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Solvent-Free Microwave Assisted Synthesis of Novel Pyrazole-Oxopyrrolidine and Pyrazole-Oxopiperidine Derivatives and Their Antimicrobial Activity

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Abstract—Herein we report an efficient one-pot multicomponent synthesis of novel pyrazole-oxopyrrolidine derivatives via the Ugi (4C3C) reaction under MW solvent-free conditions. The structures of products have been elucidated by their FTIR, ^{1}H and ^{13}C NMR, mass spectrometry, and HPLC analysis. All synthesized compounds have been tested for their antimicrobial activity and some of those characterized as highly active.

Keywords: Solvent-free synthesis, microwave, Ugi (4C3C) reaction, antimicrobial activity, pyrazole-oxopyrrolidine derivatives

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Pyrazole derivatives are characterized by a broad range of pharmacological activities [1], including antimicrobial [2], anti-inflammatory [3], anticancer [4], anti-tubercular [5], antiproliferative [6], anti-HIV [7], and many more. The combination of pyrazole and oxopyrrolidine makes versatile building blocks in organic synthesis of compounds with pronounced pharmaceutical properties. For example, compound (**I**) acts as caspase-3-inhibitor with analgesic action [8], the pyrazole derivative (**II**) was demonstrated as antifungal activity against *A. niger* and *C. albicans* [9] (Fig. 1).

Several reported methods of synthesis of pyrazole-oxopyrrolidine involved toxic organic solvents, expensive catalysts, proceeded via multiple steps, and giving unsatisfactory yields of products [10]. Among the methods that addressed such challenges were multicomponent reactions (MCRs) carried out under microwave irradiation [11–13].

The above information stimulated our search for efficient synthetic approach to novel pyrazole-oxopyrrolidine derivatives applying MW irradiation in multicomponent reactions thus producing the compounds of antimicrobial potential. Pyrazole-oxopyrrolidine and pyrazole-oxopiperidine derivatives were synthesized via the Ugi (4C-3C) reaction from different ketoacids, aminopyrazoles and cyclohexylisocyanide. Antimicrobial activity of the pyrazole-oxopyrrolidine derivatives was evaluated.

RESULTS AND DISCUSSION

Initially, synthesis of *N*-cyclohexyl-1-(1,3-dimethyl-1*H*-pyrazol-5-yl)-2-methyl-5-oxopyrrolidine-2-carbox-

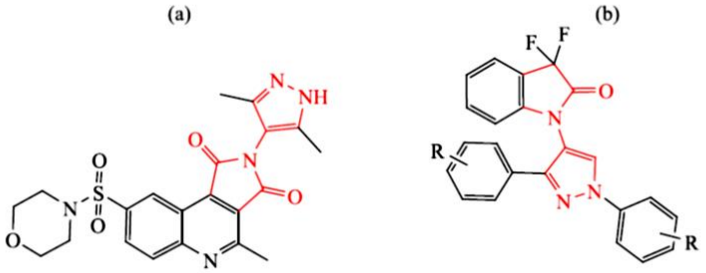

Fig. 1. Some pharmacologically active pyrazole-oxopyrrolidine derivatives: (a) caspase-3 inhibitor (**I**) and (b) antimicrobial agent (**II**).