

两类HPPD酶抑制剂的比较分子场分析研究

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收稿日期 修回日期 网络版发布日期 接受日期

摘要 用比较分子场分析法(CoMFA)研究了环己二酮类及3-烷氧基-2-环己烯酯类化合物的结构与活性的关系。本研究从蛋白酶与底物动力学模拟的复合物结构出发构建两类抑制剂化合物分子的构象,并进行了全空间搜索,CoMFA分析得到了较好的模型(交叉验证回归系数 $q^2 = 0.779$,模型的线性回归系数 $r^2 = 0.989$)。该方

程不仅可以帮助推测抑制剂与受体的结合方式,还可定量地预测结构相近的类似物活性,为设计合成新的HPPD酶抑制剂提供了理论依据。

关键词 酶 抑制剂 比较分子力场分析法 环己二酮 环己烯 结构与性能关系

分类号 [O64](#)

CoMFA of Two Classes of 4-Hydroxyphenylpyruvate Dioxygenase Inhibitors

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Abstract Comparative molecular field analysis (CoMFA) was used to perform a quantitative structure-activity relationship study of cyclohexane-1,3- diones and alkanolic acid 3-oxo-cyclohex-1-enyl analogues as 4-hydroxyphenylpyruvate dioxygenase inhibitors. The structure of the substrate abstracted from the dynamics modelling of the enzyme- substrate complex was used to design the structure of the inhibitors. Satisfactory results were obtained after all-space searching, with the leave-one out cross validation correlation coefficient $q^2 = 0.779$ and conventional $r^2 = 0.989$. The model will be used to speculate the combining mode between the inhibitors and the receptor as well as to quantitatively prognosticate the biological activity of analogues. Moreover, it provides theoretical foundation for synthesizing new HPPD inhibitors.

Key words [ENZYME](#) [INHIBITOR](#) [CoMFA](#) [CYCLOHEXANEDIONE](#) [CYCLOHEXENE](#) [STRUCTURE AND PROPERTY CORRELATION](#)

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