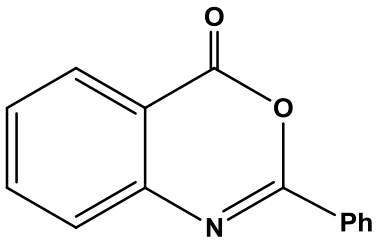
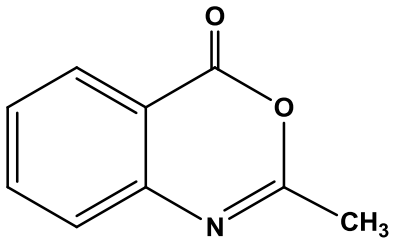
INTRODUCTION

4*H*-3,1-Benzoxazin-4-ones as a class have been known for more than a century. The phenyl derivative **1a** was first synthesized in 1883 [1] and the methyl analog **1b** seventeen years later [2].



1a



1b

The present review will cover this important fused heterocycles nearly almost the chemistry (synthesis and reactions) as well as its applications.

1. Importance of 4*H*-3,1-benzoxazin-4-ones:

4*H*-3,1-Benzoxazin-4-one derivatives are an important class of compounds, like other heterocyclic compounds, as they are used directly or indirectly in many fields[3,4].

1.1 Pharmaceutical applications of 4*H*-3,1-benzoxazin-4-ones:

A series of 6-amino-2-phenyl-4*H*-3,1-benzoxazin-4-one amino acyl, dipeptidyl derivatives in which amino acids and dipeptides are linked to the benzoxazinone moiety via an amide bond and 2-vinyl-4*H*-3,1-benzoxazin-4-one were tested for their inhibitory activity towards *human leukocyle elastase* (HLE) [5,6].

Also, a series of 2,8-disubstituted benzoxazinones were subjected to antiplatelet aggregation, inhibition of superoxide anion and inhibition of *neutrophil elastase release* assay[7].

The 2-aryl-4*H*-3,1-benzoxazin-4-ones were also tested for inhibitory activity against C1r *Serine Protease*. The interaction of 3,1-benzoxazin-4-ones with *Serine Proteases* involves enzyme acylation due to the nucleophilic attack of the active site serine on the lactone carbon, ring cleavage, and the subsequent deacylation of the acylenzyme formed [8-9].

In a modern fashion, 4*H*-3,1-benzoxazin-4-ones core linked to heterocyclyl or heteroaryl were disclosed as *Serine Hydrolase* inhibitors. They were evaluated in a human sputum neutrophil elastase assay[10]. Moreover, potent benzoxazinones are inhibitors for human Cathepsin G, and bovine chymotrypsin.[11-12]

2-Aryl-substituted 4*H*-3,1-benzoxazin-4-ones act as novel active substances for *Cardiovascular system*. They exhibit relaxing effect on smooth musculature in particular and markedly increase coronary flow through langendorff hearts[13]. Moreover, they used in the treatment of *Obesity* and also found to be novel specific *Puromycinsensitive Aminopeptidase* inhibitors [14-15]. Nevertheless, they exhibit biological activities towards *Anti-Elasteases*[16].

One of the most important feature in 4*H*-3,1-benzoxazin-4-ones chemistry is their use as a key starting materials for the synthesis of other pharmaceutically active heterocyclic compounds, mainly quinazoline derivatives[17].

For example, 2-substituted 4(3H)quinazolinone have been gaining prominence duo to the fact that its derivatives have been found to possess a wide spectrum of activities, such as tubulin polymerization inhibitor[18], cytotoxic agent[19], Hsp90 inhibitor[20-21], anticonvulsant[22-23], anti-tumer[24], anti-inflammatory[25], sedative-hypnotic[26], Anti-proliferative[27], antibacterial, and antifungal agent [28-29].

1.2. Industrial applications:

The 2- alkyl and 2-aryl-4*H*-3,1-benzoxazin-4-ones are widely used in the synthesis of polymeric materials [30] and optical bleaching agents [31-32]. Some 4*H*-3,1-benzoxazin-4-ones possessing sulfonylamino groups are fluorescent dyes [33].

4*H*-3,1-B.enzoxazin-4-one derivatives with (aryl) vinyl substituents at position-2 were reported as useful UV absorber having absorption in the long-wavelength region for cosmetics [34]. Also, some 4*H*-3,1-benzoxazin-4-one derivatives have been used to improve the light fastness of textile material[35].

Moreover, 4*H*-3,1-benzoxazin-4-one derivatives are useful UV-light stabilizers for organic materials [36]. Furthermore, 7-nitro-2-phenyl-4*H*-3,1-benzoxazin-4-ones have been reported as selective herbicides [37]. Aryl-ureido benzoxazinone compounds are useful as pigments for use in security links and fibers[38].