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Review

Surface-bonded ionic liquid stationary phases in high-performance liquid chromatography—A review

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A B S T R A C T

Ionic liquids (ILs) are a class of ionic, nonmolecular solvents which remain in liquid state at temperatures below 100 °C. ILs possess a variety of properties including low to negligible vapor pressure, high thermal stability, miscibility with water or a variety of organic solvents, and variable viscosity. IL-modified silica as novel high-performance liquid chromatography (HPLC) stationary phases have attracted considerable attention for their differential behavior and low free-silanol activity. Indeed, around 21 surface-confined ionic liquids (SCIL) stationary phases have been developed in the last six years. Their chromatographic behavior has been studied, and, despite the presence of a positive charge on the stationary phase, they showed considerable promise for the separation of neutral solutes (not only basic analytes), when operated in reversed phase mode. This aspect points to the potential for truly multimodal stationary phases. This review attempts to summarize the state-of-the-art about SCIL phases including their preparation, chromatographic behavior, and analytical performance.

Contents

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1. Introduction

Silica is undoubtedly the most used stationary phase media in reversed-phase liquid chromatography (RPLC) due to its versatility and physical characteristics [1]. It results very simple to link different materials to the siliceous particles, thereby producing a wide range of selectivity. One important disadvantage of silica-based materials arises in the analysis of basic compounds, because of the strong interaction that are established between these compounds and the free residual silanol groups on the surface of the stationary phase [2–4]. It is worthy to mention that there has been an impressive amount of works in the last decade shifted to develop new stationary phases for high-performance liquid chromatography (HPLC), in order to improve column efficiency, permeability, and stability [5–7].

Ionic liquids (ILs), which can be defined as a class of ionic, non-molecular solvents, remain in liquid state at temperatures below 100 °C. They possess a multitude of tunable physicochemical properties and have been extensively studied for synthesis and catalysis [8]. ILs have many unique properties including variable viscosity, high conductivity, high thermal stability, almost negligible vapor pressure, and a multitude of varying solvation interactions. The use of ILs has been a hot research topic in analytical chemistry in recent years due to their outstanding properties, as it has been highlighted in a number of recent review articles [9–15].

ILs have also found an important application area in HPLC. They have been mainly used as mobile phase additives with the purpose of removing the deleterious effect of free silanols on the retention of basic analytes, as an alternative to conventional alkyl amines or other amino quenchers [16–21].

ILs have been also used as stationary phases in HPLC, bonding them to silica and hence constituting surface-confined ionic liquids (SCILs) [1,21,22]. The first use of ILs in combination with silica took place in 1985, when Moreira and Gushikem [23] used silica gel functionalized with 3(1-imidazolyl)propyl groups to absorb and pre-concentrate metal ions from ethanol solutions. In 2002, Valkenberg et al. [24] reported methods for the immobilization of ILs to solid supports. Liu et al. [25] were the first authors to report the utilization of a SCIL phase for HPLC in 2004. The new stationary phase, containing the immobilized IL 1-(mercaptopropyl)alkyl-3-hexylimidazolium tetrafluoroborate, was able to separate efficiently 4 ephedrines using a mobile phase composed of 1% methanol in 0.05 mol L^{-1} KH_2PO_4 at pH 3.0. The same analytes were poorly separated on a C18 column when using similar mobile phase but without the addition of ion-pair agent [26] or triethylamine (TEA) [27]. Moreover, the separation was achieved using low amounts of organic modifier. The novelty and interest of the new developed SCIL stationary phase was followed by a number of works in which different methods were used to attach covalently various IL cations/anions to silica sorbents. Thus, the tuneability of ILs had led to the development of a high number of new SCIL phases. Among them, it must be highlighted not only the studies of Liu and co-workers [28–33], but also the works of Stalcup and co-workers focused on understanding the behavior of SCIL phases [34–40], mainly, their true multi-modal retention properties: hydrophobic, electrostatic, and hydrogen bonding.

