Exploring Fluorous Affinity by Liquid Chromatography

Martina Catani, † Roberta Guzzinati, ‡ Nicola Marchetti, † Luisa Pasti, † and Alberto Cavazzini*, †

University of Ferrara, Department of Chemistry and Pharmaceutical Sciences, via L. Borsari, 46, 44121 Ferrara, Italy, and Italian National Agency for New Technologies, Energy and Sustainable Economic Development (ENEA), RC Casaccia, via Anguillarese, 301, 00123 S.M. di Galeria, Roma, Italy

E-mail: cvz@unife.it
Phone: +39 0532 455331. Fax: +39 0532 240709

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*To whom correspondence should be addressed
† University of Ferrara
‡ University of Ferrara and ENEA
Abstract

Terms such as “fluorous affinity” and “fluorophilicity” have been used to describe the unique partition and sorption properties often exhibited by highly fluorinated organic compounds, that is molecules rich in sp$^3$ carbon-fluorine bonds.

In this work, we made use of a highly fluorinated stationary phase and a series of benzene derivatives to study the effect of one single perfluorinated carbon on the chromatographic behavior and adsorption properties of molecules. For this purpose, the adsorption equilibria $\alpha,\alpha,\alpha$-trifluorotoluene, toluene and other alkylbenzenes, have been studied by means of nonlinear chromatography in a variety of acetonitrile/water eluents.

The results of this investigation are interesting. They reveal that one single perfluorinated carbon is already enough to induce a drastic change in the adsorption properties of molecules on the perfluorinated stationary phase. In particular, it has been found that adsorption is monolayer if the perfluoroalkyl carbon is present but that, when this unit is missing, molecules arrange as multilayer stack structures. These findings can contribute to the understanding of molecular mechanisms of fluorous affinity.

Introduction

Fluorous affinity is the property that describes the capacity of highly (or heavily) fluorinated materials to selectively interact with each other by means of strong noncovalent fluorine-fluorine (F-F) interactions, in a sort of similar dissolves (or likes) similar principle. By definition, highly fluorinated materials are those where a relevant number of hydrogen atoms, typically from 7 to 20, attached to sp$^3$ carbon atoms are replaced with F atoms. This gives the molecules specific properties, different from those of their parent hydrocarbon analogs.$^1$

Fluorophilicity has been extensively employed especially in organic chemistry for the purification of fluorous-tagged molecules from other mixture components by solid phase extraction over fluorous-functionalized silica gel$^{2,3}$ and in fluorous-biphase technology to promote the high-
temperature mixing of innately immiscible fluorous and organic phases as to conduct catalytic reactions efficiently under homogeneous conditions. More recently, fluorous separations have been introduced to other fields of research such as proteomics, metabolomics and environmental analytical science for enrichment and determination of perfluorinated emerging contaminants.

The most common material for solid-based fluorous-separations is silica gel with a fluoro- carbon bonded phase. Perfluoro-functionalized silica gels have the general structure silica-O-Si(CH$_3$)$_2$(CH$_2$)$_n$-R$_f$, where the alkyl bridge is usually made by two or three alkyl units ($n = 2, 3$) and the perfluorinated portion, R$_f$, is either C$_6$F$_{13}$ or C$_8$F$_{17}$. Previous investigations with these stationary phases have shown that, when employed with aqueous/acetonitrile (ACN) binary eluents, they exhibit features very similar to traditional reversed-phase (RP) stationary phases, such as C$_{18}$. For instance, in agreement with the basic concept of RP liquid chromatography (LC) that the solubility of analytes in the mobile phase (MP) controls their retention, a linear dependence of the logarithm of retention factor on the volume fraction of the organic modifier has been observed. Another similarity comes from studies about the preferential adsorption of ACN from ACN/water binary mixtures, which have evidenced that the shape of the excess isotherm of ACN on perfluoro-functionalized silica gels is quite comparable to those typically found on C$_{18}$ phases, where the excess adsorption of ACN is positive at any MP composition with the exception of very organic-rich eluents (i.e., when the ACN amount in the MP exceeds approx. 95% v/v).

