RSC Advances

RSC Advances

www.rsc.org/advances

ROYAL SOCIETY
OF CHEMISTRY

www.rsc.org/advances

Sil-UIm-R

(1) Sil-UIm-C8, R =

(2) Sil-UIm-C18, R =

(3) Sil-UIm-EC29, R =

(4) Sil-UIm-Ant, R =
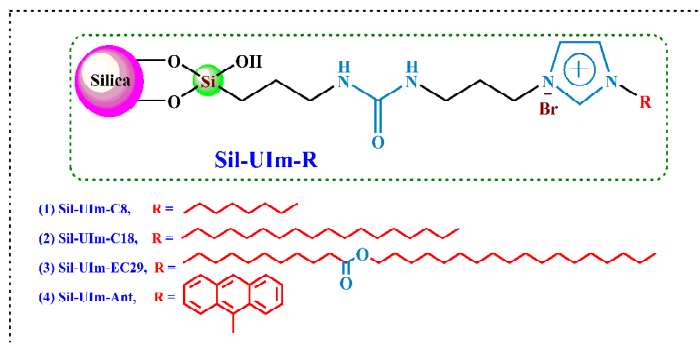
New strategy for surface modification of silica spheres was proposed on the basis of one-pot urea formation and quaternization of imidazole. The properties of the modified silica materials were of high tunability, which guarantees the controllable hydrophobicity and thus designable behaviour in high-performance liquid chromatography.

ARTICLE TYPE

Homogenous formation, quaternization of urea-functionalized imidazolyl silane and its immobilization on silica for surface-confined ionic liquid stationary phases

Mingliang Zhang,[a,b] Jia Chen,[a] Hongdeng Qiu,*[a] Abul K. Mallik,[c] Makoto Takafuji,[c] and Hirotaka Ihara[c]

A novel facile and efficient immobilization strategy was introduced on the basis of the reaction between _iso_cyanate and amine and applied in surface modification of mesoporous silica sphere with a series of urea-functionalized imidazolium salts bearing aliphatic chains of different lengths and a large aromatic group, resulting in an array of multifunctional silica materials as HPLC stationary phases with selectivity significantly influenced by the substituents and functional groups.

1. Introduction

Ionic liquids (ILs) are a class of ionic, non-molecular substances. Their beneficial characteristics, such as high thermal stability, negligible vapour pressure, non-flammability, tunable viscosity, miscibility in different solvents and conductivity etc., have greatly contributed to the successes achieved in many fields, such as synthesis, catalysis, energy reservation, biotechnology and functional materials.[1-5] "Task-specific" ILs can be obtained by modification of either ionic part or the combination of both parts.[6, 7] The electrostatic interactions involved in the cation/anion pairs, and their ability to interact with other molecules via ion exchange, hydrogen bond, π-π stacking and hydrophobic (hydrophilic) interactions, have truly made ILs as multifunctional materials.[8, 9] In separation science, ILs play a very important role in liquid-liquid extraction and solid phase extraction,[10, 11] as well as in electrophoresis and electrochromatography.[12, 13] In high performance liquid chromatography (HPLC), ILs have been used as multifunctional ligands for stationary phases in different modes.[14-16]

To obtain surface-confined ionic liquid (SCIL) stationary phase, ILs are chemically anchored on the supports by monomeric or polymeric bonding of their cations.[17, 18] Though effective for surface modification of the supports, the monomeric immobilization method requires 1-substituted imidazoles, and it cannot guarantee high bonding amount due to the heterogeneity of the reaction medium. The polymeric method is quite applicable for imidazolium salts containing alkenyl groups, whereby the bonding amount can be elevated, which is, however, sensitive to the shapes of cation and anion.[19, 20] In fact, both methods are significantly influenced by steric hindrance.

