

Y. Sun · B. Cabovska · C. E. Evans · T. H. Ridgway  
A. M. Stalcup

## Retention characteristics of a new butylimidazolium-based stationary phase

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**Abstract** A new HPLC stationary phase has been synthesized based on the ionic liquid *n*-butylimidazolium bromide. Imidazolium was covalently immobilized on a silica substrate through an *n*-alkyl tether and the retention characteristics of the resulting stationary phase were evaluated systematically. Using 28 small aromatic test solutes and reversed phase conditions, the linear solvation energy relationship approach was successfully used to characterize this new phase. The retention characteristics of the test solutes show remarkable similarity with phenyl stationary phases, despite the presence of a positive charge on the new imidazolium phase. Operated in the reversed phase mode, this new stationary phase shows considerable promise for the separation of neutral solutes and points to the potential for a truly multimodal stationary phase.

**Keywords** Butylimidazolium bromide · LSER · Reversed phase · HPLC · Ionic liquids · Retention mechanisms

### Introduction

The unique solvation properties of ionic liquids are being used to great advantage in the dissolution of a

wide range of organic and inorganic substances, including both neutral and charged species, with most applications [1–3] exploiting their unique bulk solution properties [4–7]. For instance, they have been used as solvents for organic synthesis [8–10], and matrices in matrix-assisted laser desorption/ionization (MALDI) mass spectrometry [11, 12]. Although ionic liquids have been used as additives or coatings in capillary electrophoresis [6, 13–16], most of their applications in terms of analytical separations have been as stationary phases in gas chromatography [5, 17–22]. Investigations of the physicochemical properties of ionic liquids [20] and solute/stationary phase interactions in gas chromatographic stationary phases [19, 21] suggest that ionic liquids may be useful as multimodal media in chromatographic separations. Although ionic liquids have been used as additives in the eluent in liquid chromatography [23, 24], UV absorbance and viscosity properties [25] have contributed to limited utility. In this work, butylimidazolium cations with Br<sup>−</sup> counterions were immobilized on porous silica particles and examined as a stationary phase for liquid chromatography.

Solvatochromic analysis, originally developed by Taft and Kamlet [26, 27], was adapted into a linear solvation free energy relationship (LSER) by Abraham and co-workers [28–30]. In chromatography, the LSER methodology has been used to correlate retention with fundamental solute/mobile phase and solute/stationary phase properties. In particular, this approach is valuable for describing the contribution of individual intermolecular interactions to the retention mechanism in reversed phase chromatography [30]. The retention relationship is expressed as a sum,

$$\log k = \log k_0 + rR_2 + s\pi_2^H + a \sum \alpha_2^H + b \sum \beta_2^H + vV_2 \quad (1)$$

where each term represents the contribution of a specific intermolecular interaction to the overall retention factor. Individual interactions include electron lone

*Present address:* B. Cabovska  
PPRU-Laboratory of Applied Pharmacokinetics and  
Therapeutic Drug Management, Cincinnati Children's Hospital  
Medical Center, 3333 Burnet Ave,  
Cincinnati, OH 45229, USA

*Present address:* C. E. Evans  
Department of Chemistry, 215 UCB,  
University of Colorado, Boulder, CO 80309, USA

Y. Sun · B. Cabovska · C. E. Evans · T. H. Ridgway  
A. M. Stalcup (✉)  
Department of Chemistry,  
University of Cincinnati,  
Cincinnati, OH 45221-0172, USA  
E-mail: apryll.stalcup@uc.edu

pair, dipole, hydrogen bond acidity and basicity, cavity formation and dispersion. Specifically,  $R_2$  is the excess molar refraction, which reflects polarizability contributions from  $\pi$ - and  $n$ -electrons;  $\pi_2^H$  is the solute dipolarity/polarizability;  $\sum \alpha_2^H$  and  $\sum \beta_2^H$  are the overall solute hydrogen bond acidity and basicity, respectively, which scale as the hydrogen bonding propensity of a solute to surrounding solvent molecules;  $V_2$  is McGowan's characteristic volume [31, 32]. The coefficients  $r$ ,  $s$ ,  $a$ ,  $b$  and  $v$  are distinctive for each particular mobile/stationary phase system and are obtained by multiple linear regression analysis of retention data for a training set of neutral compounds. These factors describe the difference in the associated property for solute interacting with the mobile phase and solutes interacting with the stationary phase. If the defined property is stronger in the solvated stationary phase than in the mobile phase, the corresponding system coefficient in Eq. 1 has a positive sign, contributing to solute retention [33].

