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Study on Extraction Kinetics of *α*-cyclopentylmandelic acid enantiomers with hydroxyethyl-*β*-cyclodextrin as chiral selector[☆]

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Abstract In this work, the kinetic study on reactive extraction of *α*-cyclopentylmandelic acid (*α*-CPMA) enantiomers was performed in a Lewis cell using hydroxyethyl-*β*-cyclodextrin (HE-*β*-CD) as chiral selector. The enantioselective complexation equilibrium between HE-*β*-CD and *α*-CPMA enantiomers was studied by phase solubility method. The important process parameters affecting the initial extraction rate were separately studied and the reaction rate equations were deduced. The optimal conditions for kinetic study were as follows: stirring speed of 75 $r \cdot min^{-1}$, interfacial area of 12.56 cm^2, pH of 2.5, initial HE-*β*-CD concentration of 0.05 $mol \cdot L^{-1}$, initial *α*-CPMA concentration of 5 $mmol \cdot L^{-1}$, and temperature of 278 K. The reaction has been found to be first order in *α*-CPMA and second order in HE-*β*-CD with the forward rate constants of 2.056×10^{-3} $m^6 \cdot mol^{-2} \cdot s^{-1}$ and 1.459×10^{-3} $m^6 \cdot mol^{-2} \cdot s^{-1}$ for (*S*)-*α*-CPMA and (*R*)-*α*-CPMA, respectively. The complexation equilibrium constants were evaluated as 61 $L \cdot mol^{-1}$ and 117 $L \cdot mol^{-1}$ for (*S*)-*α*-CPMA and (*R*)-*α*-CPMA, and the intrinsic enantioselectivity is estimated as 1.92.

Graphical abstract

The kinetic study on reactive extraction of α-cyclopentyl mandelic acid (α-CPMA) enantiomers was performed in a Lewis cell (a) using hydroxyethyl-β-cyclodextrin as chiral extractant. Under different conditions, concentrations of α-CPMA curve over time was obtained (b).

Keywords: kinetics, liquid-liquid extraction, chiral resolution, *α*-cyclopentylmandelic acid

1 INTRODUCTION

In pharmaceuticals industry, *α*-cyclopentylmandelic acid (*α*-CPMA, Fig. 1) is the key intermediate of soft anticholinergics, *e.g.*, glycopyrrolate which is a well-known antagonist of muscarinic receptors and used for the treatment sialorrhea [1], hyperhydrosis [2], and overactive

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