Herein, we describe a new strategy of great versatility for
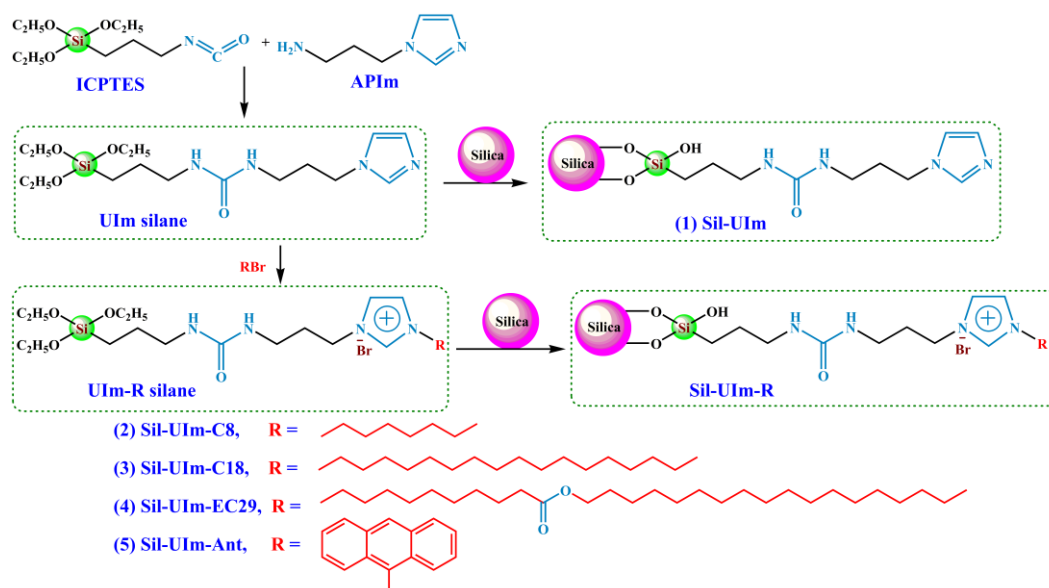
Scheme 1 Synthetic strategy for SCIL stationary phases

ARTICLE TYPE

convenient and efficient immobilization of ILs onto silica sphere, and the recommendable performance of the resulted multifunctional materials when used as SCIL stationary phases. For the first time, employment of large aromatic substituent in
5 preparation of SCIL stationary phase was demonstrated.

2. Preparation strategy

The new one-pot strategy consists of multiple steps (Scheme 1). Firstly, the urea-functionalized imidazolyl silane (UIm) was quantitatively obtained by the nucleophilic addition between γ-
10 *iso*cyanatopropyltriethoxysilane (ICPTES) and *N*-(3-aminopropyl) imidazole (APIm) in acetonitrile (MeCN). Conveniently, UIm could be isolated by evaporation of MeCN and precipitation in *n*-hexane (see Fig. S1 for 1H NMR spectrum). Then UIm could be directly used for surface functionalization of silica (Sil-UIm) or
15 further treated by 1-haloalkanes to afford ILs. Finally the silica spheres were added to produce SCIL stationary phases (Sil-UIm-R).

2.1 Synthesis of Sil-UIm

To a stirred solution of APIm (1.00 g, 8 mmol) in MeCN (30 mL)
20 cooled in ice bath was added ICPTES (2.01 g, 8 mmol) in MeCN (20 mL) dropwise. The reaction was exothermic. Ice bath was removed after 1 h, and the reaction continued at room temperature for 11 h. MeCN was removed and the residue was washed repeatedly by *n*-hexane to afford UIm as colourless oil,
25 which was soluble in water, alcohol, ether and toluene, but insoluble in *n*- and cycloalkanes. The same procedure was used but without purification of UIm for preparation of Sil-UIm. Silica (3 g) was added to the solution and the suspension was refluxed for 24 h. The modified silica, namely Sil-UIm, was filtered and
30 washed by sufficient hot MeCN, ethanol, ethanol/water (v/v=3/1) and methanol (MeOH) (100 mL for each) successively, and dried in vacuum at 80 ℃.

2.2 Synthesis of Sil-UIm-R

The same synthetic procedure was carried out between APIm and
35 ICPTES, and then 1-bromoalkane (9 mmol) was added. The solution was refluxed for 48 h. Silica was afterwards added and the resulting slurry was further stirred under reflux for 24 h. Then the modified silica was isolated and washed by hot chloroform, ethanol, ethanol/water (v/v=3/1) and MeOH in turn (100 mL for
40 each), and dried in vacuum at 80 ℃. Particularly, in the case of 9-bromomethylanthracene, MeCN was substituted by *iso*-propanol throughout the whole synthesis.

