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论文

新型抑制破骨细胞生成的化合物合成与活性研究

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摘要:

目的 寻找有抑制破骨细胞活性的苄膦酸型先导化合物。方法 用类似Arbuzov型反应合成α-烷氨苄膦酸化合物。以体外培养大鼠骨髓液中的破骨细胞样细胞(osteoclast-likecells,OLC)生成为模型,筛选上述合成产物,化合物结构经MS或^{1}HNMR得到证明。结果 得到10个α-烷氨苄膦酸化合物,均为新化合物。生物活性筛选表明,化合物2,8及9对体外大鼠的OLC的生成有显著抑制活性($P<0.01$)。结论 增强分子的芳香性及亲脂性(9)可提高抑制生成破骨细胞的活性。

关键词: 苄膦酸 合成 破骨细胞

STUDIES ON THE SYNTHESIS AND BIOACTIVITY OF α-ALKYLAMINOBENZYL-PHOSPHONIC ACIDS

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Abstract:

AIM To search for some substituted benzyl phosphonic acids as leading compounds with inhibiting effect on osteoclast formation. METHODS Target compounds were prepared from aromatic aldehydes, primary amine and phosphorous acid using tetramethylenesulfone as solvent *via* Arbuzov type reaction. The effect on inhibiting the formation of osteoclast-like cells (OLC) of related compounds was studied by incubating the extract of rat femur marrow. RESULTS Ten compounds of α-alkylaminobenzyl phosphonic acids have been synthesized and identified by MS or ^{1}HNMR analysis. Three (2, 8 and 9) of them were found to have notable effect on the inhibition of OLC formation ($P<0.01$). CONCLUSION Among the present substituted benzyl phosphonic acids, the increased aromaticity and hydrophobicity (such as compound 9) can remarkably enhance the ability to inhibit OLC formation.

Keywords: synthesis osteoclast benzylphosphonic acid

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