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ORIGINAL ARTICLE

Synthesis, characterization and evaluation of antibacterial activity of (E)-N′-(substituted benzylidene)-2-(2-fluorobenzyl)-5-ethyl-2*H*-1,2,3-triazole-4-carbohydrazides

Synthèse, caractérisation et l'évaluation de l'activité antibactérienne de (E)-N′-(substitué benzylidène)-2-(2-fluorobenzyl)-5-éthyl-2H-1,2,3-triazole-4-carbohydrazides

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Antibacterial activity;
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Summary Triazoles and their derivatives are important precursors in the pharmacological field due to their broad diversity of medicinal and biological deed. In this article, the exploration is to put an effort to produce some novel biologically active triazole 4-carbohydrazide derivatives. The structures of the newly synthesized compounds were characterized and confirmed by spectral data and were screened for anti-bacterial activity. Compounds **5(d—i)**, **5l** and **5m** were observed to possess potent anti-microbial activity.

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MOTS CLÉS
Synthèse de triazoles substitués ;
Activité antibactérienne

Résumé Le noyau triazole et ses dérivés substitués représentent d'importants précurseurs en pharmacologie en raison de leur grande diversité d'action thérapeutique et biologique. L'objectif de cet article porte sur la synthèse, la caractérisation structurale et l'évaluation de l'activité antibactérienne de vingt nouveaux composés triazoles à fonction carbohydrazide, porteurs d'un substituant fluorophényl et d'un substituant variable de type benzylidène. Comparés à l'activité antimicrobienne de la norfloxacine, les composés **5(d—i)**, **5l** et **5m** présentent une activité prometteuse.

Introduction

Heterocyclic compounds containing nitrogen play an important role in agrochemicals and pharmaceuticals. The basic heterocyclic rings present in the various medicinal agents are mainly 1,2,3-triazole and 1,2,4-triazole [1]. In recent years, triazoles containing compounds have become potential targets for drug discovery [2,3]. A large number of 1,2,3-triazoles exhibit various biological effects and are frequently used as a pharmacophore for the modification of known pharmaceuticals [3], e.g., antiviral [2], antibacterial [3], antifungal [4] and anticancer [5] activities. Also, substituted 1,2,4-triazoles play an important role in organic chemistry due to their presence as key structural units in pharmaceuticals and biologically active heterocycles [6]. Compounds possessing the 1,2,4-triazole moiety have been reported to display antimicrobial activity [7], antifungal [8], antibacterial [9,10], anti-inflammatory [11] and antituberculosis [12] activities. Encouraged by the various biological activities associated with triazole derivatives, we report herein the synthesis, characterization and antibacterial activity of twenty new triazole derivatives.

Results and discussion

Chemistry

The present paper describes the synthesis of (*E*)-*N*′-benzylidene-2-(2-fluorobenzyl)-5-ethyl-2*H*-1,2,3-triazole-4-carbohydrazide derivatives **5a-5t** as depicted in Scheme 1. Coupling of ethyl 2-pentynoate **1** with azidotrimethylsilane was carried out in the presence of triethylamine to obtain Ethyl 5-ethyl-2*H*-1,2,3-triazole-4-carboxylate **2**. Alkylation of compound **2** with 2-fluoro-benzylbromide in potassium carbonate and DMF resulted in the formation of ethyl ester derivative **3**. Reaction of ethyl ester derivative with hydrazine hydrate in presence of ethanol yields carbohydrazide derivative **4**. The condensation of compound **4** with various substituted benzaldehydes was carried out utilizing ethanol at reflux temperature to furnish novel benzylidene-1,2,3-triazole-4-carbohydrazide derivatives **5a-5t**.

Antimicrobial activities

The antimicrobial results of the twenty new triazole carbohydrazide derivatives **5a-5t** (Table 1) have established some interesting structure-activity relationships. Compounds **5 (d-i)**, **5l** and **5m** exhibited excellent activity against all the tested bacterial strains when compared with the standard drug norfloxacin, while the compounds **5b**, **5j**, **5k**, **5r**, **5s** and **5t** observed equipotent activity and compounds **5a**, **5c**, **5n**, **5o**, **5p**, **5q** displayed least activity against all the tested bacterial strains. In general, it is observed that the compounds incorporated with the fluoro-substituent exhibited excellent activity when compared to the standard drug norfloxacin and all other compounds in the series displayed equipotent to moderate activity. From the above observations, it can be concluded that by altering the substituents in the aryl ring of the triazole-carbohydrazide scaffold may lead to a promising antibacterial agent for all the tested bacterial strains such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes* and *Staphylococcus aureus*.

The antimicrobial activity of the compounds **5a-t** were compared with structurally related 1,2,3-triazole-4-carbohydrazides such as *N*′-(4-(4-fluorophenyl)-1-(hydrazono)-1-(piperidin-1-yl)but-3-en-2-ylidene)-1,2,3-triazole-4-carbohydrazide, *N*′-(1-(2-arylhydrazono)-1-(phenylsulfonyl) propan-2-ylidene)-1,2,3-triazole-4-carbohydrazide and (*E*)-*N*′-(1-(1-(4-Fluorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-ethylidene)-5-methyl-1-phenyl-1*H*-1,2,3-triazole-4-carbohydrazides [13]. Bakr F. Abdel-Wahab et al. [13] repoted the synthesis as well as antimicrobial evaluation of these 1,2,3-triazole-4-carbohydrazides, by disc diffusion method. These compounds were tested for their antibacterial activity against Gram positive bacteria (*S. aureus* ATCC 29213, *Bacillus subtilis* ATCC6633, and *Bacillus megaterium* ATCC 9885) and Gram negative bacteria (*Klebseillapeneumoniae* ATCC13883, *P. aeroginosa* ATCC27953 and *E. coli* ATCC 25922) at a concentration of 100 μg/mL in DMSO. Ciprofloxacin was used as standard antibacterial reference. They showed a zone of inhibition ranging from 15—35 mm and few compounds showed a zone of inhibition comparable or greater than the reference ciprofloxacin. The hydrazone moiety was reported to be responsible for the antimicrobial activity and the compound bearing sulfonyl group was reported to be more effective than the other tested compounds.

The compounds **5a-t** investigated presently were tested against selected Gram negative strains (*E. coli* MTCC 443 and *P. aeruginosa* MTCC 424) and two Gram positive strains (*S. aureus* MTCC96 and *S. pyogenes* MTCC442) at a concentration of 25 μg/mL by disc diffusion method. They showed a zone of inhibition ranging from 9—28 mm but at a concentration one fourth of that of the compounds reported [13]. It