3. Characterization

The proposed methodology eliminates the prerequisite of either
45 1-subsituted imidazole or alkenyl-containing imidazolium salts; only the desired haloalkane is required. Moreover, hydrophilic
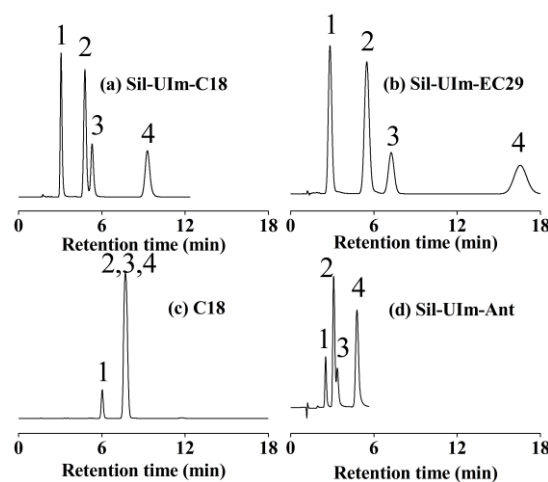

Fig. 1 Separation of *o*-terphenyl (1), *m*-terphenyl (2), *p*-terphenyl (3) and triphenylene (4) on different columns. Mobile phase: MeOH/water =
50 90/10 (v/v) for a, b and c, 70/30 for d.

halohydrocarbons could also be considered to fabricate hydrophilic surface. The conversion rate of each step of the synthetic process and the surface coverage of the silica were acceptably high, as evidenced by elemental analysis (Table S1),
55 infrared spectroscopy (Fig. S2) and contact angle (CA) tests (Fig. S3). From elemental analyses results, it can be observed that the quaternization rate of UIm tended to decline with the increase of the bulkiness of 1-bromoalkane, resulting in a lower experimental C/N ratio. However, the amount of reacted UIm was always
60 beyond 60%, 1-bromooctane produced the highest conversion rate of UIm, followed by 1-bromooctadecane. The surface coverage was significantly impacted in the same pattern, notably in the case of 9-(bromomethyl)anthracene. The CA tests using water revealed that Sil-UIm was hydrophilic, attachment of
65 aliphatic chains led to hydrophobic surface. Superhydrophobic surface was obtained in the case of *n*-octadecyl 11-bromoundecanoate. Surprisingly, attachment of 9-methylanthracene ligand induced an even hydrophilic surface, probably due to the conjugation of the imidazolium and
70 anthracene and lower bonding amount of imidazolium. The infrared spectra also indicated the successful immobilization of ILs.

Due to the replaceability of the aliphatic chains in the IL ligands, the properties of these new materials were highly tunable.
75 The surface properties of the each stationary phases varied so greatly from one another that different propellant solvents were used to perform the packing procedures. Individually, Sil-UIm-C18 and Sil-UIm-EC29 were packed using MeOH, Sil-UIm-C8 using *n*-hexane, Sil-UIm and Sil-UIm-Ant using MeCN. From the
80 viewpoint of LC application, the diversity in the substituents could provide designable and tunable hydrophobicity, which in turn influenced the retention and selectivity. Furthermore, the various polar groups in the IL ligand were able to impact the chromatographic behaviour via multiple interactions. Because of
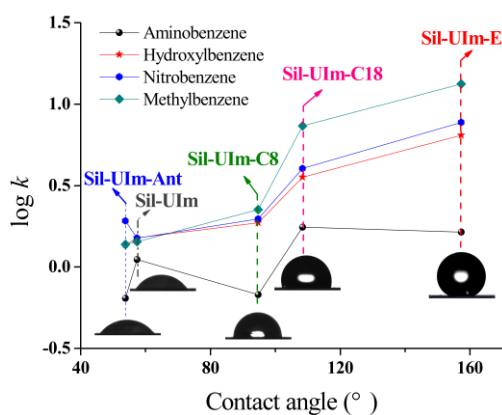
Fig. 2 Log *k* vs. CA value plots for Sil-UIm and Sil-UIm-R. Mobile phase: MeOH/water = 50/50.

