Scientific paper

A Convenient Methods for Synthetic Isomeric Structures of Pyrimido-1,2,4-triazine Derivatives as Biocidal Agents

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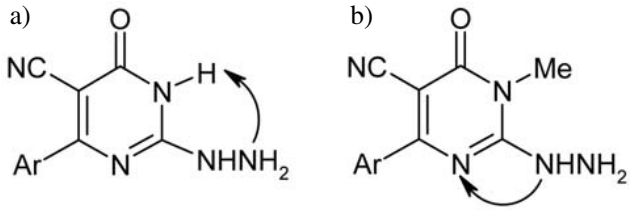
Abstract

Some new isomeric structures of pyrimido[2,1-*c*][1,2,4]triazines **4**–**8** and **10**–**14** have been synthesized via the ring closure reactions of 2-hydrazinyl-1-methylpyrimidine **3** and/or 2-hydrazinopyrimidine **9** with acyclic and cyclic oxygen compounds under various conditions. Structures of the targets have been established from their elemental analyses and spectral data (UV, IR, $^{1}H/^{13}C$ NMR and mass spectrometry). Most of the obtained compounds were evaluated as antimicrobial agents and compared with pipericillin and mycostatine as standard antibiotics. Only compound **7** had highly biocidal effects.

Keywords: Synthesis, isomeric structures, pyrimidotriazines, biocidal effects.

1. Introduction

Polyfunctional pyrimidines are highly reactive intermediates for building various heterobicyclic nitrogen systems which exhibit a broad spectrum of biological and pharmacological properties.[1–3] Diverse pharmacological properties of pyrimidine derivatives, such as anticancer,[4–6] antiinflammatory,[7,8] antimalarial,[9] antiviral,[10] and antidepressant,[11] and fused pyrimidines as antimicrobial,[12–14] antibacterial,[15] antifungal,[16] and antihypertensive[17] support the importance of their synthesis. On the other hand, 1,2,4-triazines have been proved to be very useful in the synthetic chemistry, especially in various one-step heterocyclization reactions proceeding by insertion of two carbon atoms bearing bifunctional groups.[18–20] The structural diversity and biological significance of 1,2,4-triazines have aroused much attention due to the wide range of applications.[21–25] In view of all these facts and as the continuation of our work on the synthesis of new heterocyclic derivatives,[26] the main aim of the present work is the study of the reactivity of polyfunctional pyrimidines with the aim of constructing fused heterobicyclic nitrogen systems containing 1,2,4-triazine moiety starting from 2-hydrazinopyrimidine via two routes (**A** and **B**), in view of the biocidal effects of the final products.



The isomeric structure targets

2. Results and Discussion

The original objective of this work is the formation of isomeric fused pyrimidotriazines via nitrogen atoms. Thus, starting with methylation of 4-(2-hydroxy-1-naphthyl)-2-mercapto-6-oxo-1,6-dihydropyrimidine-5-carbonitrile (**1**),[27] using methyl iodide in stirring with aqueous KOH for one day, yielded 4-(2-hydroxy-1-naphthyl)-1-methyl-2-(methylthio)-6-oxo-1,6-dihydropyrimidine-5-carbonitrile (**2**) which on hydrazinolysis by refluxing with hydrazine hydrate in ethanol produced the corresponding 2-hydrazinyl-1-methylpyrimidine **3** (Scheme 1). Compound **3** was used as starting material for building of pyrimido[2,1-*c*][1,2,4]triazine via route **B**. UV absorption