Pyridazin-3(2H)-one Derivatives as Selective Inhibitors of Monoamine Oxidase-B Isoform (MAO-B)

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Description

This invention is concerned essentially with pyridazinone derivatives substituted at C4, C5 or C6 with dithiocarbamate fragments that are selective MAO-B inhibitors, and their use for the preparation of medicaments for treating disorders resulting from MAO-B hyperactivity, including neurodegenerative diseases, such as Parkinson´s and Alzheimer's diseases and other dementias.

The pyridazine ring is a privileged fragment found in compounds with very different pharmacological properties, such as antihypertensive, antiplatelet, anti-inflammatory, antinociceptive, antidepressant, hypoglycemic, antiinfective or anticancer agents, many of them being pyridazin-3(2H)-one derivatives. The pyridazine ring is also included in polycyclic compounds acting as MAO-B inhibitors. However, simple pyridazin-3(2H)-one derivatives have not been described so far as selective MAO-B inhibitors.
The present invention provides novel pyridazin-3(2H)-one derivatives substituted at C4, C5 or C6 with several dithiocarbamate moieties that selectively inhibit the MAO-B activity and whose structure is unrelated to those currently available.

Innovative aspects and advantages

The novel pyridazin-3(2H)-one derivatives can be easily synthesized through a multi-component reaction, in which the appropriate 6(5)(4)-bromoalkyl analogue, an amine and carbon disulfide react in the presence of anhydrous potassium phosphate at room temperature. The compounds of the present invention were inactive against MAO-A. However, these simple pyridazinone derivatives are inhibitors MAO-B with IC50 values in the micromolar range.

Commercial applications and potential users

The compounds of the present invention or their salts could be used by the pharmaceutical industry for the preparation of medicaments to treat disorders resulting from MAO-B hyperactivity, including neurodegenerative diseases, such as Parkinson´s and Alzheimer's diseases and other dementias.

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Spanish patent and PCT application.

Type of collaboration

Licensing of the technology and collaboration on the commercialization of the product.

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