The present study evaluates whether the LSER approach can be used to establish a relationship between the system constants and properties of an ionic liquid-type stationary phase. In particular, the goal is to characterize this new butylimidazolium-based stationary phase and interpret retention in terms of the primary intermolecular interactions governing the observed behavior. Results are discussed in terms of the chemical meaning of the magnitude of the coefficient as well as its sign and the effect of mobile phase composition. The solute training set was chosen for these studies based on previous LSER studies [34]. Finally, this study focuses on understanding solute retention in pure methanol and methanol-water mobile phases. While it is possible that adventitious ions (for example carbonate) could affect solute retention, measured solute retention factors were highly reproducible, indicating no significant change in interaction chemistry. Shifts in equilibrium away from carbonate ion formation for  $\text{CO}_2$  in methanol and methanol-water mixtures may also diminish [35] the impact of the primary adventitious ion. Nonetheless, the contributions of the counterion to solute retention are presently under investigation. The study here focuses on characterizing solute retention using methanol and methanol-water mobile phases on this new, multi-modal stationary phase.

## Experimental

### Materials

The training set, consisting of 28 probe solutes, is listed in Table 1 along with the respective Abraham's solute descriptors [36, 37]. All chemicals, including the probe solutes, synthesis materials (8-bromo-1-octene, 1-butylimidazole, hydrogen hexachloroplatinate(IV), and anhydrous toluene), and mobile phase components

**Table 1** Solvation solute descriptors for the training set

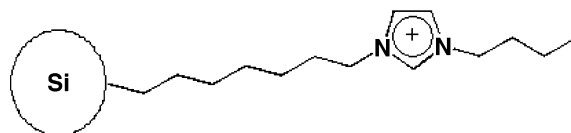
Probe solute	Descriptors				
	$R_2$	$\pi_2^H$	$\sum \alpha_2^H$	$\sum \beta_2^H$	$V_2$
1 Benzene	0.610	0.52	0.00	0.14	0.716
2 Naphthalene	1.340	0.92	0.00	0.20	1.085
3 Biphenyl	1.360	0.99	0.00	0.22	1.324
4 Anthracene	2.290	1.34	0.00	0.26	1.454
5 Toluene	0.601	0.52	0.00	0.14	0.857
6 <i>o</i> -Xylene	0.663	0.56	0.00	0.16	0.998
7 Mesitylene	0.649	0.52	0.00	0.19	1.139
8 Ethylbenzene	0.613	0.51	0.00	0.15	0.998
9 Propylbenzene	0.604	0.50	0.00	0.15	1.139
10 <i>n</i> -Butylbenzene	0.600	0.51	0.00	0.15	1.280
11 <i>tert</i> -Butylbenzene	0.619	0.49	0.00	0.16	1.280
12 Fluorobenzene	0.477	0.57	0.00	0.10	0.734
13 Chlorobenzene	0.718	0.65	0.00	0.07	0.839
14 Iodobenzene	1.188	0.82	0.00	0.12	0.975
15 1,2-Dichlorobenzene	0.872	0.78	0.00	0.04	0.961
16 Phenol	0.805	0.89	0.60	0.30	0.775
17 Benzyl alcohol	0.803	0.87	0.33	0.56	0.916
18 2-Phenylethanol	0.811	0.91	0.30	0.64	1.057
19 <i>p</i> -Cresol	0.820	0.87	0.57	0.31	0.916
20 <i>p</i> -Chlorophenol	0.915	1.08	0.67	0.20	0.898
21 Nitrobenzene	0.871	1.11	0.00	0.28	0.891
22 Benzonitrile	0.742	1.11	0.00	0.33	0.871
23 Benzaldehyde	0.820	1.00	0.00	0.39	0.873
24 Aniline	0.955	0.96	0.26	0.50	0.816
25 Acetophenone	0.818	1.01	0.00	0.48	1.014
26 2-Chloroaniline	1.033	0.92	0.25	0.40	0.939
27 Anisole	0.708	0.75	0.00	0.29	0.916
28 <i>n</i> -Butylbenzoate	0.668	0.80	0.00	0.46	1.495

Obtained from [36, 37]

(HPLC-grade water and methanol) were purchased from the Aldrich Chemical Company (Milwaukee, WI, USA) or the Fisher Scientific Chemical Company (Fair Lawn, NJ, USA) and used without further purification. Nucleosil silica (100 Å, 5  $\mu\text{m}$ , 350  $\text{m}^2/\text{g}$ ) was purchased from Alltech (Deerfield, IL, USA) and dimethylchlorosilane from Gelest, Inc. (Morrisville, PA, USA).

