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A REVIEW OF LITERATURE ON SYNTHESIS, CHARACTERIZATION, AND BIOLOGICAL ACTIVITIES OF SOME NOVEL PHENOXAZINE DERIVATIVES

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ABSTRACT

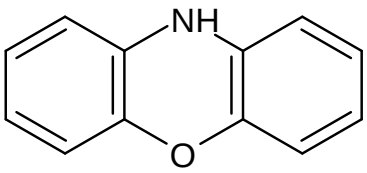
The aim of this review article is given to a systemic approach to synthetic and different biological activities related to the phenoxazine derivatives. The synthesis of phenoxazine derivatives and screening of them for various biological activities have garnered considerable attention in the last few decades. Antiprotozoal activity, Antiviral activity, Antioxidant activity, Anti-inflammatory activity, Antibacterial activity, Antifungal activity, Antiparasitic activity, Antineoplastic activity, and other biological activities are all effective with phenoxazine. Phenoxazine derivatives associate better activity than standard drugs.

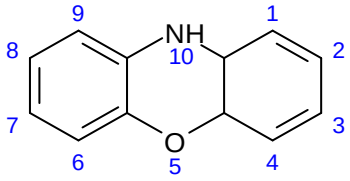
Keywords: Phenoxazine, Antibacterial, Antiviral, Antiprotozoal, Antitubercular.

I. INTRODUCTION

Phenoxazine is a heterocyclic compound that belongs to the oxazine class, which is relevant in medical chemistry and material science. Phenoxazine was first invented by Bernthsen in 1887 in the course of proof of structure studied on Meldola's blue and gallocyanine.[1] Phenoxazine is two benzene rings are fused with an oxazine [2].

Structure





1. Molecular formula: O (C6H4)2NH
2. Molar Volume: 153.1 ± 3.0 cm^3
3. Molecular weight: 183.20 gm/mole
4. Molar Refractivity: 54.13 ± 0.3 cm^3
5. Composition: C=78.67%, H=4.95%
6. Parachor: 404.1 ± 4.0 cm^3

N=7.65%, O=8.73%

7. Index Refraction: 1.624 ± 0.02
8. Density: 1.196 ± 0.06 g/cm^3
9. Polarizability: 21.46 ± 0.5 $10^{-24}cm^3$
10. Melting point: 156-159^{0}C

Phenoxazines are a group of N-heterocyclic compounds having three-ring structures with nitrogen and oxygen atoms [3]. Specifically, as effective microbial agent, Phenoxazine based on chemical probes with aryl substituents has been considered [4, 5]. Due to their biological actions, such as anticancer, anti-inflammatory, and cytotoxic effects, it is a veritable group of heterocycles in the field of medicinal chemistry. Many substituted phenoxazines shows important biological properties like antiviral, antifungal [6], antibacterial [7], tranquilizers [8], antimalarial [9], anti psychotropic [10], antiviral [11], antitubercular [12], antitumour [13,14] and etc. Stimulation of the penetration of anticancer agents via the blood-brain barrier [15] and multidrug resistance reversal activity [16]. They have also been found to prevent human amyloid disorders [17] and to protect neuronal cells from death by oxidative stress [18].

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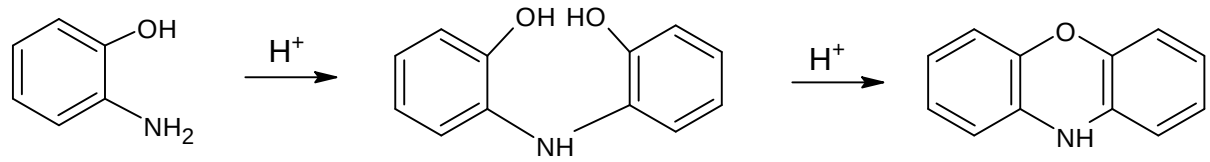
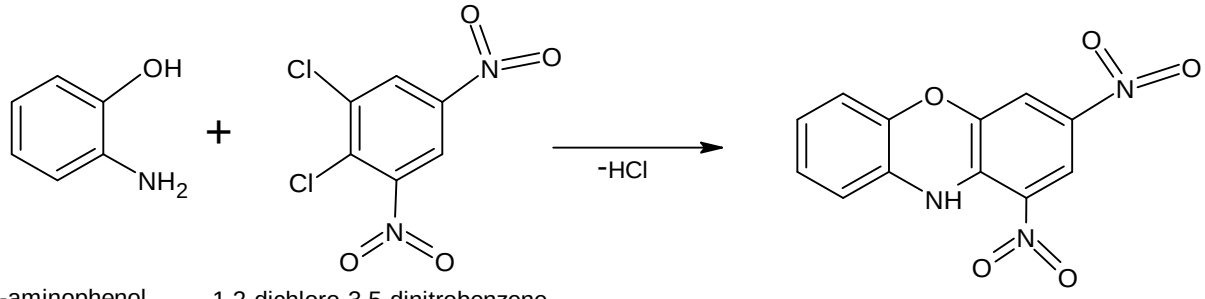
GENERAL SYNTHETIC REACTIONS OF PHENOXAZINE AND ITS DERIVATIVES

