Analytica Chimica Acta 946 (2016) 96–103

Contents lists available at ScienceDirect

Analytica Chimica Acta

journal homepage: www.elsevier.com/locate/aca

Per(3-chloro-4-methyl)phenylcarbamate cyclodextrin clicked stationary phase for chiral separation in multiple modes high-performance liquid chromatography

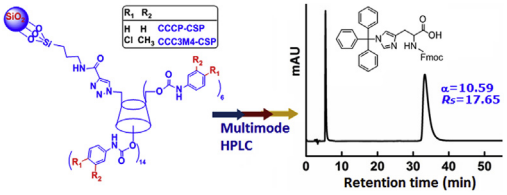
Jian Tang, Limin Pang, Jie Zhou, Shaopeng Zhang, Weihua Tang*

College of Chemical Engineering, Nanjing University of Science and Technology, Nanjing 210094, People's Republic of China

HIGHLIGHTS

- 3-Chloro-4-methyl functionality enhanced enantioselectivities for CD clicked stationary phases.
- Correlation study of chromatography separation with molecular simulation.
- Enantioseparation of 39 racemates in multimode HPLLC.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 15 July 2016
Received in revised form
19 September 2016
Accepted 9 October 2016
Available online 14 October 2016

Keywords:
Enantioselectivity
Cyclodextrin
Chiral stationary phase
High-performance liquid chromatography

ABSTRACT

In this work, a detail study has been performed on the enantioselectivity of per(3-chloro-4-methyl) phenylcarbamate-β-CD clicked chiral stationary phase (CSP) in high-performance liquid chromatography. Both normal phase and polar organic mobile phases have been explored for the enantioseparation of 39 model racemic pairs including aromatic alcohols, flavonoids, β-blockers and amino acids. Chiral resolution values over 10 were achieved for flavonoids. The comparison study with reference perphenylcarbamate-β-CD clicked CSP reveals the significance of 3-chloro-4-methyl functionality in improving the enantioselectivities. This study may provide insight on the multiple interactions between functionalized CD and analytes.

1. Introduction

High-performance liquid chromatography (HPLC) remains one of the most commonly used techniques for separation and purification. The impact of chirality on racemic drugs in terms of therapeutic and pharmacodynamic effects has strengthened the demand for chiral separation. By taking advantage of the intermolecular interactions formed between chiral stationary phases (CSPs) and analytes [1,2], the enantioseparations are generally realized with chromatographic techniques including HPLC, gas chromatography and supercritical fluid chromatography. In HPLC, the interactions may vary in normal phase (NP), polar organic (PO) and reversed phase (RP) modes [3–6]. RP is by far the most favorable mode for the separation of hydrophobic analytes [7,8], while it is not suitable for the analysis of highly polar and charged solutes. To make HPLC more powerful and versatile for wider range of analytes, functionalized CSPs have thus been developed in order to construct multiple intermolecular interactions with chiral solutes for different modes HPLC [1].

Nucleophilic or electrophilic reactions are generally used for the chemical immobilization of chiral selectors onto silica support to prepare chemically-bonded CSPs [7]. However, their low selectivity and efficacy in building linkage often leave unreacted

* Corresponding author.
E-mail address: whtang@mail.njust.edu.cn (W. Tang).

http://dx.doi.org/10.1016/j.aca.2016.10.015
0003-2670/

functionalities on support surface, resulting in low loading of chiral selectors and unstable linkage. These may greatly affect the enantioselectivity of CSPs and their tolerance to multiple modes HPLC [1]. Surface-initiated atom transfer radical polymerization and click chemistry [9] have proven to be highly efficient and selective methods in preparation of stable CSPs tailoring to multiple modes HPLC. The clicking of oligo- and polysaccharides as well as their derivatives has been explored for preparing CSPs for chiral separation [8–12].

Cyclodextrins (CDs) clicking immobilization onto silica gel have been widely developed as effective separation materials [13–15]. Especially, the class of phenylcarbamate derivatives of CDs clicked CSPs with high column efficiency stood out for multiple HPLC modes [6,16–18]. Inspired by the structure controlled enantioseparation ability of phenylcarbamated polysaccharides-based CSPs [19], the effect of substitute's types on phenylcarbamate on CDs-based CSPs was also evaluated [20]. In our earlier systematical work on functionalities tuned the enantioselectivity of phenylcarbamated CD-based CSPs, per(3-chloro-4-methyl)phenylcarbamate-β-CD clicked CSP (CCC3M4-CSP) exhibited more excellent chiral recognition ability than its analogies, including per(4-chloro-3-methyl)phenylcarbamate-β-CD clicked CSP (CCC4M3-CSP) and per(5-chloro-2-methyl)phenylcarbamate-β-CD clicked CSP (CCC5M2-CSP) due to different position of electro-withdrawing and/or electro-donating functionalities on phenylcarbamate moiety [16,17], with chiral resolution (R_s) over 10 achieved for flavonoids and aryl alcohols using CCC3M4-CSP in RP HPLC [16]. The enhanced enantioselectivities are attributed to the enlarged

