Chinese Chemical Letters Vol. 14, No. 3, pp 280 – 282, 2003
http://www.imm.ac.cn/journal/ccl.html

Chiral Separation of Erythromycin as a New Chiral Selector on CE

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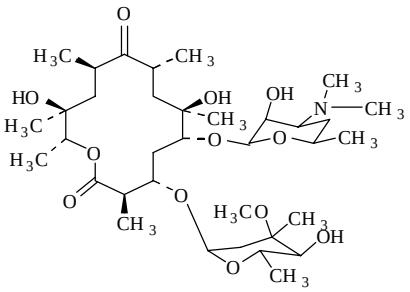
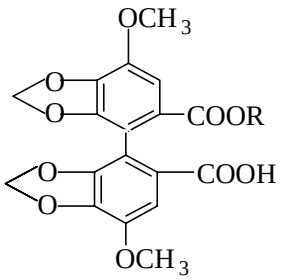
Abstract: Erythromycin as a new chiral selector was first used for chrial separation of four derivatives of biphenyldimethylester enantiomers on CE. The influence of pH, the chiral selector concentration and organic modifiers were preliminarily studied. Experiments show that the erythromycin as chiral selector is useful to CE.

Keywords: Enantiomer, erythromycin, chiral selector, CE.

The separation of optical isomers is an important subject in the pharmaceutical field. Much of the groundbreaking work in chiral separations occurred in LC. In recent years CE has gained in popularity with high efficiency, low cost, flexibility of chiral selectors and operating model, environmental friendliness[1]. The macrocyclic antibiotics have already had a significant impact on the field of separations as a new class of chiral selectors since 1994 by Armstrong[2]. The macrocylic antibiotics offer unique properties that allow the resolution of many compounds often with far greater selectivity. In this work, we introduce a macroolide antibiotic, erythromycin, as a new chiral selector. It has a characteristic fourteen-ring structure, five hydroxyl groups and is slightly soluble in water. We successfully used erythromycin as chiral selector for CE and separated stereoisomers of four derivatives of biphenyldimethylester (**B1-B4**, **Figure 1**).

Figure1 The structures of erythromycin and **B1-B4**





B1 R=-H; **B2** R=CH_3; **B3** R=-C_2H_5; **B4** R=-C_3H_7

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All the separations were performed on a Beckman P/ACE System 5510 capillary electrophoresis equipped with a 254 nm lamp and a 47/40cm×75um I.D. general fused silica capillary and reserved-polarity condition. Data processing were carried out on Beckman P/ACE 5510 ChemStation. The samples were pressure injected for 2s. The separation voltage was set at -30KV. The solution contained 30 mmol/L erythromycin, 40% 2-propanol, 60% 50 mmol/L phosphate (pH=6).

The effect of chiral selector concentration, pH and organic modifiers on chiral separation was investigated. The experiments indicated that the concentration of erythromycin was an important factor on chiral separation and above 40 mmol/L resulted in undesired peak shape and noisy baselines (**Figure 2a**). 30 mmol/L erythromycin was chosen as the optimum concentration for impressive resolution, peak shape and decrease baseline noise. Variation of pH not only changed interactions of electrostatic, hydrogen bonding but also affected the EOF, the charge and molecular recognition properties of both the analyte and the chiral selector. The best resolutions for four drugs were 3.968, 3.621, 4.531, 9.912 obtained at pH=6. When pH >7, Rs decreased. For example, the pH was further increased from 7.0 to 8.0; Rs of **B4** drastically decreased from 3.559 to 1.759. Organic modifiers had a profound effect on chiral separation. It was interesting to point out that chiral separation was not achieved in 2-propanol below 15%(v/v) but separation of four drugs was obtained in the absence of 2-propanol in buffer containing 30 mmol/L erythromycin. **Figure 2b** illustrates that the resolution increased more than 15% in the presence of 2-propanol. Electropherograms of **B1**-**B4** are shown in **Figure 3**. Interestingly, erythromycin seems particularly suited for separating the systems containing at least two benzene rings and one carboxylate group. The experiments show that erythromycin is more stable in solution and the current cost of erythromycin is lower than that of other macrocyclic antibiotics.

Erythromycin is clearly a high-performance chiral selector for resolving the chiral compounds **B1**-**B4** and provides a new chiral selector for CE.

Figure 2 Effect of (a) erythromycin concentration and (b) 2-propanol concentration on resolution.

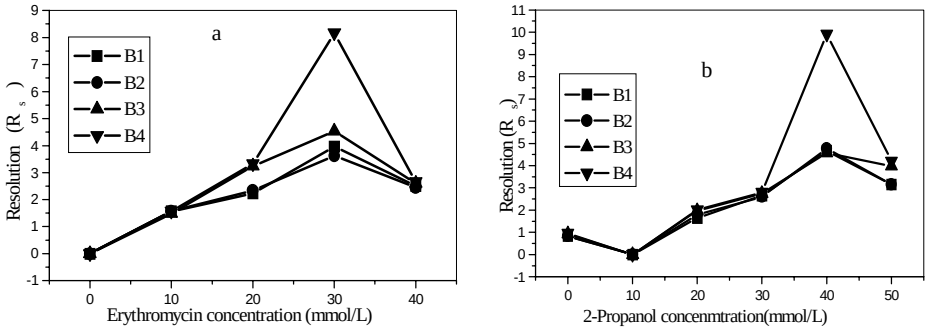
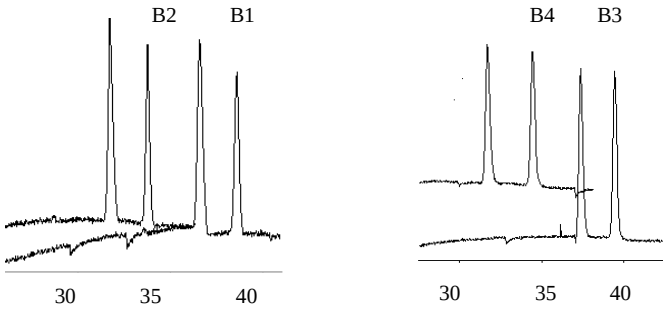


Figure 3 The electropherogram of **B1-B4**.



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Received 27 April, 2002