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研究论文

N-[2-(4-甲基)嘧啶基]-*N′*-2-硝基苯磺酰脲的合成、晶体结构、生物活性及其与酵母**AHAS**的分子对接

王建国，马宁，王宝雷，王素华，宋海斌，李正名*

(南开大学元素有机化学研究所 元素有机化学国家重点实验室 天津 300071)

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摘要 合成了磺酰脲化合物*N*-[2-(4-甲基)嘧啶基]-*N′*-2-硝基苯磺酰脲, 用元素分析、红外、核磁共振氢谱对产物进行了表征, 培养并测定了其晶体结构. 晶体属三斜晶系, 空间群, 晶胞参数a=0.54159(1) nm, b=1.1533(3) nm, c=1.1857(4) nm, α=83.907(6)°, β=81.048(5)°, γ=77.637(4)°, V=0.7126(4) nm^3, D_c=1.572 g/cm^3, Z=2, F(000)=348, R=0.0659, wR=0.1217. 在晶体结构中, 杂环上的一个N原子与脲桥上邻近的N原子上的H构成分子内氢键. 测定了对酵母AHAS的离体抑制活性, 其抑制常数K_i为(2.48±0.35)×10^{-7} mol/L. 用分子对接方法, 将目标化合物晶体结构对接到靶酶酵母AHAS的活性位点, 发现对接完毕目标化合物的构象与复合物晶体中的磺酰脲分子构象接近, 并得到了合理的生物活性预测值. 该研究为进一步理解磺酰脲类的分子结构、药物活性并设计新的分子提供了帮助和指导.

关键词 磺酰脲 合成 晶体结构 生物活性 分子对接

分类号

Synthesis, Crystal Structure and Biological Activity of *N*-(4-Methyl- pyrimidin-2-yl)-*N′*-2-(nitrophenylsulfonyl)urea and Its Docking with Yeast AHAS

WANG Jian-Guo,MA Ning,WANG Bao-Lei,WANG Su-Hua
SONG Hai-Bin,LI Zheng-Ming*
(*State Key Laboratory of Elemento-organic Chemistry, Elemento-organic Chemistry Institute, Nankai University, Tianjin 300071*)

Abstract *N*-(4-Methylpyrimidin-2-yl)-*N′*-2-(nitrophenylsulfonyl)urea has been synthesized and characterized by elemental analysis, IR and ^{1}H NMR spectra. Single crystals of the title compound have been obtained and determined. The crystal belongs to triclinic system, space group with cell parameters: a=0.54159(1) nm, b=1.1533(3) nm, c=1.1857(4) nm, α=83.907(6)°, β=81.048(5)°, γ=77.637(4)°, V=0.7126(4) nm^3, D_c=1.572 g/cm^3, Z=2, F(000)=348, R=0.0659, wR=0.1217. In the crystal structure, an intramolecular H-bond was formed be-tween a nitrogen atom of the heterocyclic ring and a neighboring hydrogen atom bonded with a nitrogen atom to connect the urea bridge. *In vitro* inhibitory activity against yeast AHAS has been determined and the inhibition constant K_i was (2.48±0.35)×10^{-7} mol/L. Molecu-lar docking was used to dock the crystal structure of the title compound to the active site of yeast AHAS. It was found that the resulting conformation was similar to sulfonylurea herbicide in complex with AHAS and the biological activity was predicted reasonably well by the program. This study will provide assistance and guidance to further understand molecular structure of sulfonylurea and its herbicidal activity and to design new compounds.

Key words sulfonylurea synthesis crystal structure biological activity molecular docking

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通讯作者 李正名 nkzml@nk.sina.net