



Preparation and evaluation of 1,3-*alternate* 25,27-bis-(pentafluorobenzyloxy)-26,28-bis-(3-propyloxy)-calix[4]arene-bonded silica gel high performance liquid chromatography stationary phase

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ARTICLE INFO

Article history:

Received 19 January 2009

Received in revised form 25 February 2009

Accepted 6 March 2009

Available online 13 March 2009

Keywords:

Fluorocarbons
Fluorinated phase
Separation
Calix[4]arene
Stationary phase
Selectivity

ABSTRACT

A 1,3-*alternate* 25,27-bis-(pentafluorobenzyloxy)-26,28-bis-(3-propyloxy)-calix[4]arene-bonded silica gel stationary phase (CalixBzF₁₀) was synthesized, structurally characterized, and used as a selector in liquid chromatography. The selectivity study of this phase was done by using fluorine-containing compounds (fluorobenzenes, fluoro-pyrimidine bases), as well as non-fluorinated analytes (non-steroidal anti-inflammatory drugs, sulfonamides, xanthines and polynuclear aromatic hydrocarbons). The effects of organic modifiers on the retention of various compounds possessing basic, acidic and neutral characteristics were studied. It was shown that only basic analytes exhibit a “U-shaped” retention profile and that retention depends on the mobile phase pH. Selectivity comparisons of the novel phase vs. the 1,3-*alternate* 25,27-bis-(benzyloxy)-26,28-bis-(3-propyloxy)-calix[4]arene phase (CalixBz) were performed. The retention mechanism is also discussed. The results indicate that the fluorinated calixarene stationary phase behaves like reversed-phase packing material; however, fluorine-fluorine interactions seem to be involved in the separation process of fluorine-containing analytes.

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1. Introduction

The search for more efficient stationary phases with the widest possible spectrum of applications has become a significant direction in the study of compound separation by high performance liquid chromatography (HPLC). Hydrocarbonaceous bonded phases (e.g., C₁₈, C₈ and phenyl) are the most widely used in reversed-phase liquid chromatography because of their selectivity in the separation of a wide variety of organic compounds. However, in many cases, the analysis may require the use of more specific phases that interact with solutes in a different manner than the classical phases. Several other organic bonded phases have been tried in attempts to increase the selectivity of the stationary phase. For example, very long alkyl chains (C₃₀) [1,2], polar-embedded alkyl chains [3,4] and hybrid materials [5] have all been investigated. Recently, there has been great interest in using fluorinated stationary phases, which offer certain advantages over conventional hydrocarbonaceous stationary phases [6,7]. A number of fluorinated stationary phases are already commercially available. These phases generally contain the pentafluorophenyl group or fluorinated alkyl chains of different

lengths. Fluorinated stationary phases have offered especially high selectivity for fluorine-containing compounds; however, they have also been employed for the separation of steroids [8], polyphenols [9], taxanes [10], corticosteroids [11] and a wide range of pharmaceuticals [12–14].

On the other hand, macrocyclic compounds (cyclodextrins, crown ethers and calixarenes), which are capable of forming inclusion complexes with guest molecules, are commonly used in modern chromatography. The exceptional interest in calixarenes as stationary phases in chromatography results from unique opportunities to influence the specificity and selectivity of these macrocycles [15]. Moreover, the host–guest interactions of calixarenes with solutes are not determined solely by their hydrophobic cavities, but are also influenced by additional functional groups attached at their rims, which can contribute to potential variations in these interactions. Several functionalized calixarenes have been utilized as selectors in liquid chromatography [16,17]. The modifications of these macrocycles comprise conformations in which the calixarene molecules are blocked, variations in the types of functional groups and substituents that are present at their upper and lower rim, ring-size, and the type of spacer fixing the macrocycle to the stationary phase. Calix[*n*]arenes (*n* = 4, 6, 8) in cone conformation functionalized at the upper rim by *tert*-butyl substituents and permanently attached to solid support attracted the great attention of researchers. However, some

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