the hydrogen acceptor nature of imidazolium and urea, which is
5 also a hydrogen donor, it is anticipated that the higher loading of
these groups induced by the proposed synthetic strategy would
enhance certain molecular interactions between stationary phase
and solute, such as hydrogen bonding with phenols and electron-
involved interactions with electron-rich polycyclic aromatics (π-π
10 and electron-transfer interactions)

4. Applications

Superior selectivity over that on conventional C18 for three
isomeric terphenyls and triphenylene was observed on new
materials (Fig. 1 and Table S2). The selectivity factors for these
15 PAHs demonstrated that the imidazole ring and urea group had a
positive effect on the separation process. Approximately, the
selectivity was improved upon quaternization of imidazole.
Heightened shape recognition ability was induced by the linear
aliphatic substituents, whereas the planar aromatic substituent did
20 not behave in the identical way. Comparing with C18, the
combination of linear aliphatic chain and imidazolium cation
seemed very effective in enhancing the shape discrimination; the
longer the aliphatic chain was, the better the selectivity was.
Notably, C18 chain offered an appreciably high selectivity factor
25 (4.74) for triphenylene/*o*-terphenyl. More interestingly, the ester-
functionalized C29 aliphatic chain offered a much higher
selectivity factor (9.37). According to literature,[21-23] such great
selectivity factor was an indication of significant solute planarity
recognition (α≥2) and "polymeric-like" nature (α>3). The ester
30 group, or carbonyl group,[24-26] was believed to elevate the
planarity selectivity via additional π-π interaction. Furthermore,
the elution order of anthracene and *o*-terphenyl on C18 was
inversed from those on Sil-UIm-C18 and Sil-UIm-EC29. This
retention inversion was identical to that observed between
35 benzo[a]pyrene (BaP) and tetrabenzonaphthalene (TBN),[27] the
linear anthracene was more retained on polymeric C18, non-
planar *o*-terphenyl on monomeric C18, highlighting the
"polymeric C18" behaviours of Sil-UIm-C18 and Sil-UIm-EC29.
  Comparative analyses of the behaviours of Sil-UIm-R was
40 conducted with four benzene derivatives bearing different
functional groups, including aminobenzene (AB, log P = 0.90,
basic, strong polarity), hydroxylbenzene (HB, log P = 1.46, acidic,
strong polarity), nitrobenzene (NB, log P = 1.85, neutral, weak
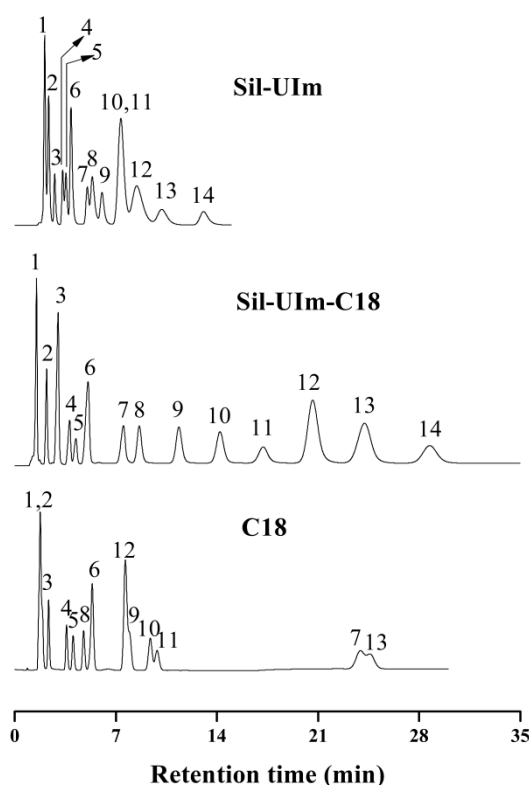polarity) and methylbenzene (MB, log P = 2.73, neutral,

45 **Fig. 3** Separation of anilines including *p*-pheneylenediamine (1), *m*-
phenylenediamine (2), *o*-phenylenediamine (3), aniline (4), *p*-
fluoroaniline (5), *o*-toluidine (6), *N,N*-dimethylaniline (7), *m*-nitroaniline
(8), *m*-chloroaniline (9), *m*-bromoaniline (10), *β*-naphthylamine (11), 2,4-
50 dinitroaniline (12), 2,4-dichloroaniline (13), 2,6-di*iso*propylaniline (14)
on different columns. Mobile phase: MeOH/water = 50/50 (v/v) for Sil-
UIm-C18 and C18, 10/90 for Sil-UIm.