What differentiates perfluorinated and C$_{18}$ stationary phases, instead, is their ability to discriminate between molecules differing by one single methylene or perfluormethylene group that is, in chromatographic terms, their methylene or perfluoromethylene selectivity. Experimentally, perfluoromethylene selectivity can be estimated by the dependence of the logarithm of retention factor on the number of CF$_2$ groups in homologous series of, e.g., perfluorinated acids. When perfluorinated stationary phases are employed in these measurements, the Gibbs free energy of phase transfer for the passage of a perfluoroalkyl carbon from the mobile to the stationary phase can be considered a sort of direct measure of fluorous affinity. As a consequence, by employing...
eluents of different composition, these experiments permit to establish how fluorous affinity varies with the composition of the eluent.  

The majority of models used to describe retention in RPLC are based on measurement performed under linear conditions, i.e. when the concentrations of solutes injected in the column are very low (ideally, infinite dilution conditions for the solute). A common example of these models are the so-called linear free-energy relationships (LFER). However, an important limitation of these approaches is that the effects of different possible interactions between molecule and stationary phase are lumped in one single parameter (the retention factor), so that some fundamental aspects of the chromatographic process might be lost. For instance, if the adsorption surface is energetically heterogeneous (i.e. composed by different kinds of adsorption sites), the retention factor cannot be used to distinguish between sites with different energy/abundance. To gather this information, indeed, one needs to extend the adsorption measurements to the nonlinear range of the adsorption isotherm.

In this work, the adsorption equilibria of $\alpha,\alpha,\alpha$-trifluorotoluene and toluene on a straight-chain perfluorinated stationary phase have been studied with the purpose of investigating the effect of one single perfluorinated sp$^3$ carbon on the adsorption behavior of these molecules. The investigation has been carried on under a variety of experimental conditions, through linear and nonlinear chromatographic measurements. For the sake of comparison and to assess the possible effect of the alkyl-chain length on the adsorption process, in addition, linear alkyl benzenes with alkyl chain lengths ranging from C$_2$ to C$_6$ have also been considered in our study.

The conclusions of these investigations are interesting, showing a drastic change in the adsorption properties of molecules due to the presence of one single CF$_3$ group. On the contrary, the adsorption mode was not found to be substantially influenced by the alkyl-chain length. These findings may contribute to the understanding of molecular mechanisms of fluorous affinity.
Theory

For the sake of space, only a short overview of the theory and equations employed in this work is given. For a detailed discussion about theoretical aspects or how these equations can be derived, readers are referred to literature (and to Supporting Information) where these features are covered in detail.

Tracer pulse chromatography

The tracer pulse method has been extensively used for measuring excess surface isotherm of binary systems.\textsuperscript{7,23–32} According to this theory, the operational definition of the excess volume of an isotopically labeled compound $i$, $V_{i}^{\text{exc}}$, is given by:\textsuperscript{24}

$$V_{i}^{\text{exc}} = (V_{R,i}^{*} - V_{R,j}^{*})\theta_{i}^{M}\theta_{j}^{M}$$  \hspace{1cm} (1)

where $V_{R,i}^{*}$ and $V_{R,j}^{*}$ are the elution volumes for each labeled component $i$ and $j$ of the binary system and $\theta_{i}^{M}$ and $\theta_{j}^{M}$ their volume fractions in the bulk MP. In the context of this model, the thermodynamic void volume (i.e., the total volume of the eluent in the column) is:

$$V_{0} = V_{R,i}^{*}\theta_{i}^{M} + V_{R,j}^{*}\theta_{j}^{M}$$  \hspace{1cm} (2)

According to the method originally proposed by Nagy and Schay,\textsuperscript{33} the capacity and thickness of the surface phase (needed to pass from excess to absolute adsorption\textsuperscript{24,30,34}) can be estimated by the linear region of the excess isotherm, being:

$$V_{i}^{\text{exc}} = V_{i}^{S} - V_{S}\theta_{i}^{M}$$  \hspace{1cm} (3)
where $V_i^S$ and $V_S$ are the volume of $i$ in the stationary phase and the stationary phase volume, respectively.

