化学学报 1995 53 (9): 900-908 ISSN: 0567-7351 CN: 31-1320/06

# 羟甲芬太尼对映异构体的^1H NMR及立体化学

高金海,王智贤,宋国强,朱友成,嵇汝运

中国科学院上海药物研究所

收稿日期 修回日期 网络版发布日期 接受日期

摘要 本文对强效镇痛剂羟甲芬太尼(OMF)八个对映异构体中的其中四个, 即(-)-cis-(3R,4S,2'R)-OMF (1), (+)-cis-(3-R,4S,2'S)-OMF (2),(+)-trans-(3S,4S,2'R)-OMF (3), 和(+)-trans-(3S,4S,2'S)-OMF (4)进行了^1HNMR研究, 归属了所有的共振谱线。对哌啶环质子间偶合常数的分析表明, 所有顺式和反式异构体中的哌啶环都呈现相同的椅式构象。在顺式异构体中3-甲基位于直立键, 而4-N-苯基丙酰胺基位于平伏键, 反式异构体中它们均位于平伏键。讨论了3-甲基和4-N-苯基丙酰胺基的立体取代对NMR的影响, 在顺式异构体中4-N-苯基丙酰胺基的构象相对固定, 而在反式异构体中则较为自由。

关键词 质子磁共振谱法 异构体 立体化学 镇痛药 羟甲芬太尼

分类号 0621

## ^1H NMR and stereochemistry of ohmefentanyl enantiomers

GAO JINHAI,WANG ZHIXIAN,SONG GUOQIANG,ZHU YOUCHENG,JI RUYUN

**Abstract** The ^1H NMR and stereochemistry of four ohmefentanyl enantiomers, (-)-cis-(3R,4S,2'R)-OMF (1), (+)-cis-(3-R,4S,2'S)-OMF (2), (+)-trans-(3S,4S,2'R)-OMF (3), and (+)-trans-(3S,4S,2'S)-OMF (4), were analyzed with the combination of several one- and two-dimensional NMR techniques. The vicinal coupling constants between the piperidine ring protons were consistent with the piperidine ring assuming a chair conformation with an equatorial 4-N-phenylpropanamide group. In cis-isomers, the 3-He and 5-He signals were 1.1 downfield and 0.5 upfield from the corresponding signals in trans-isomers due to the deshielding and shielding effects of C=O groups and N-phenyl rings, respectively. This suggested that the steric position and orientation of 4-N-phenylpropanamide groups are relatively fixed in cis-isomers, owing to the intramolecular hindrance of axial 3-methyl. While in trans-isomers, the 4-N-phenylpropanamide groups maybe possess various orientations, as investigated by the variable temperature NMR experiments.

**Key words** PROTON MAGNETIC RESONANCE SPECTROMETRY ISOMER STEREOCHEMISTRY ANALGESICS OHMEFENTANYL

DOI:

通讯作者