高等学校化学学报 2010, 31(4) 718-722 DOI: ISSN: 0251-0790 CN: 22-1131/O6

论文

甲酸铵催化转移氢化还原肽链中的芳香硝基——对氨基苯丙氨酸的间接引入

高永清[1,2], 周宁[2], 吕玉健[2], 史卫国[2], 程卯生[1], 刘克良[2]

1. 沈阳药科大学制药工程学院, 沈阳 110016;
2. 军事医学科学院毒物药物研究所, 北京 100850

摘要:

研究了用甲酸铵催化转移氢化法(AF-CTH)对不同类型肽中的芳香硝基的还原行为, 这些肽类化合物包括促黑激素(MSH: 四肽)、促黄体素释放激素(LHRH: 十肽)和强脯肽(十七肽)的类似物. 用HPLC对还原过程进行了跟踪监测, 结果显示, 除含对氯苯丙氨酸残基的LHRH类似物因发生脱氯副反应不适合用AF-CTH还原外, 其余序列还原过程中均无明显副反应发生, 硝基几乎定量地转化成为相应的氨基, 实现了对氨基苯丙氨酸向肽链的间接引入. 另外发现, 硝基还原所需的时间与肽链长度有关, 肽链越长, 还原所需时间越长, 但与其在序列中的位置关系不明显.

关键词: 促黑激素; 促黄体素释放激素; 强脯肽; 甲酸铵催化转移氢化; 硝基还原

Reduction of the Aromatic Nitro Group in Peptide by Ammonium Formate Catalytic Transfer Hydrogenation——An Indirect Introduction of *p*-Aminophenylalanine into Peptide Chain

GAO Yong-Qing[1,2], ZHOU Ning[2], LÜ Yu-Jian[2], SHI Wei-Guo[2], CHENG Mao-Sheng[1], LIU Ke-Liang[2*]

1. School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang 110016, China;
2. Beijing Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing 100850, China

Abstract:

The *p*-aminophenylalanine was a useful functional amino acid in the design of peptide drugs, and it was usually prepared by the reduction of *p*-nitrophenylalanine. Ammonium formate catalytic transfer hydrogenation(AF-CTH) was confirmed feasible in transforming the aromatic nitro group into the amino group in a dipeptide, and the orthogonal protection for p-aminophenylalanine in traditional route could be avoided in this method. Therefore, we wondered if this method could be widely used for the reduction of *p*-nitrophenylalanine residue in various peptides, such as the MSH(tetrapeptide), LHRH (decapeptide) and dynorphin(heptadecapeptide) analogues. The reduction processes were monitored by HPLC and the results showed that all sequences could be smoothly transformed into the desired products, except the LHRH analogue containing *p*-chlorophenylalanine due to the dechlorination. It suggested that AF-CTH was an effective method for the reduction of the nitro group in a peptide. In addition, it was found that the reduction rate of the nitro group was slower in longer peptide and not obviously correlative to its site in peptide.

Keywords: Melanocyte-stimulating hormones(MSH); Luteinizing hormone-releasing hormone(LHRH); Dynorphin; Ammonium formate catalytic transfer hydrogenation; Nitro group reduction

收稿日期 2009-05-18 修回日期 网络版发布日期

DOI:

基金项目:

国家自然科学基金(批准号: 30500629)和国家重大新药创制科技重大专项基金(批准号: 2009ZX09301-002, 2009ZX09103-027)资助.

通讯作者: 刘克良, 男, 研究员, 博士生导师, 从事多肽药物和核酸化学研究. E-mail: keliangliu@yahoo.com

作者简介:

参考文献：

[1]Sewald N., Takubke H. D.. Translated by LIU Ke-Liang(刘克良), HE Jun-Lin(何军林). Peptides: Chemistry and Biology(肽: 化学与生物学)[M], Beijing: Science Press, 2005: 268—296
[2]ZHOU Ning(周宁), FU Hui-Jun(付慧君), RONG Di(荣嫡), et al.. Chem. J. Chinese Universities(高等学校化学学报)[J], 2007, 28(4): 668—671
[3]Jiang G. C., Stalewski J., Galyean R., et al.. J. Med. Chem.[J], 2001, 44: 453—467
[4]Samant M. P., Jozsef G., Hong D. J., et al.. J. Med. Chem.[J], 2005, 48(15): 4851—4860
[5]Samant M. P., Hong D. J., Croston G., et al.. J. Med. Chem.[J], 2006, 49(12): 3536—3543
[6]Theobald P., Porter J., Rivier C., et al.. J. Med. Chem.[J],1991, 34: 2395—2402
[7]Ram S., Ehrenkaufer R. E.. Tetra. Lett.[J], 1984, 25(32): 3415—3418
[8]Rajagopal S., Spatola A. F.. J. Org. Chem.[J],1995, 60(5): 1347—1355
[9]Dean Y., Maeda F. B., Thomas F. M., et al.. J. Med. Chem.[J], 2000, 43(26): 5044—5049
[10]Jerry R. H., Rayna M. B., Xiang Z. M., et al. . J. Med. Chem.[J], 2002, 45: 2801—2810
[11]ZHOU Ning(周宁), FU Hui-Jun(付慧君), CHENG Jun-Ping(程军平), et al.. Chem. J. Chinese Universities (高等学校化学学报)[J], 2008, 29(6): 1141—1144
[12]Gao Y. Q., Zhou N., Lü Y. J., et al.. Chin. Chem. Lett.[J], 2009, 20: 668—671
[13]Avram G., Walter F., Louise I. L., et al.. Proc. Natl. Acad. Sci. USA[J], 1981, 78(11): 7219—7223
[14]Mohmed K. A., Douglas S. B., Gordon R. J., et al.. J. Org. Chem.[J], 1989, 54(6): 1284—1289

本刊中的类似文章

文章评论

反馈人		邮箱地址	
反馈标题		验证码	9595