**Retention factor and selectivity**

The (phase) retention factor, $k$, is defined as:

$$ k = \frac{V_R - V_M}{V_M} \quad (4) $$

where $V_R$ is the solute retention volume and $V_M$ is the kinetic void volume:

$$ V_M = V_0 - V_S \quad (5) $$

The selectivity, $\alpha$, is the ratio of the retention factor, $k$, of two solutes (here, 1 and 2):

$$ \alpha = \frac{k_1}{k_2} \quad (6) $$

When alkyl homologues are employed for the evaluation of $\alpha$, the so-called methylene selectivity is defined; analogously, the perfluoromethylene selectivity is when perfluoroalkyl homologues are used to calculate $\alpha$. With homologous series, in addition, $\alpha$ is best calculated by the slope of the plot of $\ln k$ vs. the carbon number in the chain. The natural logarithm of methylene or perfluoromethylene selectivity multiplied by the factor $-RT$ (being $R$ the gas constant and $T$ the temperature) gives the change of Gibbs free energy for the transfer, respectively, of a methylene or perfluoromethylene group from the mobile to the stationary phase, $\Delta G_{CX_2}^o$:

$$ -RT \ln \alpha = \Delta G_{CX_2}^o \quad (7) $$

where $X$ is either $H$ (methylene selectivity) or $F$ (perfluoromethylene selectivity).
Finally, following Martin, the total free energy $\Delta G^\circ$ for the transfer of a molecule from the mobile to the stationary phase can be calculated by assuming that each group $g$ of the molecule is associated with its own unique change $\Delta G^\circ_g$ in free Gibbs energy, independent of the presence of other groups, that is:

$$\Delta G^\circ = \sum_g \Delta G^\circ_g$$

### Inverse Method

The inverse method permits to determine adsorption isotherms in chromatography through a numerical procedure in which the parameters of an isotherm model are derived from overloaded (non-linear) band profiles of compounds. It is based on nonlinear least-squares method. The numerical constants of the isotherm models are tuned so that the calculated and the measured band profiles match as much as possible. Calculated band profiles are derived by numerically solving the equilibrium-dispersive model of chromatography, once an isotherm isotherm model has been chosen to correlate the concentration of the component in the mobile, $C$, and stationary, $q$, phases (more information under Supporting Information). In the equilibrium-dispersive model of chromatography, it is assumed instantaneous equilibrium between the stationary and the mobile phases, and an apparent dispersion term ($D_a$) accounts for both the axial dispersion and the finite rate of the mass transfer kinetics. The differential mass balance equation is written as:

$$\frac{\partial C(z,t)}{\partial t} + F \frac{\partial q(z,t)}{\partial t} + u \frac{\partial C(z,t)}{\partial z} = D_a \frac{\partial^2 C(z,t)}{\partial z^2}$$

where $z$ is the length, $t$ the time, $u$ the MP linear velocity, and $F$ the phase ratio ($V_S/V_M$). $D_a$ is the apparent dispersion coefficient that can be calculated from the number of theoretical plates ($N$) determined by an analytical injection:

$$D_a = \frac{uL}{2N}$$
being $L$ the column length. Initial and boundary conditions employed to solve Eq. 9 are reported under Supporting Information.

**Experimental Section**

**Column and materials**

A commercial $150 \times 2.1$ mm stainless steel column, packed with perfluorohexylpropylsiloxane-bonded silica, $5 \mu$m particle size, 100 Å pore size (Fluophase-RP, Thermo Scientific) was used for all measurements. Toluene, ethylbenzene, propylbenzene, pentylbenzene, hexylbenzene and $\alpha,\alpha,\alpha$-trifluorotoluene were purchased from Sigma Aldrich. Ultra-high quality Milli-Q water was obtained by a Milli-Q water purification system (Millipore). ACN was LC-MS grade from Sigma Aldrich. Deuterated water, $D_2O$, and deuterated ACN, $D_3$-ACN, were from Cambridge Isotope Laboratories Inc.

