inefficiently due to their poor water solubility. Thus for example, where such compounds are administered orally, only a small fraction of the drug is taken up into the blood during transit of the gastro-intestinal tract. As a result, to achieve adequate drug uptake it may be necessary to administer high doses of the drug compound, to prolong the period of drug administration or to make frequent administrations of the drug compound. Indeed, the poor solubility and hence poor bioavailability of a drug may cause an alternative drug, perhaps one with undesired side effects or one which requires invasive administration (e.g. by injection or infusion), to be used in place of the poorly soluble drug.

Therefore it is an object of the present invention to produce more bioavailable compounds with a broad antifungal spectrum or to provide useful alternative compounds, maintaining adequately high therapeutic efficacy and adequately low toxicity or other side effects.

Unexpectedly, the antifungal compounds of the present invention or part of the compounds of the present invention may have improved metabolic stability properties, improved PK (pharmacokinetic) properties, improved solubilities, reduced cytochrome P450 liabilities, or improved bioavailability compared with the compounds disclosed in the prior art.

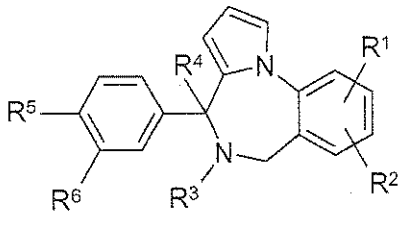
The compounds of the present invention are useful as squalene epoxidase inhibitors.

It is accordingly an object of the present invention to provide novel compounds with antifungal activity to overcome or ameliorate at least one of the disadvantages of the prior art, or to provide a useful alternative.

Summary ~~of the invention~~

It has been found that the compounds of the present disclosure~~invention~~ are useful as antifungal compounds.

The present disclosure, in a first aspect,~~invention~~ concerns novel compounds of Formula (I):



(I)

or~~and~~ stereoisomeric forms thereof, wherein

R^1 is hydrogen, chloro or fluoro;

R^2 is hydrogen, chloro, fluoro or methyl;
R^3 and R^4 are hydrogen;
or R^3 and R^4 taken together form a bond;
R^5 is 1,1-difluoroethyl, and R^6 is hydrogen or fluoro;
or R^5 is hydrogen or fluoro, and R^6 is 1,1-difluoroethyl;
and the pharmaceutically acceptable addition salts, and the solvates thereof.

The present disclosure~~invention~~ also concerns methods for the preparation of compounds of Formula (I) and pharmaceutical compositions comprising them.

The present disclosure, in a second aspect, concerns a pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of a compound as defined above.

The present compounds are useful agents for combating fungi *in vivo*.
The present disclosure, in a third aspect, concerns a compound as defined above for use as a medicament.

The present disclosure, in a fourth aspect, concerns a compound as defined above for use in the treatment or prevention of a fungal infection.

The novel compounds described in the present disclosure~~invention~~ may be useful in the treatment or prevention of infections caused by dermatophytes, systemic fungal infections and onychomycosis.

The novel compounds described in the present disclosure~~invention~~ may be active against a wide variety of fungi, such as *Candida* spp., e.g. *Candida albicans, Candida glabrata, Candida kruceï, Candida parapsilosis, Candida kefyr, Candida tropicalis; Aspergillus* spp., e.g. *Aspergillus fumigatus, Aspergillus niger, Aspergillus flavus; Cryptococcus neoformans; Sporothrix schenckii; Epidermophyton floccosum; Microsporum* spp., e.g. *Microsporum canis, Microsporum gypseum; Trichophyton* spp., e.g. *Trichophyton mentagrophytes, Trichophyton rubrum, Trichophyton quinckeanum, Trichophyton tonsurans, Trichophyton verrucosum, Trichophyton violaceum, Trichophyton interdigitale, Trichophyton soudanense*; *Fusarium* spp., e.g. *Fusarium solani, Fusarium oxysporum, Fusarium proliferatum, Fusarium* verticillioides; *Rhizomucor* spp., e.g. *Rhizomucor miehei, Rhizomucor pusillus*; *Mucor circinelloides; Rhizopus* spp., e.g. *Rhizopus oryzae, Rhizopus microspores; Malassezia furfur; Acremonium* spp.; *Paecilomyces; Scopulariopsis; Arthrographis* spp.; *Scytalidium; Scedosporium* spp., e.g. *Scedosporium apiospermum, Scedosporium prolificans*; *Trichoderma* spp.; *Penicillium spp.*; *Penicillium marneffei; Blastoschizomyces.*

In view of the aforementioned pharmacology of the present compounds, it follows that they are suitable for use as a medicament.

The disclosure~~invention~~ also relates to a compound according to the general Formula (I), the stereoisomeric forms thereof and the pharmaceutically acceptable addition salts and the solvates thereof, for use in the treatment or prevention of fungal infections.

One advantage of the compounds or a part of the compounds of the present disclosure~~invention~~ may lie in their enhanced bioavailability, improved metabolic stability properties,

improved PK properties, reduced hERG channel inhibition, or reduced cytochrome P450 liabilities compared with the compounds disclosed in the prior art.

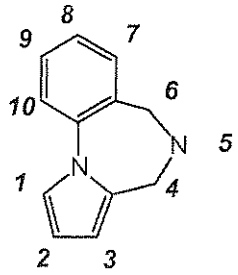
The present disclosure~~invention~~ will now be further described. In the following passages, different aspects of the disclosure~~invention~~ are defined in more detail. Each aspect so defined may be combined with any other aspect or aspects unless clearly indicated to the contrary. In particular, any feature indicated as being preferred or advantageous may be combined with any other feature or features indicated as being preferred or advantageous.

Detailed description

The chemical names of the compounds of the present invention were generated according to the nomenclature rules agreed upon by the Chemical Abstracts Service, using Advanced Chemical Development, Inc., nomenclature software (ACD/Name product version 10.01; Build 15494, 1 Dec 2006).

In case of tautomeric forms, it should be clear that the other non-depicted tautomeric form is also included within the scope of the present invention.

The atoms in the tricyclic system are numbered as shown in the following formula (XX):



(XX)

It will be appreciated that some of the compounds of Formula (I) and their pharmaceutically acceptable addition salts and solvates may contain one or more centers of chirality and exist as stereoisomeric forms.

Hereinbefore and hereinafter, the term "compound of formula (I)" is meant to include the addition salts, the solvates and the stereoisomers thereof.
The terms "stereoisomers", "stereoisomeric forms" or "stereochemically isomeric forms" hereinbefore or hereinafter are used interchangeably.
The invention includes all stereoisomers of the compound of Formula (I) either as a pure stereoisomer or as a mixture of two or more stereoisomers.
Enantiomers are stereoisomers that are non-superimposable mirror images of each other. A 1:1 mixture of a pair of enantiomers is a racemate or racemic mixture.
Diastereomers (or diastereoisomers) are stereoisomers that are not enantiomers, i.e. they are not related as mirror images. If a compound contains a double bond, the