooxazolo[3,2-a]pyridinium salts would therefore be N-phenacylated derivatives of readily available 5-nitro-2-pyridone or 5-nitro-2 halopyridines. Our attempts to perform phenacylation of 2-chloro-5-nitropyridine were unsuccessful. On the other hand, selective N-alkylation of the salts of 5-nitro-2-pyridone was reported in literature. It was found that the sodium salt of 5-nitro-2-pyridone undergoes selective N-alkylation in reactions with phenacylbromides leading to phenacyl pyridones I. [4-5] The reaction is complete after 10-12 hours, and the yields vary from 40% (X=NO2) up to 80% (X=Cl). The alkylation is easily monitored by TLC (since the Rf values of the products I lay in between the values of the reactants), and there were no signs of formation of alternative O-alkylated products (for spectral differences between N- and O-phenacylated isomers of 2-hydroxypyridine



Synthesis of 2-aryl-6-nitrooxazolo[3,2-a]pyridinium perchlorates

The usual technique of cyclodehydration of N-phenacylpyridones to oxazolopyridinium salts (dissolving a compound in concentrated sulfuric acid, diluting with water, and precipitating the product with perchloric acid) was not appropriate for the case of nitropyridones I. The most successful procedure required complete avoidance of water. This was achieved by pouring the reaction mixture of pyridone I in sulfuric acid (containing few drops of HClO4) into anhydrous diethyl ether. The precipitate formed corresponds to pure perchlorate II.



Screening of Antimicrobial activity

A suspension of Staphylococcus aureus (SA) was added to sterile nutrient agar at 45ºC. The mixture was transferred to sterile petri dishes to give a depth of 3 to 4 mm and allowed to solidify. Precautions were observed to reduce uniform layer of medium on the plate. Sterile discs 5 mm in diameter (made from Whatman Filter paper) were immersed in the solutions of synthesized compounds (250 µg/mL) and maintain an untreated control sample for comparison. Leave the plates to stand for 1 hour at room temperature as a period of pre incubation diffusion to minimize the effects of variations in different time. Then the plates were incubated at 37ºC for 24 hours and observed. The diameter of the zone of inhibition was measured for each plate in which the zone of inhibition was observed. The average zone of inhibition was calculated and compared with that of standard. A similar procedure was adopted for studying the antibacterial activity against the other organisms.

Results and Discussion

Phenacylation of 5-nitro-2-pyridone

It was found that the sodium salt of 5-nitro-2-pyridone undergoes selective N-alkylation in reactions with phenacylbromides leading to phenacyl pyridines. The findings of physical data of compounds were reported in table 1.1.

Synthesis of 2-aryl-6-nitrooxazolo[3,2-a]pyridinium perchlorates

The precipitate formed corresponds to pure perchlorate II. The findings of physical data of compounds were reported in table 1.1.

Table 1.1: Physical Data of Compounds

Compound	Yield %	Melting Point
BN1	85	175-178
BN2	72	138-140
BN3	74	145-148

Assessment of screening of antimicrobial activity

The diameter of the zone of inhibition was measured for each plate in which the zone of inhibition was observed. The average zone of inhibition was calculated and compared with that of standard. A similar procedure was adopted for studying the antibacterial activity against the other organisms. The findings of antimicrobial activities of the synthesized compounds were reported in table 1.2

Table 1.2: Antimicrobial activities of the synthesized compounds

S.N.	Microorganisms	Zone of Inhibition (in mm)		
		BN1	BN2	BN3
1	Staphylococcus aureus	12	20	18
2	Bacillus Subtilis	16	16	18
3	Escherichia Coli	18	20	24

Conclusion

The heterocyclic moiety being so versatile in nature offers the medicinal chemist to explore more about it in medicinal field and the data mentioned in this article will be a great help to prospective researchers working in this area for further study of this scaffold. Oxazole moiety is an important heterocyclic compound as they are being an essential constituent of large number of marketed drugs. Having such diverse spectrum of biological activities, oxazoles has immense potential to be investigated for newer therapeutic possibilities and is an important class of lead compounds for development of new chemical entities (NCE) to treat various diseases of clinical importance.

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