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Short communication

Cyclodextrin clicked chiral stationary phases with functionalities-tuned enantioseparations in high performance liquid chromatography

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ABSTRACT

In this work, two cyclodextrin (CD) chiral stationary phases (CSPs) have been developed by clicking per-4-chloro-3-methylphenylcarbamoylated mono-6^A-azido-β-CD (CSP1) and per-5-chloro-2-methylphenylcarbamoylated mono-6^A-azido-β-CD (CSP2) onto alkynylated silica support. The enantioslectivies of the as-obtained new CSPs have been evaluated using 29 model racemates including aromatic alcohols, flavonoids, β-blocker and FMOC-amino acids in both reversed-phase (RP) and normal-phase (NP) high performance liquid chromatography (HPLC). The CD functionalities tuned enantioselectivities were elucidated in different HPLC elution modes. Higher chiral resolutions were achieved in RP-elution mode with the aid of the inclusion complexation in comparison to NP-elution mode. The π-π stacking interaction and dipole–dipole interaction provided by phenylcarbamate moieties can also contribute to the enantioseparation.

1. Introduction

Chiral analysis and purification has become a prerequisite process prior to the clinical use of drugs [1]. High-performance liquid chromatography (HPLC) is a versatile approach for both chiral analysis and manufacturing [2–4]. Enantioseparation can be achieved by the utilization of chiral mobile phases (CMPs) [5,6] or chiral stationary phases (CSPs) [7,8]. The CSPs have aroused prominent interests due to their practicability and chemical stability in different modes of HPLC. Chemically bonded cyclodextrin (CD) CSPs are developed by immobilizing CD derivatives onto silica support [9,10]. The 'click chemistry' [11] has recently evolved as a facile and efficient synthesis approach in the field of biological science and material science, e.g. the preparation of CSPs [12–15].

The introduction of an electron-donating methyl group or an electron-withdrawing halogen at the 3- and/or 4-position of the phenyl ring on phenylcarbamated polysaccharide (cellulose and amylose) CSPs was found to improve their chiral recognition ability towards many racemates [16]. Now, various carbamates including chlorinated and methylsubsituted phenylcarbamates substituted CDs CSPs has been reported in [17–19], but only own one electron-donating group or one electron-withdrawing group.

As a continuation of our research in developing chemically bonded perphenylcarbamoylated CD CSPs [20,21], we herein report per-4-chloro-3-methylphenylcarbamoylated β-CD clicked CSP1 and per-5-chloro-2-methylphenylcarbamoylated β-CD clicked CSP2. The enantioselectivities of these CSPs were evaluated with 29 racemates including aryl alcohols, flavanoids, adrenergic drugs and FMOC-amino acids in both normal-phase (NP), and reversed-phase (RP) modes. The enantioseparation was tuned by optimizing the composition of mobile phases.

2. Experimental

2.1. Chemicals and materials

Reagents including β-CD, 4-chloro-3-methylaniline and 5-chloro-2-methylphenyl isocyanate were purchased from Energy Chemical (Shanghai, China). Kromasil spherical silica gel (5 μm, 100 Å) was obtained from Eka Chemicals (Bohus, Sweden). HPLC-grade methanol (MeOH), acetonitrile (ACN), *n*-hexane (HEX), 2-propanol (IPA) and ethanol (EtOH) were purchased from Tedia (USA). HPLC-grade trifluoroacetic acid (TFA) and triethylamine (TEA) were purchased from J&K (Shanghai, China). The structures of racemates and CSPs are depicted in Fig. 1. Among of them, A6 and A9 were purchased from Sigma–Aldrich (St. Louis, MO), the other racemates were procured from J&K (Shanghai, China).

