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论文

含有脂环的三苯乙烯化合物的合成和抗雌激素受体活性的研究

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摘要:

目的 为寻找高效低毒的雌激素受体拮抗剂，设计合成了新结构骨架的三苯乙烯类化合物。方法 通过McMurry反应得到三苯乙烯中间体，再经醚化反应得到目的物。通过抗小鼠子宫增重实验测定化合物的拮抗活性，竞争性结合雌激素受体实验测定化合物对受体的亲和力。结果 本文共合成了35个新化学实体，并利用X-射线晶体衍射和氢谱确定了化合物的构型。结论 所有化合物均能与受体结合(IC_{50}<10^{-6} mol.L^{-1})，其中化合物35与受体的亲和力最大。某些化合物抑制子宫的增长，表现为拮抗作用；有的则促进子宫的增长，表现为激动作用。其中化合物14和27对子宫的抑制作用强于或相当于他莫昔芬，有待进一步研究。

关键词： 抗雌激素受体活性 三苯乙烯

SYNTHESIS OF TRIPHENYLETHYLENE WITH ALIPHATIC CYCLIC MOIETY AND ITS ANTAGONISM ON ESTROGEN RECEPTOR

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Abstract:

AIM In order to improve the biological activity and reduce the side effects and toxicity, a series of novel estrogen receptor antagonists were designed. METHODS The key triphenylethylene intermediates were obtained by the McMurry reaction. The target compounds were prepared by etherification. The binding affinities of the target compounds for the estrogen receptor in rat uterine cytosol were measured by a competitive binding assay and their estrogen agonistic/antagonistic properties were investigated in the 3-day uterine weight assay in the immature rats. RESULTS Thirty-five new compounds have been synthesized and their geometric configuration were determined by X-ray crystallography and ^{1}HNMR spectral data. CONCLUSION All of the test compounds showed affinity for the estrogen receptor (IC_{50}<10^{-6} mol.L^{-1}), especially compound 35 with IC_{50} 1.07×10^{-8} mol.L^{-1}. Some compounds are antagonists, inhibiting uterus growth; others are agonists, promoting uterus growth. Compounds 14 and 27 are superior antagonists to tamoxifen.

Keywords: triphenylethylene antagonism on estrogen receptor

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