药学学报 1990, 25(12) 891-897 DOI: ISSN: CN:

论文

抗胆碱药3-(2-苯基-2-环戊基-2-羟基-乙氧基)奎宁环烷的立体化学和构效关系

高建华;文广伶;张其楷

军事医学科学院毒物药物研究所,北京100850

摘要:

研究了强效抗胆碱药dl-3-(2-苯基-2-环戊基-2-羟基-乙氧基)-奎宁环烷的四个光学异构体的两种不对称合成方法,用HPLC检测了异构体含量,讨论了构效关系。

关键词: 抗胆碱药 不对称合成 光学纯3-取代奎宁环烷 构效关系

STUDIES ON THE STEREOCHEMISTRY AND STRUCTURE-ACTIVITY RELATIONSHIP OF CHOLINOLYTIC COMPOUNDS 3-(2-PHENYL-2-CYCLOPENTYL-2-HYDROXYL-ETHOXY)-QUINUCLIDINES

JH Gao; GL Wen and QK-Zhang

Abstract:

Four optical isomers of the new cholinolytic compound 3 - (2 - phenyl - 2 - cyclopentyl - 2 - hydroxyl - ethoxy) - quinuelidine (Ⅰ) have been asymmetrically synthesized by two methods. Method one: Recemic 1 - phenyl - 1 - cyclopentylepoxy ethane reacting with 3Ror 3S-quinuclidinol produces a mixture of (R-1) and (R-2)or (S-1) and (S-2) respectively. The chemical yields varied from 57% to 78%. The highest % de is 22 and the major product is (R- 1)or (S- 1). Method two: Grignard reaction of 3R or 3S - benzoyl - methoxy - quinuclidine with cyclopentyl magnesium bromide yields a mixture of(R- 1)and (R- 2)or (S- 1)and (S-2). The chemical yield is 80%. The highest % de is 81 and the major product is (R- 2)or (S-2). Preliminary evaluation of the four new optical isomers revealed the following series of biological potencies: (R - 2)>(Ⅰ)>(S - 1)>(R - 1)>(S-2). In the coupling of the compounds with the active centers of M receptors, the absolute Configurations in carbon-3 of the quinuclidinyl group and carbon-2 of the substituted ethyl group play an important role. The influence of carbon-2R is greater than that of carbon-3R on cholinolytic potency.

Keywords: Asymmetric synthesis Optically pure substituted quinuclidine Structure — activity relationship Cholinolytic

收稿日期 1988-09-08 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者:

作者简介:

参考文献:

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