药学学报 2006, 41(6) 537-543 DOI: ISSN: CN:

论文

抗高血压药奥美沙坦酯合成新路线和相关杂质的研究

吴泰志;刘晓华;张福利;谢美华

1. 上海医药工业研究院， 上海 200437; 2. 青岛国风药业股份有限公司， 山东 青岛 266510

摘要：

目的研究奥美沙坦酯的新合成方法，并对合成中产生的主要杂质进行结构确证和有效控制。方法4-(1-羟基-1-甲基乙基)-2-丙基咪唑-5-羧酸乙酯水解，环合成4,4-二甲基-2-丙基-4,6-二氢呋喃并［3,4-d］咪唑-6-酮，与4-［2-(2-三苯甲基四唑-5-基)苯基］苄基溴缩合，经分离纯化，皂化成钠盐，与4-氯甲基-5-甲基-2-氧代-1,3-二氧杂环戊烯成酯，脱保护基得奥美沙坦酯。对缩合反应的主要杂质应用X-ray单晶衍射谱确证其结构为咪唑位置异构体，并用其合成奥美沙坦酯的咪唑位置异构体。通过优化反应条件抑制异构体的量，从而保证奥美沙坦酯的质量。结果用新路线合成了奥美沙坦酯，总收率60%，纯度大于99.0%；成品中异构体含量小于0.1%。结论本文合成路线是奥美沙坦酯的新合成方法，并首次报道奥美沙坦酯的咪唑位置异构体。

关键词： 奥美沙坦酯 合成 异构体

A novel synthesis of olmesartan medoxomil and examination of its related impurities

WU Tai-zhi; LIU Xiao-hua; ZHANG Fu-li; XIE Mei-hua

Abstract:

AimTo develop a new synthetic route for olmesartan medoxomil. MethodsOlmesartan medoxomil was prepared from ethyl 4-(1-hydroxy-1-methylethyl)-2-propylimidazole-5-carboxylate via hydrolysis and lactonization to afford 4,4- dimethyl-2-propyl-4,6-dihydrofuro ［3,4-d］-1*H*-imidazole-6-one which was condensed with 2-(triphenylmethyl)-5-［4′-(bromomethylbiphenyl)-2-yl］tetrazole, followed by esterification with 4-chloromethyl-5-methyl-1,3-dioxol-2-one, and deprotection. The chemical structure of the major impurity in condensation reaction is the regio-isomer in the imidazole moiety, and confirmed by single crystal X-ray diffraction. The corresponding regio-isomer of olmesartan medoxomil was synthesized from the impurity by similar method. Optimization of the condensation conditions reduced the impurity to a negligible quantity. ResultsSynthesis of olmesartan medoxomil by the new route gave a product of 60% yield and above 99.0% purity. The content of olmesartan medoxomil regio-isomer was effectively controlled to less than 0.1%. ConclusionA novel synthetic route for olmesartan medoxomil was developed successfully. The olmesartan medoxomil regio-isomer is reported for the first time.

Keywords: synthesis regio-isomer olmesartan medoxomil

收稿日期 2005-11-03 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 张福利

作者简介:

参考文献：

本刊中的类似文章

文章评论 (请注意:本站实行文责自负, 请不要发表与学术无关的内容!评论内容不代表本站观点.)

反馈人		邮箱地址	
反馈标题		验证码	3671