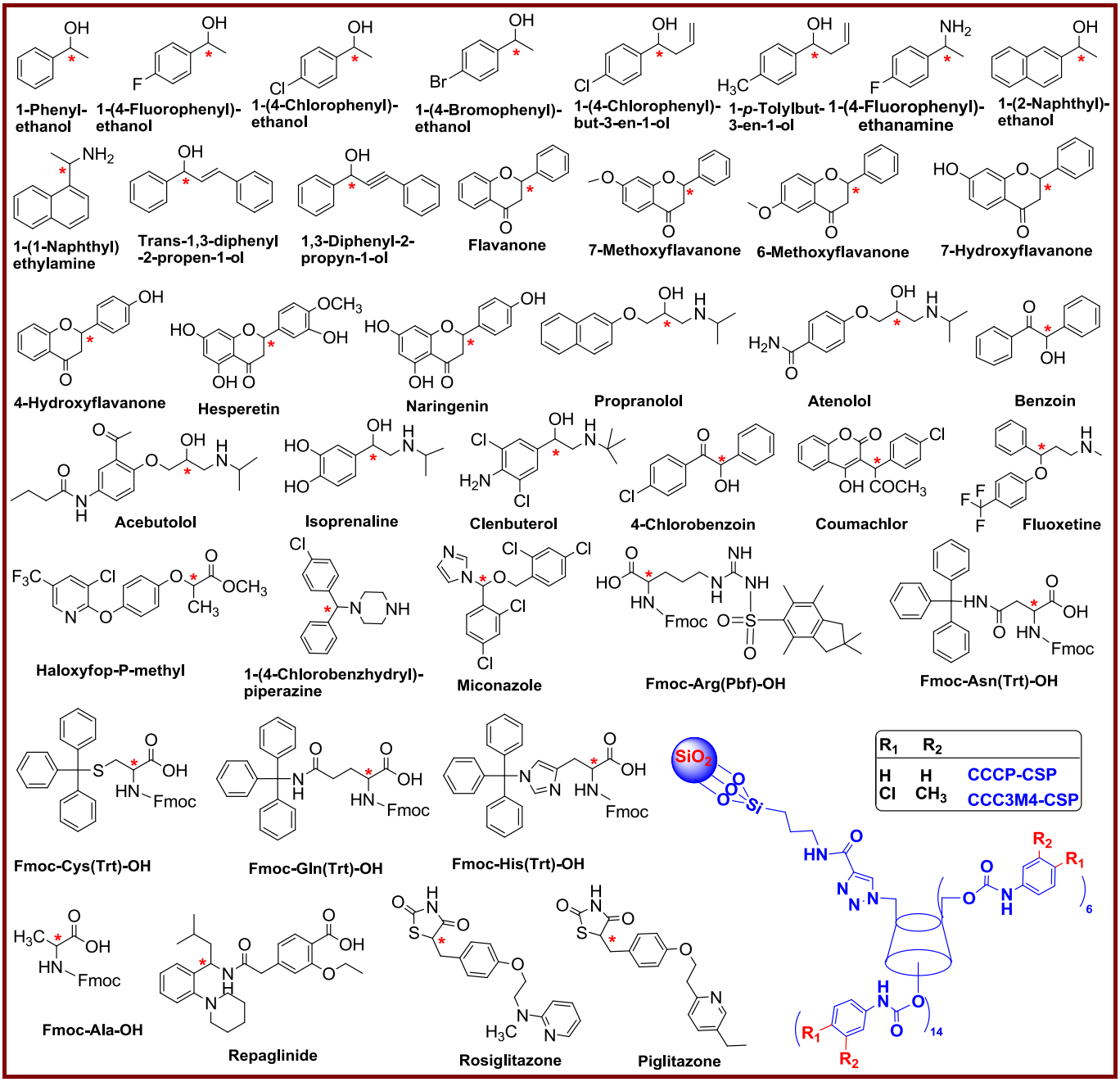


Fig. 1. Structures of racemates and two CD clicked CSPs employed in this study.