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Synthesis of novel phosphorus heterocycles as antimicrobial agents

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Background and Aims: The emergence of multi-drug resistant strains of bacteria is a problem of ever increasing significance. Consequently, the development of new antimicrobial agents will remain an important challenging task for medicinal chemists. This study aimed at the synthesis of novel phosphoramidates and to elucidate the potential role of these compounds as antibacterial agents in order to establish structure-activity relationship.
Methods: We synthesized 19 new compounds from the reaction of N-phenylureidophosphoryl dichlorides with 2,2-dimethyl-1,3-diaminopropane or ethylene diamine in the presence of an HCl scavenger (an excess amount of the corresponding diamine). The structural elucidation of the compounds was performed by IR, 1H, 13C and 31P NMR spectroscopy and elemental analysis. Antimicrobial activity of the newly obtained derivatives was tested against three Gram-positive and three Gram-negative bacteria by cup-plate agar and microdilution methods. Gentamycin and Tetracyclin have been used as reference for inhibitory activity against bacteria.
Results: The screening data reveal that five-Membered derivatives having substituent at meta position of the phenyl ring exhibited potent antimicrobial activities against B. subtilis. Also, the data show that all of the five-Membered derivatives were almost inactive against the selected gram-negative bacteria. The results indicate that B. subtilis was more sensitive to the toxicity of the synthesized compounds than other microorganisms.
Conclusions: A series of phosphoramidate derivatives have been synthesized and evaluated for their antibacterial. In general, the results of antimicrobial assays indicated that six-Membered phosphoramidates was the more potent than their five-Membered derivatives against the tested microorganisms. The data exhibited that gram-positive bacteria were more sensitive to the toxicity of the titled compounds than gram negative bacteria. Among the compounds tested three of them (containing the 4-NO2 group and six-Membered ring) showed the most favorable antimicrobial activity.

Keywords: Synthesis; P-heterocycle; Antimicrobial