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Communication

Synthesis, crystal structure and 3D-QSAR studies of antifungal (bis-)1,2,4-triazole Mannich bases containing furyl and substituted piperazine moieties

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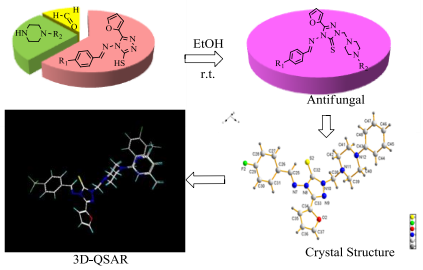
Graphical abstract



This article exhibited the synthesis, crystal structure and 3D-QSAR studies of antifungal furyl- and piperazine- containing (bis-)1,2,4-triazole Mannich bases.

ABSTRACT

A series of novel title compounds **6a**-**6r** and **7a**-**7c** have been synthesized by Mannich reaction of the new triazole Schiff base intermidiates, substituted piperazine and formaldehyde under mild conditions in excellent yields. The crystal structure of compound **6i** was determined to show a chair conformation of the piperazine ring and an (*E*)-configuration of the C=N double bond. The bioassay results indicated that most of the newly synthesized compounds exhibited excellent *in vitro* inhibitory activities and broader spectrum against several plant fungi, and were more effective than the control Triadimefon. Several compounds also displayed favourable *in vivo* antifungal activities. The relationships between the compound structures and various biological activities were discussed. Furthermore, the CoMFA calculation based on the antifungal activity data of compounds **6** against *R. cerealis* was carried out to establish a 3D-QSAR model, which revealed that steric and electrostatic fields were two most important factors for contributing the bioactivity of the compounds. The present work will provide significant information for guiding optimization of such new structures to develop novel agrochemicals with higher antifungal activities.

Keywords:
Triazole
Furan-2-yl
Mannich base
Antifungal activity
Herbicidal activity
3D-QSAR

It is well known that the application of agrochemicals has resulted in increased yields, healthy crops and economic benefits for over half a century. According to the FAO report, some 20%-40% of the world's potential crop production is already lost annually because of the effects of crop diseases, weeds and pests. Such crop losses would be doubled without using the existing agrochemicals [1]. For example, fungal and bacterial pathogens which are recently main reasons for plant diseases have led to severe losses to agriculture and even constituted an emerging threat to the global food security [2-4]. Undoubtedly, agrochemicals play a very important role in agriculture industry. In view of the emergence of resistance and pollution problems associated with conventional agrochemicals, the research and development for all kinds of agrochemicals that have novel structures, super bioactivities and eco-friendly properties are urgently needed in the pesticide chemistry research [5,6].

Heterocyclic compounds, an important class of organic compounds, have attracted much attention in diverse areas because of their interesting structural properties and versatile biological activities. Particularly, they are indispensable part in almost all kinds of agrochemicals. Like many other five-membered heterocyclic compounds, triazoles are used very often in agricultural applications. The compounds containing a triazole ring, such as 1-(substituted phenyl)-3-(1-alkoxycarboxyl alkoxy)-1,2,4-1*H*-triazoles have shown versatile and useful biological properties, and been developed as herbicides, fungicides, or plant growth regulators [7]. As shown in Fig. 1, many 1,2,4-triazole derivatives (*e.g.*, Triadimefon) represent the most important category of fungicides to date and have excellent protective, curative, and eradicant activity against a broad spectrum of foliar, root, and seedling diseases caused by many ascomycetes, basidiomycetes, and imperfect fungi [8-10]. Meanwhile, some structures with a triazole ring also exhibited outstanding

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