

## Enantiomeric Separation of Amino Alcohols by Ion-pair Chromatography

Ming Hua HU, Xiu Zhu XU\*

Department of Chemistry, Zhejiang University, Hangzhou 310027

**Abstract:** Enantiomers of four amino alcohols were resolved by ion-pair chromatography with (+)-10-camphorsulphonic acid as chiral counter ion. Studies of the influence of the mobile phase composition, the solute structure and the mobile phase flow-rate on separation are presented. Under the optimized conditions, enantiomeric propranolol, norephedrine, metropolol and salbutamol were separated using dichloromethane -1-pentanol (97:3, v/v) as mobile phase on Lichrospher-100-DIOL column.

**Keywords:** Ion-pair chromatography, chiral separation, amino alcohols, (+)-10-camphorsulphonic acid.

Many drugs or physiologically important compounds are chiral molecules and the optical isomers of them may differ in their pharmacological activities. In some instances differences in undesirable side-effects of these enantiomers are important. So the separation of chiral compounds is becoming increasingly important. Liquid chromatography (LC) is well known as an excellent method for separating and analyzing mixtures of stereoisomers. For resolving the ionic chiral compounds it is available to use ion-pair chromatography. The separation of enantiomers with ion-pair chromatography is based on the assumption that transient diastereomeric ion pairs between optical isomers and a chiral counter ion can be formed, and diastereomeric ion pairs have different distributions between the mobile phase and the stationary phase or have different stabilities in the mobile phase. The interaction between enantiomers and a chiral counter ion includes electrostatic attraction and hydrogen bonding. (+)-10-camphorsulphonic acid is often used as a chiral counter ion for separation of amino alcohols in ion-pair chromatography.

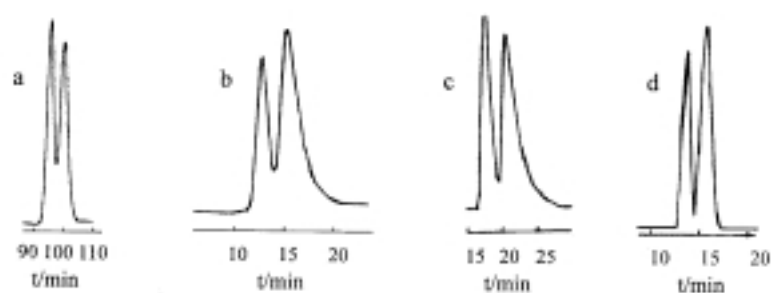
Propranolol, norephedrine, metropolol and salbutamol are four amino alcohol basic drugs and are widely used for the treatment of hypertension and angina pectoris. It is well known that the pharmacological properties of these compounds are mainly due to the (s)-(-)isomer. In previous literatures these compounds were often resolved by using chiral stationary phases<sup>1-3</sup>. In this paper, we successfully used ion-pair chromatography with (+)-10-camphorsulphonic acid as the chiral counter ion on Lichrospher-100-DIOL column which is cheaper than the chiral column.

All the separation were performed on a Shimadzu LC-4A HPLC system equipped with a Waters 991 Photodiode Array Detector, the detection wavelength was set at 225 nm. Lichrospher-100-DIOLcolumn (5  $\mu$ m, 250 mm  $\times$  4.0 mm i.d.) was obtained from E. Merck (Darmstadt, G.F.R). Methylene chloride and 1-pentanol were of analytical grade and

methylene chloride was free from water before use by molecular sieve (4Å). Four amino alcohols were kindly provided by Dr. Wei Wang. (+)-10-Camphorsulphonic acid was obtained from East China Normal University. All other reagents were of analytical grade.

The effects of the mobile phase composition, the solute structure and the mobile phase flow-rate were investigated. The experiment result indicated that both the retention and the resolution of solutes significantly decreased with increasing the concentration of 1-pentanol or other polar solvents in the mobile phase. The reason was that the ability of forming hydrogen bonding between 1-pentanol or other polar solvents in the mobile phase and diastereomeric ion pairs might increase, which reduced the retention on the column and the different distributions between the organic mobile phase and the stationary phase. The result also suggested that the resolution of propranolol was smaller than others, maybe due to the interaction between naphthyl ring and the adsorbing stationary phase was stronger than phenyl ring. Flow-rate was found to strongly influence the separation of those compounds and increase the flow-rate of mobile phase evidently decrease the resolution of these compounds. The reason was that the interaction between enantiomers and (+)-10-camphorsulphonic acid was not sufficiently strong so the solutes were eluted quickly with increasing flow-rate. After optimizing the chromatographic conditions, higher separation factors ( $\alpha$ ) of these four compounds were achieved: 1.06, 1.29, 1.21 and 1.20 for propranolol, norephedrine, metropolol and salbutamol, respectively. Chromatograms of four compounds are showed in **Figure 1**. In short, using ion-pair chromatography with (+)-10-camphorsulphonic acid as chiral counter ion, the separation of these four chiral amino alcohols is successful.

**Figure 1** Chiral separation of four amino alcohols



## References

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