### Methods

The butylimidazolium bromide stationary phase was prepared on silica via hydrosilylation of the alkenylbromide [38], followed by immobilization of the silane with subsequent attachment of the butylimidazole. Elemental analysis (Galbraith Labs, Knoxville, TN, USA) revealed that the linker loading was  $\sim 2.0 \mu\text{mol}/\text{m}^2$  while the imidazolium surface concentration was  $\sim 0.7 \mu\text{mol}/\text{m}^2$ . A schematic of the immobilized ligand is shown below.



All HPLC experiments were performed using a Shimadzu (Columbia, MD, USA) LC-10AT pump at room temperature. Detection was accomplished using a SPD-10A UV detector set at 254 nm or 310 nm. The butylimidazolium column (packed by Advanced Separations Technology, Inc., Whippany, NJ, USA) was a 250×4.6 mm I.D. stainless steel column.

All samples were dissolved (0.004~0.5 mg/mL) in methanol or methanol/water mixtures. A 20  $\mu$ L aliquot of the sample was injected using a Rheodyne injection valve (Cotati, CA, USA) with all experiments performed in triplicate. The flow rate was 1 mL/min or less of methanol or methanol/water mixtures (60–100% v/v methanol–water). The multimodal nature of the stationary phase complicated selection of a suitable neutral void volume marker. For this reason, the void volume was determined by measuring the difference in column weights when the column was filled with methylene chloride or with hexane. Chromatographic retention data was acquired with a Chrom & Spec Chromatography Data System (Ampersand International, Inc., Beachwood, OH, USA).

Multiple linear regression analysis and statistical tests of the chromatographic data were performed on a PC using Excel. Based on Eq. 1, the system constants were obtained from multiple linear regression analysis of experimental  $\log k$  values for the training set against the Abraham's solute descriptors.

## Results and discussion

### Evaluation of the selection of probe solutes

It is important to initially evaluate cross-correlation among the descriptors to ensure the suitability of the selected training set. The variance–covariance matrix of the solute descriptors calculated using the 28 probe solutes listed in Table 1 is shown in Table 2.

While the interpretation of the correlation coefficient is clear when the experimental value is either unity or zero, it can be ambiguous in intermediate cases. If there is no systematic error, analogy with the autocorrelation literature [39, 40] can provide some insight. In this formalism, the reciprocal of  $v$ , the number of degrees of freedom, is treated as an estimate of  $s$ , the variance in the correlation coefficient. In the present case, this would be

$$s = 1/\sqrt{v} = 0.19$$

**Table 2** Correlation coefficient matrix of solute descriptors

	$R_2$	$\pi_2^H$	$\sum \alpha_2^H$	$\sum \beta_2^H$	$V_2$
$R_2$	1	0.702	0.013	0.089	0.405
$\pi_2^H$		1	0.306	0.502	0.070
$\sum \alpha_2^H$			1	0.358	-0.300
$\sum \beta_2^H$				1	0.049
$V_2$					1

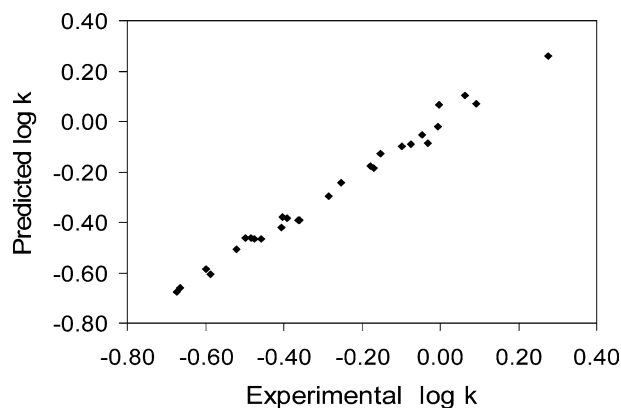
Comparison of the Table 2 coefficients to zero via the Student  $t$ -distribution indicates that any correlation coefficient greater than 0.45 could be considered significant at the 95% confidence level. Accordingly, the solute dipolarity/polarizability coefficient ( $\pi_2^H$ ) seems to be only weakly coupled to the overall hydrogen bond basicity ( $\sum \beta_2^H$ ) (correlation coefficient = 0.502) whereas  $\pi_2^H$  and  $R_2$  exhibit a slightly higher correlation (correlation coefficient = 0.702). This latter correlation has been previously noted [33] and is expected since both  $\pi_2^H$  and  $R_2$  reflect the polarizability characteristics of the solutes.