Evidently, it can be argued that once bound to a solid support, the cation/anion pair no longer constitutes a true ionic liquid. However, the ability to modify the properties of the silica-based stationary phase by changing easily the structural make-up of the cation/anion pair draws obvious correlations to the tuneability of classic ionic liquids. Because of the variety of possible SCIL phases that could be synthesized and the multiple retention modalities in which these new bonded phases can participate, the study of this new type of HPLC stationary phases results of interest.

Several authors have already included the use of SCIL phases in HPLC as part of their review articles regarding ILs in separation science and HPLC [10,21,22], or regarding novel HPLC stationary phases [1]. This review focuses on summarizing all SCIL phases synthesized up to date by describing their preparation and physicochemical characterization, and by discussing the studies conducted to account for their behavior. Their potential multimodal behavior when interacting with a variety of analytes is undoubtedly highlighted, as well as recent analytical validation properties published.

2. Types of surface-confined ILs stationary phases

A group of around 20 SCIL stationary phases has been described up to date [25,28–48]. The main structures of the reported SCILs are shown in Table 1. The name and abbreviations used for the SCILs (Table 1) correspond to the final IL that results attached to the silica; and do not follow the criteria of several authors; in which the starting IL of the synthesis is used to name the SCIL phase.

SCIL stationary phases have been mainly prepared using 4 different synthetic approaches. One of them consists of grafting bromoalkyl-1-trichlorosilane linking ligand to a silica substrate, and the phase is then endcapped with chlorotrimethylsilane. The subsequent modification of the linker and endcap-modified silica with either an ionic liquid precursor compound (imidazole, alkylimidazole, or pyridine) or an ionic liquid (for example: 3-(*n*-butanesulfonate)-imidazole), leads to the formation of the SCIL phase, as it is shown in Fig. 1(A). This approach has been used in a high number of works [34–40]. Other approach starts by modifying the activated silica with a silane-coupling agent, 3-mercaptopropyltrimethoxysilane (MPS). Then, the MPS-modified silica is reacted with an ionic liquid containing 1-allyl as substituent of the imidazolium cation, in the presence of azodiisobutyronitrile (AIBN) as the initiator via the radical chain transfer addition [25,32,43,47]. The procedure is shown in Fig. 1(B). Another approach also used activated silica but modified with another silane-coupling agent: 3-chloropropyltrimethoxysilane, as it is shown in Fig. 1(C). The modified silica is then reacted with imidazole, alkyl-imidazole, or pyridine [28–32,41,44,46], to form the SCIL phase. Colón and co-workers followed a different approach, which is shown in Fig. 1(D) [42]. Authors first synthesized the IL by reacting 3-bromopropyl-trimethoxysilane with 1-alkylimidazole and then, the resulting IL was easily bonded to the silica.

A recent work of Zhou et al. [45] has also described the preparation of four novel ILs functionalized β-cyclodextrins (β-CDs) and their bonding to silica gel to be used in HPLC as stationary phases.

3. Characterization of surface-confined ILs stationary phases

3.1. Physicochemical characterization

The physicochemical characterization of these new SCIL phases has been carried out using different methods and techniques such as elemental analysis, thermogravimetric analysis, X-ray photoelectron spectroscopy (XPS), Raman spectroscopy, infrared spectroscopy, and ^{13}C and ^{29}Si nuclear magnetic resonance (NMR) spectroscopy analysis. Table 2 summarizes the data obtained from such studies. Thus, elemental analysis has been applied to verify if immobilization of the IL on the surface was successful, and also to calculate the surface coverage of the chemically modified silica [30,43]. The thermogravimetric analysis gives information on the thermal stability of SCIL phases and also confirms the amount of the compounds successfully immobilized [28]. XPS is a very useful analytical technique for characterizing different chemical/physical forms of elements of surface layers. Infrared, Raman, and ^{13}C and