**Equipment and Measurements**

**Tracer pulse experiments**

The excess isotherm of ACN from binary water/ACN mixtures was measured through the tracer pulse technique by using a LC/MS/MS instrumentation made of a micro-HPLC (Finnigan Surveyor Plus) interfaced to a LTQ-XL linear ion trap MS detector (Thermo Scientific) through an APCI source. Ion source operational conditions are reported under Supporting Information. $5 \mu$L injections of $D_3$-ACN and $D_2O$ were done in column equilibrated with different ACN aqueous solutions. ACN concentration was varied with increase of 10% in the range 0-80%. Between 80-100%, the following concentrations were prepared: 85, 90, 93, 95, 97 and 100%. Measurements were done triplicate. Retention times of perturbations were determined through peak moments.
Linear and nonlinear measurements of benzene derivatives

A 1290 Infinity ultra high-performance liquid chromatography system (from Agilent Technologies) equipped with degasser, binary pump, autosampler, column thermostat and UV-Vis diode array was employed.

Under linear conditions, 1 μL of diluted solutions of benzene derivatives (0.02% v/v) were injected. Chromatograms were recorded at 214 nm. Four different binary water/ACN MP compositions were considered, with ACN ranging from 60 to 90% v/v (in increments of 10%). Peak retention times were estimated through peak moments.

High-concentration injections (needed for estimating the adsorption isotherm through the inverse method) of toluene, butylbenzene and α,α,α-trifluorotoluene were performed at two different MP compositions, namely 60/40 and 70/30% v/v ACN/water. The highest injected concentrations were close to the empirically evaluated solubility limits of the analytes in the actual MP. In particular, at 60/40% v/v ACN/water, these were: 13 g/L (toluene), 10 g/L (butylbenzene) and 20 g/L (α,α,α-trifluorotoluene). At 70/30% v/v ACN/water, on the other hand, we found solubilities of 35, 30 and 48 g/L, respectively for toluene, butylbenzene and α,α,α-trifluorotoluene. Large volume (up to 20 μL) injections were performed by using the available binary solvent delivery system. One channel was used to deliver the sample solution and the other to pump the pure MP. The low volume (35 μL) of the jet-weaver mixer of the 1290 chromatograph allows for an efficient mixing of solvent streams without loss of performance (with the column employed in this work).

Under nonlinear conditions, the detector was calibrated at 266 nm for butylbenzene and at 278 nm for toluene and α,α,α-trifluorotoluene.

All chromatographic measurements (including tracer pulse experiments) were performed at 0.1 ml/min at 25±0.1°C. Temperature was controlled by a digital contact thermometer (IKA Laboratory Equipment). All measurements were performed as triplicate determinations.

For the calculation of the simulated profiles, Eq. 9 was solved by using a finite difference scheme. The isotherm parameters were optimized by using a super modified downhill simplex
search routine. All programs were written in Matlab.

Results and Discussion

A rigorous description of thermodynamic equilibria in complex systems such as in RPLC would require simultaneously measuring the competitive isotherms of all the species in the system, that is both the eluent components and the analytes. These measurements, however, are very difficult to perform. Usually, therefore, the distribution isotherms of the eluent components are measured on the entire concentration range without regard to analytes (excess isotherms), while those of analytes are measured at a fixed MP composition when a convention for the determination of the volume of the mobile and the stationary phase has been established (absolute isotherms). A common approach for fixing the position of the boundary between mobile and stationary phase (or, in other words, to define the position of the Gibbs dividing surface) is by employing a purportedly unretained compound, from the retention time of which it is possible to estimate $V_M$.

The very common example is uracil with traditional C$_{18}$ silica gel in RP conditions. This is the so-called “component J not adsorbed” (JNA) convention, according to Riedo and Kováts.