### Evaluation of the LSER model and system coefficients

The LSER model was evaluated by comparison of the experimentally-determined retention factors with the predicted values. As can be seen from the typical result illustrated in Fig. 1, there is excellent agreement between calculated and experimental  $\log k$  values. Hence, the selected molecular descriptors do a good job of accounting for interactions between solutes and the butylimidazolium-based stationary phase under reversed phase conditions. This result is even more interesting because of the presence of the cation in the stationary phase (data not shown).

Regression coefficients for  $\log k_{\text{predicted}}$  versus  $\log k_{\text{exp}}$  as a function of methanol mobile phase composition are shown in Table 3. For mobile phase compositions of 60–80% MeOH, the regression coefficients were all higher than 0.98 and the standard deviations of the fits were less than 0.05. Observed correlation was somewhat lower for high organic compositions, presumably because short retention led to a greater uncertainty in the determination of  $k$ .

Insight into the interaction properties affecting solute retention for this new media may be derived from examining the sign and magnitude of individual system coefficients. Moreover, system coefficient dependence on mobile phase composition also affords insight into stationary phase properties that may not be constant along



**Fig. 1** Plot showing  $\log k_{\text{predicted}}$  versus  $\log k_{\text{experimental}}$  using 60% MeOH

**Table 3** System coefficients as a function of mobile phase composition (volume fraction) for the solvent system methanol–water on the butylimidazolium bromide stationary phase

Composition MeOH–H <sub>2</sub> O	System coefficients						Statistics			
	$\log k_0$	$r$	$s$	$a$	$b$	$v$	$R$	$SE$	$F$	$n$
60-40	$-0.97 \pm 0.04$	$0.10 \pm 0.03$	$-0.04 \pm 0.05$	$-0.13 \pm 0.03$	$-0.90 \pm 0.05$	$0.89 \pm 0.03$	0.995	0.027	452	28
70-30	$-1.00 \pm 0.03$	$0.12 \pm 0.02$	$-0.05 \pm 0.04$	$-0.11 \pm 0.02$	$-0.79 \pm 0.04$	$0.66 \pm 0.03$	0.995	0.022	485	28
80-20	$-1.28 \pm 0.04$	$0.06 \pm 0.03$	$0.11 \pm 0.05$	$-0.10 \pm 0.03$	$-0.85 \pm 0.05$	$0.57 \pm 0.04$	0.989	0.030	200	28
90-10	$-1.51 \pm 0.07$	$0.06 \pm 0.05$	$0.29 \pm 0.08$	$-0.02 \pm 0.06$	$-0.94 \pm 0.09$	$0.41 \pm 0.06$	0.961	0.052	53	28
100-0	$-1.66 \pm 0.13$	$0.07 \pm 0.10$	$0.62 \pm 0.16$	$-0.02 \pm 0.11$	$-1.06 \pm 0.17$	$0.15 \pm 0.12$	0.897	0.097	18	28

*MeOH* methanol,  $R$  overall correlation coefficient,  $SE$  standard error in the estimate,  $F$  statistic,  $n$  number of solutes

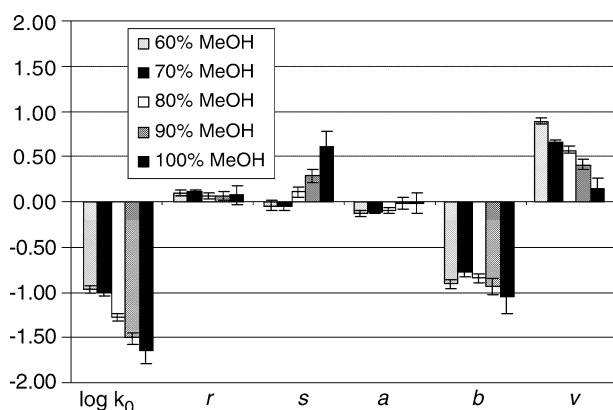
a range of mobile phase compositions. Comparisons of solute/stationary phase interactions are illustrated on the system map in Fig. 2, where the error bars indicate the standard deviations of the coefficients. Consistent with other reversed phase systems [33, 34, 41], the cavity formation process (the  $v$  coefficient) and the solute hydrogen bond basicity interactions (the  $b$  coefficient) are the most significant interactions governing retention. Likewise,  $\log k_0$  provides the significant negative contribution to retention expected for reversed phase separations [33]. In addition, system coefficients shown in Fig. 2 indicate that the  $s$  and  $v$  LSER coefficients are affected by mobile phase composition, whereas  $r$ ,  $a$ , and  $b$  appear to be independent of mobile phase composition. This interesting behavior is addressed below, with each system coefficient specifically detailed.

