

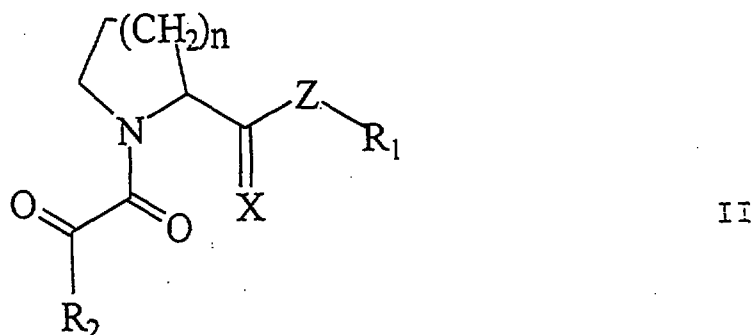
HETEROCYCLIC THIOESTERS AND KETONES

ABSTRACT

This invention relates to neurotrophic low molecular weight, small molecule heterocyclic thioesters and ketones having an affinity for FKBP-type immunophilins, and their use as inhibitors of the enzyme activity associated with immunophilin proteins, particularly peptidyl-prolyl isomerase, or rotamase, enzyme activity.

This invention relates in particular to :

compounds of formula II:



or a pharmaceutically acceptable salt thereof, wherein:

n is 1 or 2;

X is O or S;

Z is S;

R₁ is selected from the group consisting of C₁-C₃ straight or branched chain alkyl, C₂-C₃ straight or branched chain alkenyl, Ar, and mixtures thereof, wherein said R₁ is unsubstituted or substituted with halo, nitro, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl, hydroxy, C₁-C₄ alkoxy, C₂-C₄ alkenyloxy, phenoxy, benzyloxy, amino, Ar, or a mixture thereof;

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R_2 is selected from the group consisting of C_1-C_8 straight or branched chain alkyl, C_2-C_8 straight or branched chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl and Ar_1 , provided that R_2 is not methyl when n is 1, X is O, and R_1 is phenyl;

Ar_1 is phenyl, benzyl, pyridyl, fluorenyl, thioindolyl or naphthyl wherein said Ar_1 is unsubstituted or substituted with halo, trifluoromethyl, hydroxy, nitro, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, amino or a mixture thereof.

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