In this work, the determination of the stationary and MP volumes has been done through an approach, originally proposed by Schay and Nagy, which involves measuring the excess adsorption isotherm of ACN from water/ACN binary mixtures and the use of Eqs. 3, 2 and 5. Briefly: Eq. 3 shows that the estimation of $V_S$ can be obtained by considering the region of the excess isotherm where the excess of ACN decreases linearly with $\theta_{ACN}^M$ (i.e., the zone of saturation of the stationary phase by ACN); then, through Eqs. 2 and 5, the estimation of $V_M$ is straightforward (so is the calculation of $F$ in Eq. 9). This approach has some advantages over the simpler JNA method. Indeed, it not only shows when (i.e., for which eluents) the composition of the stationary phase is constant and independent on that of the MP (saturation region) but it also permits an estimation of the composition of the stationary phase at saturation.
The excess isotherm of ACN is represented in the main part of Figure 1 in the form of excess volume of adsorbed ACN per column. The excess volume increases gradually in the first part of the isotherm (roughly up to $\theta_{\text{ACN}}^M \approx 0.4$), it reaches a maximum and then it decreases quasi-linearly for $0.5 < \theta_{\text{ACN}}^M < 0.9$. For very organic-rich eluents, the excess of ACN becomes negative in consequence of a positive excess of adsorbed water. This is due to the presence of residual unreacted surface silanols, that under these conditions have not been yet completely saturated by water molecules. The analysis of the linear region of the excess isotherm by means of Eq. 3 leads to estimated values of $V_S$ and $V_S^{\text{ACN}}$ roughly of 75 and 68 $\mu$L, respectively. In other words, at saturation, the stationary phase is made by more than 90% of ACN. Accordingly, being $V_0 = 351 \mu$L (from Eq. 2), the phase ratio was 0.27.

All measurements of benzene derivatives have been performed in this zone of the excess isotherm. Indeed, since retention in LC involves equilibria in both the stationary and the MP, it is very important to work where these phases can be properly defined and characterized.\textsuperscript{8,24,43} Initially, the dependence of $\ln k$ on $\theta_{\text{ACN}}^M$ for a series of six alkyl-benzenes (namely, toluene, ethylbenzene, propylbenzene, butylbenzene, pentylbenzene and hexylbenzene) has been investigated. The inset of Figure 1 shows the experimental data. From them it can be observed that, at a given MP composition, retention increases as the hydrophobic portion of the molecule increases (thus with a typical RP behavior) and that, for all compounds, $\ln k$ decreases linearly with $\theta_{\text{ACN}}^M$. The linear fitting of experimental data, in fact, led to correlation coefficients $R^2$ larger than 0.99 in all cases (straight lines not shown to avoid overcrowding the figure). Therefore, these data can be used for the calculation of the methylene selectivity\textsuperscript{14} and, by means of Eq. 7, of the free energy change for the transfer of a CH$_2$ unit from the mobile to the stationary phase. Calculated $\Delta G_{CH_2}^\circ$ values, in function of the eluent composition, are listed in the second column of Table 1 (more information under Supporting Information).

By considering now the chromatographic behavior of $\alpha,\alpha,\alpha$-trifluorotoluene, i.e. of a molecule that differs from toluene only for the aromatic ring substituent (a CF$_3$ vs. a CH$_3$ group), some
Table 1: Gibbs free energy for the transfer of either a methylene group, $\Delta G_{CH_2}^\circ$, or a perfluoromethylene group, $\Delta G_{CF_2}^\circ$, from the mobile to the stationary phase as a function of the MP composition. $\Delta G_{CF_2}^\circ$ s were taken from.\textsuperscript{8} Free energy values in J mol\textsuperscript{-1} ($T = 298$ K). See text for details.