negligible polarity). To intuitively depict the possible connection
between the surface chemistry and the retention and the
55 involvement of different intermolecular interactions, log *k* vs. CA
value plots were constructed (Fig. 2). It could be vividly seen that
roughly the retention of solute increased with the climb of CA
value, attachment of either aliphatic or aromatic substituents had
substantially increased the selectivity. Remarkably, retention
60 ofAB showed irregular variation, and retention of NB was
stronger than that of MB on Sil-UIm and Sil-UIm-Ant. These
particularities could be explained by corresponding functional
groups and the alternation of dominant interactions governing the
chromatographic process. The amino group was highly electron-
65 donating, which intensified the electron density of the benzene
ring, thus a more vigorous electrostatic repulsion force took place
between solute and imidazole and/or anthracene, reducing the
retention of solute. This rationale was true in the case of Sil-UIm-
C8, which had the highest imidazolium density, namely π-
70 electron density, among Sil-UIm-R. Due to the considerably
higher hydrophobicity of Sil-UIm-C18 and Sil-UIm-EC29,
retention of AB increased. However, the ester group contained on
the latter caused an augmented repulsion interaction between AB
and stationary phase. Conversely, the nitro group as the strongest
75 electron-withdrawing group reduced the electron density of
benzene ring, hence stronger electrostatic attraction between NB
and imidazole and/or anthracene occurred. This charge-transfer
phenomenon has been noted for stationary phases functionalized

by fluorene, anthracene and pyrene.[28-31] The log *k* for HB and MB monotonically increased with the CA value. Nevertheless, the effect of the polarity of hydroxyl group on the retention was significant on Sil-UIm, where retention of HB was the strongest, indicating the acid-base equilibrium and dipole-dipole interaction between solute and imidazole ring.

The unique selectivity was further illustrated by separation of aromatic amine on Sil-UIm, Sil-UIm-C18 as representative SCIL stationary phase and commercial C18 (Fig. 3). Sil-UIm could nearly discern the whole solute set, and the best separation performance and resolution was obtained on Sil-UIm-C18. Elution of 2,6-di*iso*propylaniline in 40 min failed on C18. The elution orders were the same on Sil-UIm series, yet strikingly different from that on C18. The strong electrostatic interaction between mononitro-substituted aromatic and urea/imidazole was once again observed. In the case of dinitro-substituted aromatic, the electrostatic interaction was much more obvious, enabling the sharply enhanced retention of 2,4-dinitroaniline over those more hydrophobic solutes. The predominant π-π stacking between naphthalene and urea/imidazole was observed, as reflected by the stronger retention of *β*-naphthylamine on Sil-UIm series. Different retention order of diphenylamine (not included) and 2,6-di*iso*propylaniline was observed on Sil-UIm-C18 and C18, further validating the supremacy of π-π stacking.

5. Conclusions

In conclusion, we have established a novel synthetic strategy for surface modification of silica sphere with ionic liquids, leading to a series of SCIL stationary phases for HPLC. The new methodology has several advantages, such as facile preparation, high bonding amount and excellent designability. These materials can be used as multifunctional stationary phases with satisfactory performance and unique selectivity. Some of the materials had potential for application in hydrophilic interaction LC (HILIC) mode. The proposed synthetic strategy is believed to be beneficial in other fields, such as catalysis and electrochemistry, etc. In-depth evaluation of these new materials is currently underway.

