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A MINI REVIEW OF THIOPHENE DERIVATIVES

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ABSTRACT

A variety of biological and pharmacological importance of thiophene makes it an essential pharmacophore in the field of medicinal chemistry. Already marketed drugs like Clavix, Plavix which acts by irreversible inhibition of P2Y12 receptor, Tioconazole, a proven fungicidal agent which acts by inhibition of cell wall synthesis having thiophene core has been proven to be efficacious drugs in present respective disease scenario. Thus the synthesis and characterization of novel thiophene moieties with wider therapeutic consequences is a topic of interest for the medicinal chemist. This mini review enumerates the reported synthetic strategy to synthesize thiophene and its major therapeutic field as exploited in the literature. Thereby it is expected that this review will be beneficial for the researchers working in the same.

INTRODUCTION

Thiophene is a five member heterocyclic ring with general formula C_4H_4S [1]. Thiophene moiety have attracted great attention in medicinal field due to its diversified biological activities such as anti-microbial activity [2], anti-fungal activity [3], anti-tubercular activity [4,5], anti-oxidant activity [6,7], local anaesthetic activity [8], 5-HT_1A receptor antagonist [9], 5-HT_6 receptor antagonist [10], anti-inflammatory activity [11], analgesic activity [12], anti cancer activity [13], anti-convulsant activity [14], anti-allergy [15], Phosphodiesterase-IV inhibitors [16] and many more.

Thiophenes and their derivatives are important class of compounds. From literature survey it is revealed that thiophene in different forms like thienopyrimidine [17], benzothiophene [18], bithienyl [19], thienopyridine [20], possesses a wide spectrum of biological activities. Thiophenes and their fused derivatives have shown diverse pharmacological activities including antibacterial, antifungal, immunomodulatory, antiviral, anticancer, antifungal and antitubercular activity.

CHEMISTRY

Thiophene was discovered as a contaminant in benzene [21]. Victor Meyer discovered Thiophene in 1882. The compound was found to be a heterocyclic compound - Thiophene [22].

Thiophene belongs to a class of heterocyclic compounds containing a five membered ring made up of one sulphur as heteroatom [Fig. 1]. Thiophene and its derivatives exist in petroleum or coal. Thiophene is taken from the word “Theion”, the Greek word for sulfur, and another Greek word “Phaino” which means shinning [23]. Thiophene structure can be found in certain natural products and is also incorporated in several pharmacologically active compounds [24].

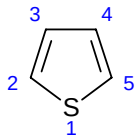
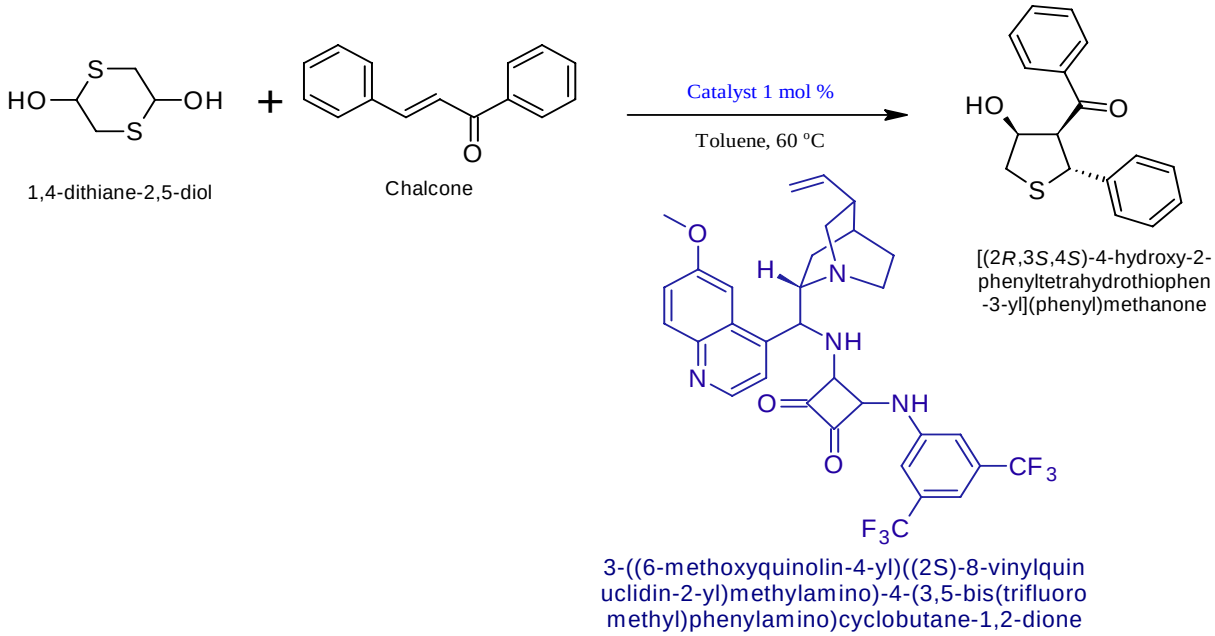