<table>
<thead>
<tr>
<th>$\theta_M^{M\text{ACN}}$</th>
<th>$\Delta G_{CH_2}^\circ$</th>
<th>$\Delta G_{CF_2}^\circ$</th>
<th>$4 \times \Delta G_{CH_2}^\circ$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6</td>
<td>-562</td>
<td>-2006</td>
<td>-2248</td>
</tr>
<tr>
<td>0.7</td>
<td>-456</td>
<td>-1775</td>
<td>-1824</td>
</tr>
<tr>
<td>0.8</td>
<td>-359</td>
<td>-1677</td>
<td>-1436</td>
</tr>
<tr>
<td>0.9</td>
<td>-280</td>
<td>-1426</td>
<td>-1120</td>
</tr>
</tbody>
</table>

interesting things can be observed. Figure 2 reports the dependence of $\ln k$ on $\theta_M^{M\text{ACN}}$ for $\alpha,\alpha,\alpha$-trifluorotoluene in the same range of eluent compositions previously considered. For the sake of comparison, in the same plot also the data for toluene and butylbenzene (see later on) have been shown. By looking at these data, it is evident that the presence of the CF$_3$ group provokes a drastic change in the retention behavior of the molecule inducing an increase in retention of roughly 60\% (compare retention of toluene and $\alpha,\alpha,\alpha$-trifluorotoluene). This finding is still more significant by considering that solubility of $\alpha,\alpha,\alpha$-trifluorotoluene in water/ACN mixtures is noticeably larger than that of toluene and that, in RP chromatography, retention is expected to decrease when the solubility in MP increases.\textsuperscript{13,36} As an example, at 70/30\% v/v ACN/water, the experimentally measured solubility limit for $\alpha,\alpha,\alpha$-trifluorotoluene was approx. 48 g/L vs. only about 35 g/L for toluene. This is, however, only apparently in contrast with our understanding of retention in RP liquid chromatography. The explanation lies in the concept of fluorous affinity. From a thermodynamic viewpoint, indeed, it is largely more favorable to transfer one CF$_3$ group from the aqueous/ACN MP to the perfluorinated stationary phase than one CH$_3$ unit. This has been demonstrated, e.g., in reference [8] where $\Delta G_{CF_2}^\circ$ s were evaluated, at different MP compositions, by using a series of perfluorinated acids. For the sake of comparison, the $\Delta G_{CF_2}^\circ$ values calculated in [8] have been reported in Table 1 (third column). They are indeed significantly more negative than the corresponding $\Delta G_{CH_2}^\circ$ s.
Another interesting information that can be derived from Figure 2 is that, since retention of \(\alpha,\alpha,\alpha\)-trifluorotoluene is comparable to that of butylbenzene, in terms of energy transfer change, four methylene units should correspond to one single perfluoromethylene group. This comes directly from the application of the group additivity principle (Eq. 8) to these molecules, as detailedly shown under Supporting Information. Indeed, by comparing, at each MP composition, the free energy change for the transfer of the CF\(_2\) group with four times the value of \(\Delta G_{CH_2}^\circ\) (third column of Table 1), one observes that, within the limits of experimental errors and the simplification introduced by the model of additivity of the free energies per functional group, these values are reasonably comparable.

From a more fundamental viewpoint, however, the most interesting thing that can be observed in Figure 2 is probably the inversion of the elution order of \(\alpha,\alpha,\alpha\)-trifluorotoluene and toluene induced by a change in the MP composition (to emphasize this aspect, the linear regressions of experimental data have been represented in the figure). Indeed one may observe that, at organic-rich MP compositions, the former is more retained than the latter but, when the MP becomes more polar, the opposite is true. An inversion of the elution order in liquid chromatography is very often an intriguing phenomenon. The most relevant case is definitely the temperature-induced inversion of elution order of enantiomers in chiral chromatography.\(^{44}\) However, even in RP chromatography the inversion of the elution order following a change of experimental conditions (in this case the eluent composition) might suggest the presence of different chromatographic recognition mechanisms or adsorption modes for the involved molecules.\(^{36,45}\)

