
目 录

摘 要.....	错误!未定义书签。
Abstract.....	错误!未定义书签。
第一章 前言.....	错误!未定义书签。
1.1 研究背景.....	错误!未定义书签。
1.2 本论文的主要工作.....	1
1.3 仪器.....	1
1.4 试剂.....	2
第二章 综述.....	3
2.1 心力衰竭概述.....	3
2.2 低钠血症概述.....	3
2.3 托伐普坦.....	3
2.4 具体合成路线比较分析.....	错误!未定义书签。
2.5 结论.....	9
2.6 研究目的.....	10
第三章 实验的研究路线、小试.....	11
3.1 实验的研究路线.....	11
3.2 小试阶段.....	12
第四章 讨论.....	16
第五章 注意事项.....	17
第六章 总结.....	18
参考文献.....	19
附 录.....	20
致 谢.....	21

托伐普坦新合成路线探索

摘 要

目的：建立在前人学者专家的托伐普坦合成路线的基础之上，先进行以测试为目的的实验来检验合成路线的可行性，通过分析该些路线的合成过程，找出其中所存在的问题，特别是以工业化生产的角度去发现问题。优化出一条生产成本相对较低，环境相对友好，杂质相对较少，产率理想的合成路线。方法：以2-甲基-4-硝基苯甲酸为原料药，与2-甲基苯甲酰氯反应，再与中间体7-氯-5-氧代-2,3,4,5-四氢-1H-苯氮卓反应，利用油浴，冰浴，搅拌，调pH等反应条件，薄层色谱，质谱等鉴别方法，通过萃取，旋蒸，重结晶等操作，最终得到目标产物托伐普坦。结果，在前辈专家学者的研究基础之上，进一步分析合成路线，并经过一系列合理的处理、鉴别方法，找到更加合理的合成路线与反应条件。结论，本工艺的合成路线并不复杂，整体产率乐观，在成本较高的中间体利用率上有了明显的提高，有效的降低了成本，反应条件温和，易于操作，后处理操作简便，适合于应用到工业化生产中。

【关键词】托伐普坦；路线优化；工业化生产

Exploration of the new synthetic route of tolvaptan

Abstract

Purpose: Based on the tolvaptan synthetic route of previous scholars and experts, first carry out test-oriented experiments to verify the feasibility of the synthetic route, and analyze the synthesis process of these routes to find out the existence Problems, especially to find problems from the perspective of industrial production. Optimized a synthesis route with relatively low production cost, relatively friendly environment, relatively few impurities and ideal yield. **Method:** Take 2-methyl-4-nitrobenzoic acid as raw material, react with 2-methylbenzoyl chloride, and then react with intermediate 7-chloro-5-oxo-2,3,4,5-tetra Hydrogen-1H-benzodiazepine reaction, using oil bath, ice bath, stirring, pH adjustment and other reaction conditions, thin layer chromatography, mass spectrometry and other identification methods, through extraction, rotary evaporation, recrystallization and other operations to finally obtain the target product Torval Putan. As a result, based on the research of senior experts and scholars, the synthetic route was further analyzed, and after a series of reasonable processing and identification methods, a more reasonable synthetic route and reaction conditions were found. In conclusion, the synthesis route of this process is not complicated, the overall yield is optimistic, the utilization rate of intermediates with higher cost has been significantly improved, the cost has been effectively reduced, the reaction conditions are mild, the operation is easy, and the post-processing operation is simple, It is suitable for application in industrial production.

【Keywords】 tolvaptan; route optimization; industrial production

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