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论文

2-甲基-2-取代-7-羟基-2,3-二氢-4H-1-苯骈吡喃-4-酮及其衍生物的合成和抗真菌活性研究

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摘要：

目的：对自行设计的抗真菌先导化合物进行衍生物合成和抗真菌活性研究，以验证设计思想，检验模建结果的可靠性。方法：设计合成18个化合物，所有目标化合物经元素分析、^{1}HNMR谱和红外光谱确证，部分化合物还进一步用^{13}CNMR谱、MS-EI谱和高分辨质谱确证。用8种人类致病真菌对所有目标化合物测试体外最小抑菌浓度值。结果：合成的18个化合物中，14个(JS1b～d,JS2a～d,JS3a～b,JS4a～d和JS5c)为新化合物。结论：对所合成的化合物进行抗真菌活性测试，结果表明设计合成的衍生物的抗真菌活性变化规律与设计思想吻合，从配体角度验证了模建的靶酶三维结构的可靠性，检测了活性位点力场的分布。

关键词： 羊毛甾醇14α去甲基化酶 白色念珠菌 抗真菌活性 4H-1-苯骈吡喃-4-酮 衍生物

SYNTHESIS AND ANTIFUNGAL ACTIVITIES OF 2-METHYL-2-SUBSTITUTED-7-HYDROXYL-2,3-DIHYDRO-4H-1-BENZOPYRAN-4-ONE AND THEIR DERIVATIVES

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Abstract:

AIM: A series of derivatives were designed to identify the distribution of molecular field energies in the cavity and to testify the reliability of the model of Lanosterol 14α demethylase of *Candida albicans*. METHODS: All of the 18 title compounds were synthesized and confirmed by elementary analysis, ^{1}HNMR and IR spctrum. Some were confirmed further by ^{13}CNMR, MS-EI and high-resolution MS spectrum. Their antifungal activities were evaluated *in vitro* against 8 common human pathogenic fungi. RESULTS: All the compounds, except JS1a, JS5a, JS5b, JS5c, were first reported, while all of 18 title compounds were first reported as antifungal agents. CONCLUSION: Antifungal activities of the derivatives were in accord with the distribution of molecular field energies in the cavity, and the reliability of the model was validated by way of ligand design.

Keywords: *Candida albicans* antifungal activity synthesis 4H-1-benzopyran-4-one derivatives lanosterol 14α demethylase

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