Auto-condensation of o-Aminophenols



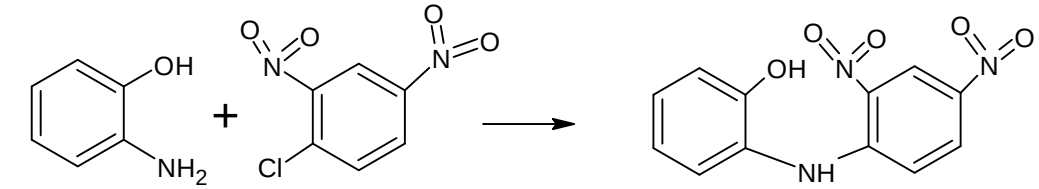
2-aminophenol 2,2'-azanediyldiphenol 10*H*-phenoxazine

Cyclization of 2-Chloro-2'-hydroxydiphenylarnine

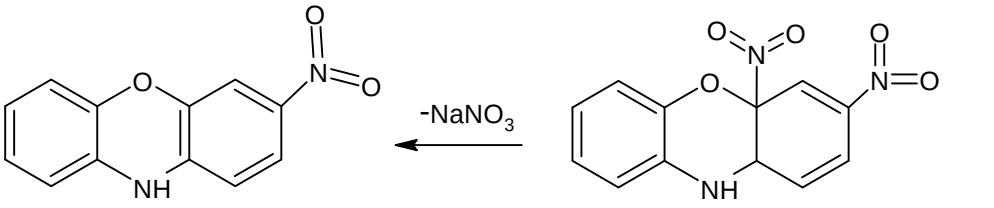


2-aminophenol 1,2-dichloro-3,5-dinitrobenzene 1,3-dinitro-10H-phenoxazine

Turpin Reaction



2-aminophenol 1-chloro-2,4-dinitrobenzene 2-(2,4-dinitroanilino)phenol

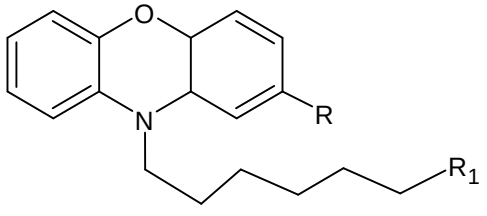


3-nitro-10*H*-phenoxazine 3,4a-dinitro-10,10a-dihydro-4a*H*-phenoxazine

PHARMACOLOGICAL ACTIVITIES

Antibacterial activity

Kumara et al synthesized some hexyl phenoxazine derivatives. It shows potent antibacterial activity [15].

GENERAL STRUCTURE	R	R_1	COMPOUND NAME
	-Cl	$-N(CH_2CH_3)_2$	10-[6'-[N-Diethylamino]hexyl]-2-chloro-phenoxazine
	-Cl	$-N(CH_2CH_2OH)_2$	10-[6'-[N-Bis(hydroxyethylamino)hexyl]-2-chloro-phenoxazine

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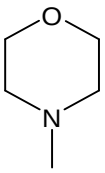
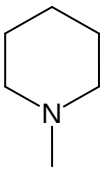
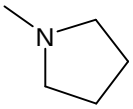
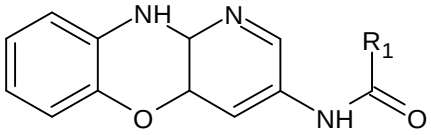
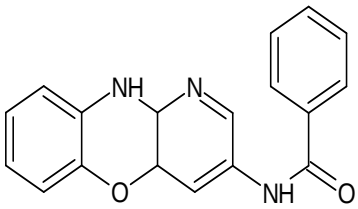
	-Cl		10-[6'-[N-Morpholino]hexyl]-2-chloro-phenoxazine
	-Cl		10-[6'-[N-Piperidino]hexyl]-2-chloro-phenoxazine
	-Cl		10-[6'-[N-Pyrrolidino]hexyl]- 2-chloro-phenoxazine

Antifungal activity

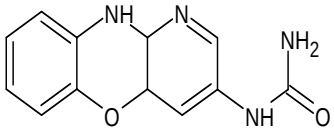
Agbo SA et al studied Phenoxazine carboxamide derivative, the synthesized derivative screened for antifungal activity against different strains of fungi (absidia corymbifera, fusarium solani) using the serial broth dilution method [19].