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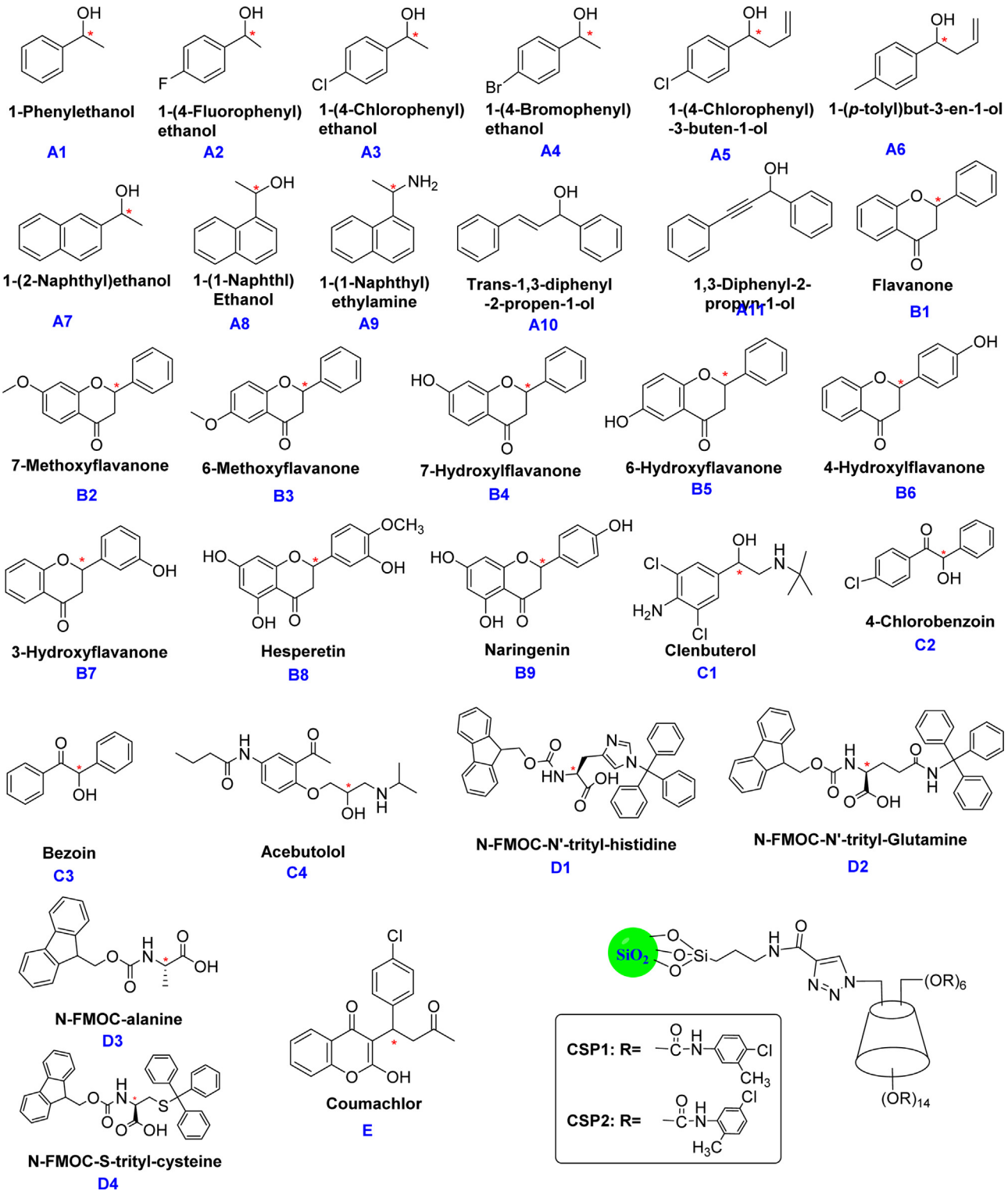

Fig. 1. Chemical structure of 29 analytes and CSPs studied.

2.2. Instruments

NMR spectra were collected on Bruker AVANCE 500 (500 MHz, Bruker Daltonics, Bremen, Germany). Fourier transform infrared spectra (FTIR) were recorded on Thermo Scientific Nicolet iS-10 FT-IR (Thermo Fisher Scientific, Waltham, MA). Elemental analysis was conducted on Vario EL-III CHONS record (Elementar Analysensysteme GmbH, Frankfurt, Germany). HPLC experiments were performed at Agilent 1260 system (Agilent Technologies, Palo Alto, CA) equipped with G1315D diode array detection (DAD) system, G1329B quaternary pump, G1331 C automatic injector, G1316A temperature controller and Agilent ChemStation data manager software (Version No.C.01. 04).

2.3. HPLC procedures

In HPLC, all analytes were prepared as 200 μg/ml in MeOH for RP mode and 200 μg/ml in IPA for NP mode. Each sample solution was