

Synthesis, Characterization and Evaluation of the Activity of Ten Mesoionic Compounds Against Microorganisms

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SUMMARY. Three mesoionic 1,3,4-thiadiazolium-2-thiolates and seven 1,3,4-triazolium-2-thiol chlorides have been synthesised and tested for activity against a range of microorganisms. The chemical structures were confirmed by Elemental Analysis, IR, Mass, ¹H and ¹³C NMR spectrometry. The biological tests indicate that the compounds have substantial activity against Gram-positive and alcohol-acid-resistant bacteria; moderate activity against yeasts and little activity against other fungi and are inactive against Gram-negative bacteria.

RESUMEN. "Síntesis, Caracterización y Evaluación de la Actividad de diez Compuestos Mesoiónicos contra Microorganismos". Tres mesoiónicos 1,3,4-tiadiazolio-2-tiolato y siete cloruros 1,3,4-triazolio-2-tiol se han sintetizado y se ha probado su actividad contra distintos microorganismos. Las estructuras químicas se determinaron por Análisis Elemental, IR, Masa y espectrometría de RMN ¹H e ¹³C. Las pruebas biológicas indican que los compuestos tienen actividad sustancial contra bacterias Gram positivas y alcohol-ácido-resistentes, actividad moderada contra levaduras, escasa actividad contra otros hongos y son inactivos contra las bacterias Gram negativas ensayadas.

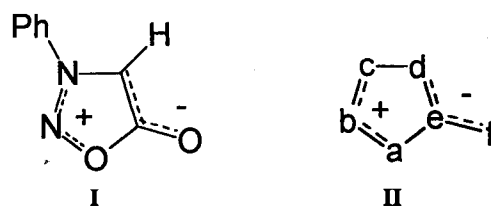
INTRODUCTION

Compounds now classified as mesoionic were first prepared around 100 years ago by Fischer and Besthorn and by Busch *et. al.*¹⁻⁴. Even so it was only in 1949 that the first definition was launched by Baker and Ollis^{5,6} referring especially to the sydnones (**I**), although important fundamental concepts were put forward by Schönberg in 1938⁷.

The concept of mesoionic compounds evolved somewhat over the years although they were generally classified as aromatic betaines. However in 1996 Miller, Simas and their co-workers⁸ put forward a new definition, *viz*: "Mesoionic compounds are heterocyclic betaines with a least one side-chain whose a-atom is also in the ring plane and with dipole moments of the order of 5D (1D = 3,33564x10⁻³⁰ cm). Electrons are delocalized over two regions separated by what are essentially single bonds. One region which includes the α-atom of the side-chain is associated with the HO-

MO and negative π-charge whereas the other is associated with the LUMO and positive π-charge". This is equivalent to indicating that mesoionic compounds are not aromatic.

Structure **II** is a convenient generic representation of mesoionic compounds, according to this definition, in which a, b, c, d, e and f are usually C, N, O, S or Se.



As a result, mesoionic compounds interact strongly with many biomolecules, leading to a very wide range of biological activity: *inter alia* analgesic, anti-convulsant, anti-depressive/psycho-stimulant, anti-inflammatory, anti-malaria, an-

PALABRAS CLAVE: Compuestos mesoiónicos, Bacteria Gram negativa, Bacteria Gram positiva, Hongos, Levaduras.

KEY WORDS: Fungi, Gram-negative bacteria, Gram-positive bacteria, Mesoionic compounds, Yeasts.

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