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Synthesis and Elastase Inhibitory Evaluation of Phosphate Esters and Mixed Phosphate Anhydride of Penam Sulfones*

María A. Laborde and O. A. Mascaretti**

Instituto de Química Orgánica de Síntesis (IQUIOS-UNR), Casilla de Correo 991, 2000 Rosario, Argentina
E-mail: iquiosra@citynet.net.ar

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**Author to whom correspondence should be addressed.

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Abstract: The evaluation of human leucocite elastase inhibition by phosphate esters (**1**-**2**) and phosphate mixed anhydride (**3**) of penicillin sulfones and their precursor sulfides is described.

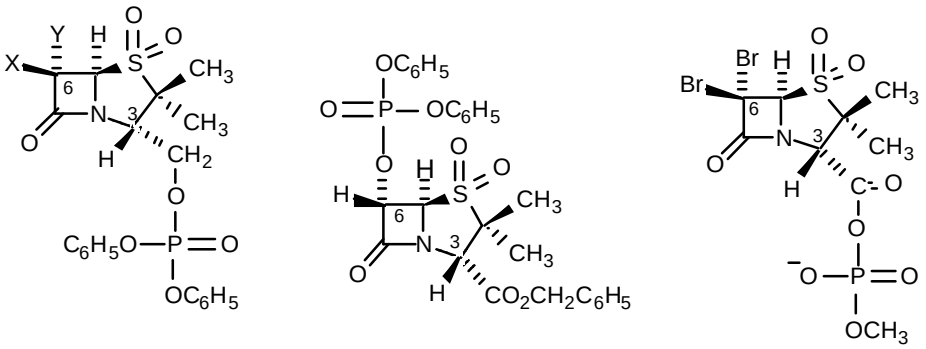
Keywords: Elastase Inhibition, Phosphate Esters, Phosphate Anhydride, Penam Sulfones.

Introduction

Human Leukocyte Elastase [1] (HLE, EC 3.4.21.37) is a serine proteinase found in the azurophilic granules of polymorphonuclear leukocytes. This enzyme has been the subject of extensive studies, both in terms of its biological role in numerous diseases [2] and in the development of suitable inhibitors to be used as potential therapeutic agents. This interest has led over the past fifteen years to the synthesis of a wide variety of inhibitors based on the β-lactam nucleus.

Results and Discussion

We have recently reported the structure-activity relationship (S.A.R) of several benzyl and methyl 6-α-substituted penicillanate sulfones [3]. In this communication we describe the synthesis and our initial structure-activity relationship study of a series of phosphate triesters (**1**-**2**) and phosphate-carboxylate mixed anhydride (**3**) of penicillin sulfones. These new penicillin derivatives were evaluated as elastase inhibitors using H.L.E.



1a X=Y=Br
1b X=H; Y=Cl

2 **3**

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References and Notes

1. a) Edwards, P.D.; Bernstein, P.R. *Med. Res. Rev*. **1994**, *14*, 127; b) Hlasta, D.J.; Pagani, E.D. *Ann. Rep. Med. Chem.* **1994**, *29*, 195; c) Durette, P.L.; Chabin, R.M. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 271.
2. Weinbaum, G.; Giles, R.E.; Krell, R.D. *Ann. N.Y. Acad. Sci.*, **1991**, *624*, 1-370.
3. Boschetti, C.E.; Mata, E.G.; Mascaretti, O.A.; Cricco, J.A.; Coux, G.; Roveri, O.A. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 2033; b) Boschetti, C.E.; Mascaretti, O.A.; Cricco, J.A.; Roveri, O.A. *Bioorg. Med. Chem.* **1995**, *3*, 95; c) Boschetti, C.E.; Mata, E.G.; Mascaretti, O.A.; Cricco, J.A.; Coux, G.; Lodeyro, A.; Roveri, O.A. *J. Braz. Chem. Soc.* **1996**, *7*, 285.