Notes and references

[a] Key Laboratory of Chemistry of Northwestern Plant Resources and Key Laboratory for Natural Medicine of Gansu Province, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000, China.
[b] University of Chinese Academy of Sciences, Chinese Academy of Sciences, Beijing 100049, China.
[c] Department of Applied Chemistry and Biochemistry, Kumamoto University, Kurokami, Kumamoto 860-8555, Japan.
*Corresponding author. Tel.: +86 931 4968877; fax: +86 931 8277088; E-mail: hdqiu@licp.cas.cn (H. Qiu)

1. S. Zhang, J. Sun, X. Zhang, J. Xin, Q. Miao and J. Wang, *Chem. Soc. Rev.*, 2014, DOI: 10.1039/C3CS60409H.
2. N. V. Plechkova and K. R. Seddon, *Chem. Soc. Rev.*, 2008, 37, 123-150.
3. Q. Zhang, S. Zhang and Y. Deng, *Green Chem.*, 2011, 13, 2619-2637.
4. R. Giernoth, *Angew. Chem. Int. Edit.*, 2010, 49, 2834-2839.
5. H. Zhao and G. A. Baker, *J. Chem. Technol. Biotechnol.*, 2013, 88, 3-12.
6. S. G. Lee, *Chem. Commun.*, 2006, 1049-1063.
7. J. H. Davis, *Chem. Lett.*, 2004, 33, 1072-1077.
8. G. A. Baker, S. N. Baker, S. Pandey and F. V. Bright, *Analyst.*, 2005, 130, 800-808.
9. W. Bi, J. Zhou and K. H. Row, *Talanta*, 2011, 83, 974-979.
10. L. Vidal, M. L. Riekkola and A. Canals, *Anal. Chim. Acta*, 2012, 715, 19-41.
11. H. Yu, T. D. Ho and J. L. Anderson, *Trends Anal. Chem.*, 2013, 45, 219-232.
12. Y. Huang, S. Yao and H. Song, *J. Chromatogr. Sci.*, 2013, 51, 739-752.
13. C Liu, Q. Deng, G. Fang, H.. Liu, J. Wu, M. Pan and S. Wang, *Anal. Chim. Acta*, 2013, 804, 313-320.
14. W. Bi, J. Zhou and K. H. Row, *Separ. Sci. Technol.*, 2012, 47, 360-369.
15. T. D. Ho, C. Zhang, L. W. Hantao and J. L. Anderson, *Anal. Chem.*, 2014, 86, 262-285.
16. V. Pino and A. M. Afonso, *Anal. Chim. Acta*, 2012, 714, 20-37.
17. M. Zhang, X. Liang, S. Jiang and H. Qiu, *Trends Anal. Chem.*, 2014, 53, 60-72.
18. W. Bi, M. Tian and K. H. Row, *Analyst.*, 2012, 137, 2017-2020.
19. H. Qiu, A. K. Mallik, T. Sawada, M. Takafuji and H. Ihara, *Chem. Commun.*, 2012, 48, 1299-1301.
20. H. Qiu, A. K. Mallik, M. Takafuji and H. Ihara, *Chem. Eur. J.*, 2011, 17, 7288-7297.
21. K. Jinno, T. Ibuki, N. Tanaka, M. Okamoto, J. Fetzer, W. Biggs, P. Griffiths and J. Olinger, *J. Chromatogr. A*, 1989, 461, 209-227.
22. K. Jinno, K. Yamamoto, H. Nagashima, T. Ueda and K. Itoh, *J. Chromatogr. A*, 1990, 517, 193-207.
23. H. Engelhardt, M. Nikolov, M. Arangio and M. Scherer, *Chromatographia*, 1998, 48, 183-189.
24. A. K. Mallik, Makoto Takafuji, and Hirotaka Ihara, *Anal. Chem.*, 2010, 82, 3320-3328.
25. M. M. Rahman, M. Takafuji, H. R. Ansarian and H. Ihara, *Anal. Chem.*, 2005, 77, 6671-6681.
26. A. K. Mallik, H. Qiu, T. Sawada, M. Takafuji and H. Ihara, *Anal. Chem.*, 2012, 84, 6577-6585.
27. S. Wise, W. J. Bonnett, F. R. Guenther and W. E. May, *J. Chromatogr. Sci.*, 1981, 19, 457-465.
28. L. C. Sander, R. M. Parris, S. A. Wise and P. Garrigues, *Anal. Chem.*, 1991, 63, 2589-2597.
29. M. Verzele and N. Velde, *Chromatographia*, 1985, 20, 239-241.
30. R. Brindle and K. Albert, *J. Chromatogr. A*, 1997, 757, 3-20.
31. C. H. Lochm üller, M. L. Hunnicutt and R. W. Beaver, *J. Chromatogr. Sci.*, 1983, 21, 444-446.