

间体未被胺化,至使未反应的中间体和反应过程中产生的有色杂质混在一起,较难分离,经摸索,采用制备薄层分离,然后进行重结晶,所得产品纯度较高。

### 参考文献

- 1 Charlier RH. *US* 3038004
- 2 Thomis J, Tentorey P. Prolonged ventricular repolarisation

- a prevention of severe arrhythmia? *Ann Rep Med Chem*, 1983, 118:99
- 3 Lynch JJ, Lucchesi BR. In life-threatening arrhythmias during ischemia and infarction; Hearse DJ, *et al.* Eds; Raven Press; New York, NY, 1987;169~196
  - 4 Lawson JW. Antiarrhythmic activity of some isoquinoline derivatives determined by a rapid screening procedure in the mouse. *J Pharmacol Exp Ther*, 1968, 160:22
  - 5 Gubin J, Rosseels G. Indolizine derivatives. *Ger Offen.* 2, 707,048

## Synthesis of Indolizine Compounds and Their Antiarrhythmic Activity

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Nine 2-ethyl-3-[4-(2-hydroxy-3-alkylaminopropanoxy) benzoyl] indolizines (alkyl = *iso*-Pr, *n*-butyl, *iso*-butyl, *tert*-butyl, diethyl, benzyl, cyclopentyl, 3,4-dimethoxyphenethyl, 3,4-methylene-doxyphenethyl) were prepared. Screening test of 9 compounds indicated that **II**<sub>2</sub>(R=*tert*-butyl) and **II**<sub>6</sub>(R=3,4-dimethoxyphenethyl) could markedly antagonize CHCl<sub>3</sub>-induced arrhythmia in mice. 2-picoline was treated with 4-(4-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>)C<sub>6</sub>H<sub>4</sub>COCl, 2-ethyl-3-(4-tosyloxybenzoyl) indolizine deprotected, the hydroxybenzoyl-indolizine treated with epoxy chloropropane and *tert*-butylamine to give **II**<sub>2</sub>, which could antagonize CHCl<sub>3</sub>-induced arrhythmia in mice.

**Key words** Indolizines; Antiarrhythmic activity

【文摘 001】7-氨基-3-甲氧甲基-3-头孢烯-4-羧酸的合成 胡树琛,周慧殊,段廷汉. 中国医药工业杂志,1993,24(9):417

7-氨基-3-甲氧甲基-3-头孢烯-4-羧酸是合成第三代口服头孢菌素头孢泊肟酯(cefepodoxime proxetil)的关键母体。作者结合以往工作的基础,选用新的合成路线。

【文摘 002】头孢菌素类抗生素的 HPLC 测定法的研究, 丁丽霞, 于如赟, 倪坤仪等. 中国医药工业杂志,1993,24(10):465

将色谱优化过程分为 4 步:(1)应用不完全因子设计从多个影响保留时间的因素中选择两个主要因素作为待优化的参数,经 8 个实验确定以 RP-HPLC

分离头孢菌素及相关物质时,流动相中甲醇的浓度和 pH 值往往是影响保留时间的主要因素。(2)应用 Doehlert 均匀外壳设计,进行选择优化实验,经 7 个实验找出同时满足特定分离度和分析时间的优化区间。(3)应用色谱优化专家系统处理数据,预测组分的保留时间和分离度。(4)通过实验验证优化色谱条件。应用 RP-HPLC,紫外检测,及色谱优化,成功地分离了头孢噻吩钠及其相关物质,头孢唑啉钠及其相关物质,建立了测定两药的 HPLC 系统。应用稳定性实验考察实验条件有微小变化时方法的波动性,表明以 HPLC 分离测定头孢菌素,具有高选择性、高灵敏度、高分离度、快速简便等优点。特别适用于多组分分析。