**The  $r$  coefficient** The  $r$  coefficient reflects the tendency of the system to interact with the solute through  $\pi$ - and  $n$ -electron pairs. As shown in Fig. 2 and Table 3, the  $r$  coefficients are slightly positive and consistent with solutes undergoing  $\pi$ - $\pi$  interactions with the stationary phase. Indeed, Cabovska and co-workers [13] reported that interactions between imidazolium cations and halophenols in aqueous solution occurred through  $\pi$ - $\pi$  stacking. A positive  $r$  is indicative of the higher polarizability of the imidazolium ring compared to water or methanol. The positive sign also suggests that retention on the butylimidazolium stationary phase is more simi-

lar to retention on the polarizable [33] phenyl phases than on the aliphatic phases.

**The  $s$  coefficient** The  $s$  coefficient is attributed to the difference in stationary and mobile phase dipolar interactions with solutes. Dipole/induced-dipole interactions between the solute and stationary phase should have a larger magnitude than solute/mobile phase interactions on the butylimidazolium phase because the stationary phase contains a cation and has a higher polarizability than either of the mobile phase components. Indeed, in this system, at high organic mobile phase composition (above 80% MeOH), the  $s$  coefficient is positive. The increase in the  $s$  coefficient on the butylimidazolium phase with increasing methanol concentration presumably resides in the growing importance of ion–dipole interactions at high organic compositions. This behavior is in contrast to the trends observed on alkyl-based reversed phase systems [42] where the  $s$  coefficient is insensitive to mobile phase composition. However, at 60% and 70% methanol, the dipole–dipole and/or ion–dipole interactions between solute and the solvated stationary phase are almost of the same magnitude as those in mobile phase. Reta and co-workers [33] also found the  $s$  coefficient to be essentially zero for phenyl-based phases at 60% MeOH, which they attributed to mobile phase sorption controlling dipolar interactions in the aromatic stationary phase.

**The  $a$  coefficient** The  $a$  coefficient is a measure of the difference in hydrogen bond basicity between the solvated stationary phase and the mobile phase; because the HB acceptor ability of the aqueous methanol is higher than that of the bonded stationary phase, the  $a$  coefficient is expected to be negative at all mobile phase compositions used in this study. In fact, the  $a$  coefficient is essentially zero for 90–100% methanol and only slightly negative for lower methanol concentrations. The relatively low magnitude of the  $a$  coefficient at all mobile phase conditions used in this study is consistent with reports for conventional reversed phases [33] and was attributed to mobile phase sorption into the stationary phase thereby decreasing the differences between the mobile phase and stationary phase environments. While mobile phase sorption may seem reasonable and has been established for alkyl-bonded phases [43], it has yet

**Fig. 2** System map

to be established on the butylimidazolium phase. Also, as in the case of the  $r$  coefficient, because of the small values of  $a$  and their large uncertainties, further conjecture about the impact of mobile phase composition on  $a$  is not presently possible.

**The  $b$  coefficient** The  $b$  coefficient is a measure of the difference in hydrogen bond (HB) acidity between the solvated stationary phase and the mobile phase. Overall, it is large and negative. Because both water and methanol are HB acids, the mobile phase acidity is much stronger than the stationary phase which is aprotic, so  $b$  is negative. Further, the  $b$  coefficient values are close to those obtained for phenyl stationary phases and smaller than those typically obtained for aliphatic stationary phases [33] suggesting that the butylimidazolium-based stationary phase behaves somewhat like a phenyl stationary phase. Reta and co-workers [33] postulated that greater sorption of mobile phase components into aromatic stationary phases probably played a role in reducing the contribution of hydrogen bond acidity differences for aromatic phases relative to alkyl phases. Interestingly, in contrast with alkyl-based reversed phases [42], the  $b$  coefficient does not exhibit a strong dependence on mobile phase composition on the butylimidazolium phase.