To further investigate these aspects, therefore, our study has been extended to the nonlinear range of the adsorption isotherm. Thus, the adsorption isotherm of toluene, butylbenzene and \(\alpha,\alpha,\alpha\)-trifluorotoluene have been measured, through the inverse method, at different MP compositions. As mentioned above, these measurements have been performed under conditions where the composition of the stationary phase is constant. To minimize the perturbation of the adsorption equilibria of the MP constituents following the injection of analytes, the inverse method has
been preferred to other, more common techniques of isotherm determination such as, for instance, frontal analysis as it allows to gather the information about the isotherm through relatively small-volume injections of compounds (in the case of this work the largest injected volume was 20µL).

The results of the nonlinear investigation are surprising. They are summarized in Figure 3 and Figure 4 where the overloaded band profiles recorded for toluene, butylbenzene and α,α,α-trifluorotoluene, at the maximum injected concentrations and two different eluent compositions (70/30 and 60/40 % v/v ACN/water), have been reported. As it can be seen, the shapes of the nonlinear peaks of alkyl-benzenes (Figure 3 and Figure 4, squares a and b) are remarkably different from those of α,α,α-trifluorotoluene (same figures, squares c). Indeed, in the former cases, the profiles present a so-called diffuse boundary in their front and a shock in the rear. The opposite, instead, can be observed for α,α,α-trifluorotoluene, where the shock comes before the diffuse boundary. According to the theory of nonlinear chromatography,\textsuperscript{13} we may conclude that for toluene and butylbenzene the isotherm must be convex downward (anti-Langmuirian) while, on the contrary, for the perfluoro-substituted compound the isotherm must be convex upward, or Langmuirian. Based on this preliminary information, the adsorption isotherms were determined through the inverse method. The anti-Langmuir isotherm has been used for modeling the overloaded band profiles of alkyl-benzenes.\textsuperscript{46} It is written:

\[ q = \frac{aC}{1 - bC} \] (11)

where \( a \) and \( b \) are numerical coefficients. On the other hand, for α,α,α-trifluorotoluene, we employed the Tóth isotherm, which has been often successfully employed to describe monolayer adsorption on heterogeneous surfaces.\textsuperscript{13,47}

\[ q = \frac{q_sK^{1/\nu}C}{[1 + (KC)^{\nu}]^{1/\nu}} \] (12)

where \( \nu \) is the so-called heterogeneity parameter, \( K \) the equilibrium constant (L/g) and \( q_s \) the
The results of the inverse method calculations have been also represented in Figure 3 and Figure 4, with continuous lines, overlaid to experimental profiles. These peaks have been obtained by solving Eq. 9 and using, as isotherm models, either Eq. 11 (alkyl-benzenes) or Eq. 12 ($\alpha,\alpha,\alpha$-trifluorotoluene), with the optimized isotherm parameters given by the inverse method (more details under Supporting Information). Table 2 lists their values. Other comparisons between experimental and simulated peaks, for different injection volumes and concentrations, have been reported under Supporting Information. In all cases, included those of Figure 3 and Figure 4, the matching between calculated and empirical profiles has been very satisfactory. This allows to conclude that the models proposed to describe the adsorption behavior of alkyl-benzenes (Eq. 11) and $\alpha,\alpha,\alpha$-trifluorotoluene (Eq. 12) take into account, within experimental error, the main features of the adsorption process.

Table 2: Best isotherm parameters calculated according to the inverse method for toluene and butylbenzene (anti-Langmuir model, Eq. 11) and $\alpha,\alpha,\alpha$-trifluorotoluene (Tóth model, Eq. 12). See text for details.