Phenoxazine carboxamide



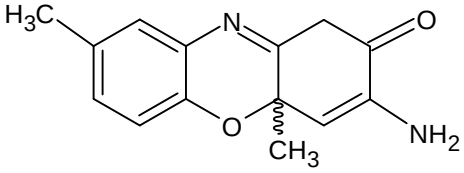
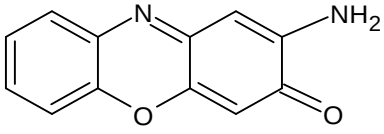
N-(10,10a-dihydro-4a*H*-pyrido[3,2-*b*][1,4]benzoxazin-3-yl)benzamide



N-(10,10a-dihydro-4a*H*-pyrido[3,2-*b*][1,4]benzoxazin-3-yl)urea

Anticancer activity

Macías et al have studied a series of easily affordable phenoxazine derivatives and tested compounds are evaluated for multidrug resistance reverting activity and full antitumor profile [20].

PHENOXAZINE DERIVATIVES	STRUCTURE
Phx_1	 3-amino-4a,8-dimethyl-1*H*-phenoxazin-2(4a*H*)-one
Phx_2	 2-amino-3*H*-phenoxazin-3-one

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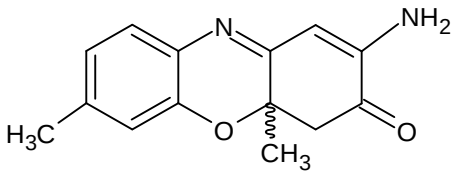
Antiviral activity

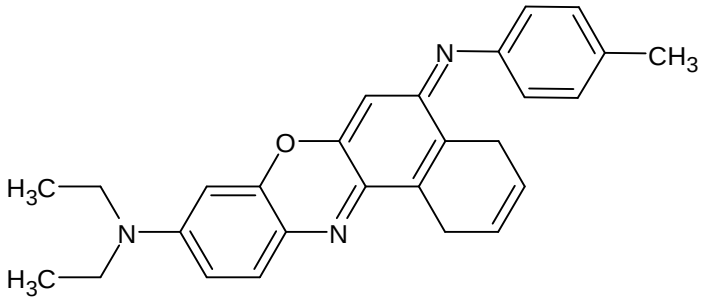
Sato K et al has synthesized 2-amino-4a, 7-dimethyl-4,4a-dihydro-3H-phenoxazin-3-one, that blocked the poliovirus proliferation in Vero cells from 0.2 5µg/ml to 2µg/ml concentrations with better antiviral activity at 1µg/ml [11].



2-amino-4a,7-dimethyl-4,4a-dihydro-3*H*-phenoxazin-3-one

Anti-protozoal activity

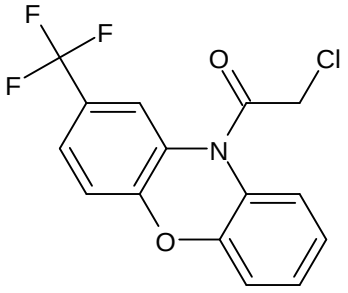
Jian-Feng Ge et al has synthesized N, N-Diethyl-5-((4-methoxyphenyl)imino) -5H-benzo [a] phenoxazin-9 amine. The in vitro anti-protozoal properties were evaluated against several organisms, such as Leishmania donovani, Plasmodium falciparum K1, Trypanosoma brucei rhodesiense, Trypanosoma cruzi, etc. N, N-Diethyl-5-((4-methoxyphenyl)imino)-5H-benzo[a]phenoxazin-9 amine shows IC50 = 0.040 l molL with a selective index of 1425 mainly against Plasmodium falciparum [21].



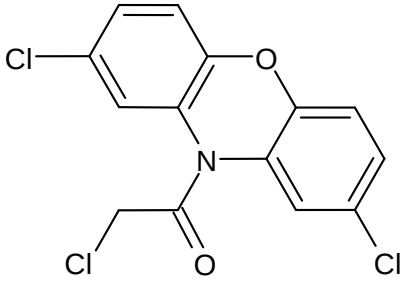
N,N-Diethyl-5-((4-methoxyphenyl)imino)-5H-benzo[a]phenoxazin-9amine

Antiparasitic activity

Müller K et al has synthesized haloacetamide of phenoxazine derivatives, the haloacetamide derivatives proved to be suitable to inhibit Leishmania major is a parasitic species that causes cutaneous leishmaniasis, a tropical disease that generates a large number of adverse effects on human health, mainly affecting the skin and mucous membranes [22].



2-chloro-1-[2-(trifluoromethyl)-10*H*-phenoxazin-10-yl]ethan-1-one



2-chloro-1-(2,8-dichloro-10*H*-phenoxazin-10-yl)ethan-1-one

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II. CONCLUSION

In this paper, we review the recent literature data on the synthesis and biological activities of some phenoxazine derivatives. Phenoxazine is found to be an important lead nucleus possessing a wide range of promising biological activities and this compound needs to be further investigated to unleash a range of molecules with useful activities. Some phenoxazine derivatives have better activity than standard drugs and could become new drugs for the market in the future.

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