Figure 1: General Structure of Thiophene

In medicinal chemistry, thiophene derivatives have been very well known for their therapeutic applications. The simple thiophenes are stable liquids which closely resemble the corresponding benzene compounds in boiling point and even in smell [25]. They occur in coal tar distillates. The discovery of thiophene in coal tar benzene provides one of the classic anecdotes of organic chemistry. Thiophene has a structure that is analogous to structure of pyrrole, and due to pie electron cloud, it behave like extremely reactive benzene derivative [26]

SYNTHESIS OF THIOPHENE DERIVATIVES [27-28]

A mixture of 1,4-dithiane-2,5-diol with chalcone with quinolin 1 mol% of catalyst in toluene at 25 ^{0}C for 48 hr proceeded as anticipated furnishing the cyclic product.



Scheme 1: Synthesis of Thiophene derivatives

BIOLOGICAL ACTIVITY OF THIOPHENE DERIVATIVES

Nowadays, much interest also has been focused on aza-analogs such as thiophene which showed a very similar classical pharmacological profile. Over the past few years several lead-compounds were developed that are superior in potency and duration of antihypertensive activity to classical high-throughput screening (HTS) drugs and comparatively favorable with second-generation analogs such as **Tiagabine hydrochloride** (GABITRIL) [29] is indicated as adjunctive therapy in adults and children 12 years and older in the treatment of partial seizures. Tiagabine HCl is an antiepilepsy drug [30].

Thiophene moiety containing drugs such as, **Clopidogrel** [31] is an oral, thienopyridine class antiplatelet agent used to inhibit blood clots in coronary artery disease, peripheral vascular disease, and cerebrovascular disease. It is marketed under the trade name ‘Clavix, Plavix’ etc. The drug works by irreversibly inhibiting a receptor called P2Y12, an adenosine diphosphate ADP chemoreceptor on platelet cell membranes. Adverse effects include hemorrhage, severe neutropenia, and thrombotic thrombocytopenic purpura (TTP). Many HTS analogs have now been synthesized and numerous second-generation commercial products have appeared on the market.

Duloxetine hydrochloride [32] is a white to slightly brownish white solid, which is slightly soluble in water. Cymbalta is indicated for the treatment of major depressive disorder (MDD). The efficacy of Cymbalta was established in four short-term and one maintenance trial in adults.

Some thiophene derivative like **Tioconazole** [33] has reported and used as antifungal agent. **Ticlopidine** [34] is an antiplatelet drug in the thienopyridine family. Rivaroxaban [35] is an oral anticoagulant.

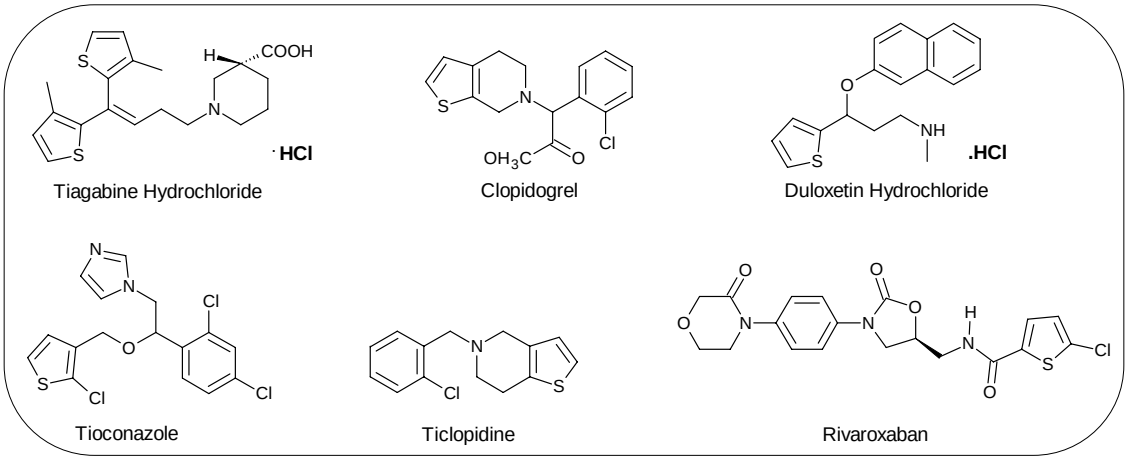


Figure 2: Example of Thiophene Ring containing Drugs

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