**The  $\nu$  coefficient** The  $\nu$  coefficient is closely related to the “hydrophobic selectivity” of the stationary phase [33] and emanates from a combination of cavity effects and dispersive interactions [44]. For the cationic butylimidazolium-based stationary phase, this behavior is manifested in the generally shorter retention times obtained with higher methanol concentrations in the mobile phase. The  $\nu$  coefficient is the most significantly positive among the five coefficients, which is consistent with observations for conventional RP-HPLC stationary phases [42]. Thus, it is reasonable to conclude that the imidazolium-based stationary phase is more hydrophobic than the mobile phase, despite the presence of the cation. It should also be noted that, as observed for conventional RP-HPLC stationary phases, the  $\nu$  coefficient becomes more positive as  $\phi_{\text{MeOH}}$  is decreased because decreasing the methanol concentration in the mobile phase decreases mobile phase hydrophobicity.

Understanding retention behavior of the immobilized butylimidazolium bromide

**Hydrophobic selectivity** In Fig. 3, the retention of  $n$ -alkylbenzenes from benzene to  $n$ -butylbenzene measured under identical conditions is plotted versus carbon number of the alkyl chain. As can be seen in Fig. 3, increasing the number of carbons in the alkyl chain increased retention while increasing the amount of water in the mobile phase also increased retention, both consistent with reversed phase behavior. The slope of the

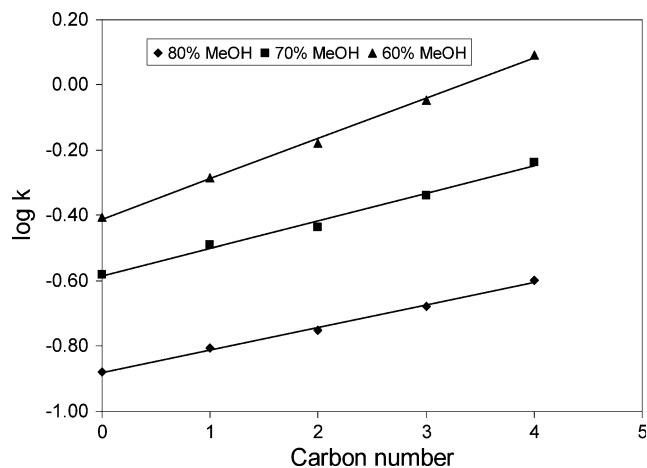


Fig. 3 Dependence of  $\log k$  on the carbon number of the alkyl chain in  $n$ -alkylbenzenes. 80% MeOH: slope = 0.069,  $r^2 = 0.9966$ ; 70% MeOH: slope = 0.084,  $r^2 = 0.9896$ ; 60% MeOH: slope = 0.123,  $r^2 = 0.9978$

lines obtained for these plots can also be regarded as a measure of the hydrophobic selectivity of the phase [45]. Indeed, a linear correlation is observed between the slope values and the  $\nu$  coefficient shown in Table 3.

**Selected separations** Further insight can be gained by closer examination of selected solutes. In addition to alkylbenzenes, halogen-substituted benzenes and benzene alcohols were also included in the training set. A chromatogram of their separation at 60% MeOH is shown in Fig. 4. It is important to note that while ion exchange columns typically generate 12–20,000 plates per meter for neutral organic compounds [46], 24–38,000 plates/m were obtained for iodobenzene using 60–100% MeOH on the butylimidazolium-based column despite the presence of the cation in the stationary phase. This behavior is indicative of the faster interaction kinetics observed for reversed phase type interactions.

The separation mechanism for specific solutes may be inferred by examining the corresponding LSER terms, calculated using the individual molecular descriptors from Table 1 and the system coefficients from Table 3.