<table>
<thead>
<tr>
<th>$\theta_{ACN}^M$</th>
<th>Toluene</th>
<th>Butylbenzene</th>
<th>$\alpha,\alpha,\alpha$-trifluorotoluene</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6</td>
<td>$a = 6.85$</td>
<td>$a = 14.5$</td>
<td>$q_s = 2472$</td>
</tr>
<tr>
<td></td>
<td>$b = 0.012$</td>
<td>$b = 0.034$</td>
<td>$K = 0.088$</td>
</tr>
<tr>
<td></td>
<td>$\nu = 0.46$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.7</td>
<td>$a = 4.26$</td>
<td>$a = 7.42$</td>
<td>$q_s = 667$</td>
</tr>
<tr>
<td></td>
<td>$b = 0.00050$</td>
<td>$b = 0.017$</td>
<td>$K = 0.076$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$\nu = 0.57$</td>
</tr>
</tbody>
</table>

Accordingly the conclusion can be drawn that the adsorption nature of benzene derivatives on highly-fluorinated stationary phases changes radically depending if the molecule bears a perfluorinated carbon or not. Indeed, in the former case, adsorption leads to formation of Langmuir monolayers while, in the latter, of multilayer stack structure. These data emphasize the importance of the F-F interaction to drive the adsorption process. The information and the approach proposed in this study might useful for a better understanding not only of the specificity of the F-F inter-
action at a molecular level but also, more in general, of other properties of highly perfluorinated materials, such as the fact that they do not mix with most organic solvents or their tendency to bioaccumulate in body compartments high in protein content such as the liver, kidney, and blood.

Conclusions

The comparison between toluene and $\alpha,\alpha,\alpha$-trifluorotoluene has evidenced that the presence of one single CF$_3$ group provokes a drastic change in the adsorption behavior of molecules on a highly perfluorinated stationary phase from water/ACN solutions. In particular, this study has revealed that $\alpha,\alpha,\alpha$-trifluorotoluene molecules interact with the stationary phase to form a monolayer, while, on the contrary, the adsorption of toluene is multilayer. An analogous anti-Langmuirian adsorption behavior has been observed also for linear alkyl-benzenes with longer alkyl chain. This information can contribute to the understanding, at a molecular level, of the nature of F-F interactions. The interaction was found to be effective already when one single fluorinated sp$^3$ carbon interacts with an highly perfluorinated moiety. This is interesting if one considers that, in the fluorous literature, a fluorous label or tag (i.e., that portion that properly introduced into a molecule, for example as a part of a protecting group, “exerts primary control over the separability characteristics of the molecule in fluorous separation techniques”) is defined to contain at least six fully fluorinated sp$^3$ carbons.

Supporting Information Available

Acknowledgments

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References


Figures

Figure 1: Main: excess adsorption isotherm of ACN (µL per column) from binary water/ACN mixtures. Straight line: linear regression for the evaluation of $V_S$ and $V_{ACN}^S$, according to Eq. 3. Inset: dependence of the logarithm of retention factor of alkyl-benzenes on the volume fraction of acetonitrile in MP: toluene (□); ethylbenzene (△); propylbenzene (■); butylbenzene (○); pentyln benzene (▲); hexylbenzene (●).

Figure 2: Dependence of the logarithm of retention factor of benzene derivatives on the volume fraction of acetonitrile in MP: toluene (□); propylbenzene (■); α,α,α-trifluorotoluene (○). Linear regressions have been shown to stress the inversion of the elution order between propylbenzene and α,α,α-trifluorotoluene as a function of $\theta_{ACN}$

Figure 3: Comparison between experimental (points) and simulated (continuous line) overloaded profiles. (a) Toluene (injected volume: 20 µL, injected concentration: 13 g/L); (b) Butylbenzene (20 µL, 10 g/L); (c) α,α,α-trifluorotoluene (20 µL, 20 g/L). MP: 60/40 ACN/water, v/v.

Figure 4: Comparison between experimental (points) and simulated (continuous line) overloaded profiles. (a) Toluene (injected volume: 20 µL, injected concentration: 35 g/L); (b) Butylbenzene (20 µL, 30 g/L); (c) α,α,α-trifluorotoluene (20 µL, 48 g/L). MP: 70/30 ACN/water, v/v.
Figure 1
Figure 2
Figure 3
Figure 4
Graphical TOC Entry

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