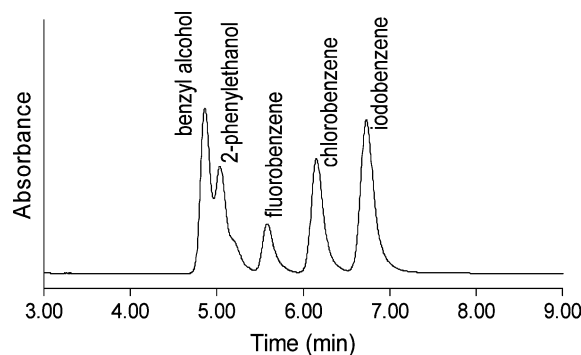


Fig. 4 Chromatographic separation of selected solutes using 60% MeOH on the butylimidazolium-based stationary phase

**Table 4** LSER terms and retention for selected solutes on the butylimidazolium-based phase using 60% methanol mobile phase

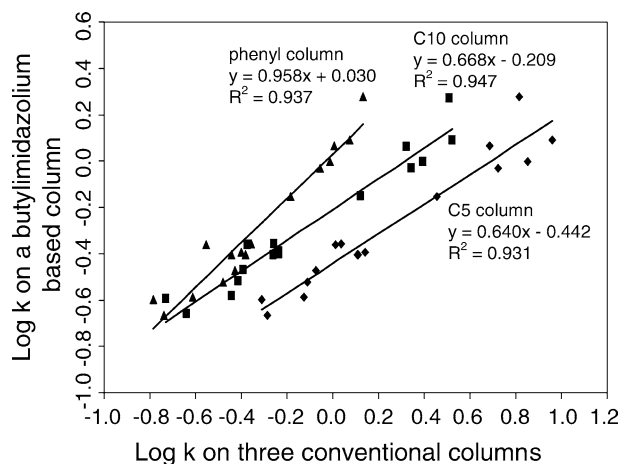
Compound	Calculated LSER terms <sup>a</sup>					Retention log <i>k</i>
	$rR_2$	$s\pi_2^H$	$a\Sigma\alpha_2^H$	$b\Sigma\beta_2^H$	$\nu V_2$	
Benzyl alcohol	0.08	-0.03	-0.04	-0.50	0.82	-0.67
2-Phenylethanol	0.08	-0.04	-0.04	-0.58	0.94	-0.61
Fluorobenzene	0.05	-0.02	0	-0.09	0.65	-0.37
Chlorobenzene	0.07	-0.03	0	-0.06	0.75	-0.23
Iodobenzene	0.12	-0.03	0	-0.11	0.87	-0.15

<sup>a</sup>Product of corresponding system coefficient and compound descriptor

As shown in Table 4, because monohalogenated benzenes do not have HB acidity while the  $rR_2$  and  $b\Sigma\beta_2^H$  terms cancel each other, the LSER terms show that their separation by the stationary phase can be attributed to the significant contributions from the  $\nu V_2$  term, which is related to dispersion interactions. In contrast, for benzyl and phenethyl alcohols, while the  $\nu V_2$  term still dominates the separation, it is partially offset by both the  $a\Sigma\alpha_2^H$  (hydrogen bond acidity) and  $b\Sigma\beta_2^H$  (hydrogen bond basicity) terms.

#### Comparison with conventional reversed phases

To quantitate similarities and differences between conventional reversed phases and the butylimidazolium column, log *k* data obtained on the butylimidazolium-based stationary phase were plotted versus log *k* data reported [33] for three different reversed phase stationary phases using the same mobile phase conditions (Fig. 5). These plots serve as a tool for comparing the energetics of solute retention for different stationary phases [47]; a high degree of behavioral similarity is indicated by the slope and regression coefficients ( $R^2$ ), which are close to unity. As can be seen in Fig. 5, the



**Fig. 5** Plot of log *k* obtained using 60% MeOH on the butylimidazolium column versus log *k* obtained on conventional reversed phase columns under the same mobile phase conditions

slope of the log  $k_{\text{butylimidazolium}}$  versus log  $k_{\text{phenyl}}$  is closest to unity (0.958). This result is further evidence that the retention behavior of the butylimidazolium-based stationary phase has marked similarities with phenyl phases operated in the reversed phase mode. In contrast, significant deviations from unity slope are observed for the aliphatic phases, indicating not only that the butylimidazolium phase is significantly different from the alkyl phases but that the residual alkyl linker does not play a large role in the retention process.

#### Conclusions

A new stationary phase based on the *n*-butylimidazolium cation has been successfully synthesized and characterized. Retention properties under reversed phase conditions are remarkably similar to conventional phenyl-based stationary phases. Despite the presence of significant ionic character in the stationary phase, LSER-derived system coefficients and direct comparison with a conventional phenyl phase provide substantial evidence for comparable retention behavior. As a result, this new stationary phase shows considerable promise for truly multi-modal retention properties and advances the goal of more universally applicable separation media.

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