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Eluotropic strength of solvents for parallel-displaced π–π interaction chromatography

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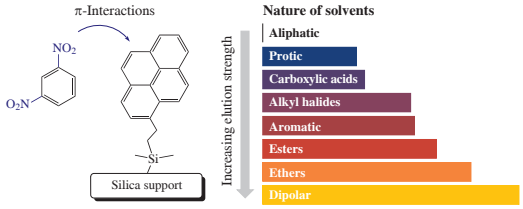
A solvent eluotropic strength series for liquid chromatography in the parallel-displaced π–π interaction mode was established. Experiments were carried out on a pyrenylethyl group bonded stationary phase with 1,3-dinitrobenzene as a marker compound and a 40 : 60 isopropanol–*n*-hexane mixture as the initial mobile phase, in which 1, 3, 5, 10, 15 and 20% were replaced by the solvent under study.



Keywords: quasi-normal phase, PYE, pyrenylethyl stationary phase, π-interactions, solvent eluotropic series.

Parallel-displaced π–π interaction liquid chromatography is based on π-interactions between stationary phase aromatic selectors, eluent and analytes. These π-interactions involve a variety of interacting groups such as another aromatic system, halogen, hydrogen-bonding group, lone electron pair, –CH, –OH, –NH and others.[1,2] Moreover, π-interactions are classified depending on the configuration of interacting aromatic systems into three categories: edge-to-face T-shape, parallel-displaced and parallel-stacked.[3] The nature of the interacting aromatic systems, heteroatoms and substituents significantly affects the distribution of the electron density of the aromatic system and, therefore, the strength and direction of π-interactions.[2] Together, these factors determine the high directionality of π-interactions and, as a result, potentially high selectivity when implemented in liquid chromatography.

Many researchers, realizing the uniqueness of π-interactions, synthesize and study stationary phases with aromatic selectors[4–8] or use them to improve chromatographic selectivity.[9,10] However, π-interactions are rarely taken into account in the development of HPLC methods. In a few pioneering studies, it is mentioned as a quasi-normal phase mode.[11–14] Only one study demonstrates a limited eluotropic series based on seven solvents.[15] Acetonitrile, which is the most popular HPLC solvent, largely suppresses π-interactions.[16–18] However, a significant number of researchers using stationary phase with aromatic selectors still use a mobile phase based on acetonitrile.[19,20] Few authors used a mobile phase based on methanol[10,16,21–26] or other organic solvents.[16,27,28] Establishing an eluotropic series of solvents capable of parallel-displaced π–π interactions provides a better understanding of the nature of π-interactions and helps in the choice of solvent for selectivity control.

Parallel-displaced π–π interactions are among the most common and powerful. In this work, a stationary phase with bonded pyrenylethyl (PYE) groups was chosen, which possess a large aromatic condensed system capable of strong π-interactions. 1,3-Dinitrobenzene (13DNB) was chosen as a marker compound. A mixture of isopropanol and *n*-hexane (40 : 60) was chosen as the initial mobile phase (retention factor $k'_{13DNB} = 8.56$), since pure *n*-hexane has low elution strength, unstable retention time (retention factor $k'_{13DNB} \approx 38$) and is immiscible with acetonitrile, methanol, water and propylene carbonate, which were supposed to be studied. To conduct the experiment, 1, 3, 5, 10, 15 and 20% of the initial composition of the mobile phase was replaced by the solvent under study.

Water and propylene carbonate were added up to 5% due to their limited miscibility with the initial mobile phase. Carboxylic acids were added up to 5%, 1,4-dioxane was added up to 3%, and dichloromethane was added up to 15% to prevent their aggressive effect. CCl_4 was not studied due to its toxicity and corrosive effect on stainless steel. Some physicochemical properties of the studied solvents are presented in Online Supplementary Materials. The equipment used and chromatographic conditions are presented in the footnote.†

The diagrams of the 13DNB retention factor k' dependence on the type and amount of the replaced solvent were plotted (Figures 1–3). The dependence graph is presented by a trend line (except for dipolar solvents, for which the trend line had a strong deviation from the experimental data).

Alkanes have the lowest elution strength, as the addition of any other solvent studied reduces the 13DNB k' retention. Protic solvents (alcohols and water) demonstrate a wide range of eluotropic strength, which decreases with increasing alkyl chain length (Figure 1).

The elution strength of alkyl halides decreases with decreasing alkyl chain length and increasing number of halide atoms (Figure 2), but for 1,2-dichloroethane and 1,2-dichloropropane it is approximately the same when converting the solvent volume fraction into the number of

† A Cosmosil PYE column (5 μm particle size, 4.6 mm i.d. × 250 mm length) was purchased from Nacalai Tesque (Japan). Chromatography was performed using an Agilent 1200 system equipped with a 1100/1200 quaternaty pump, 1200 variable wavelength detector, 1100/1200 column thermostat, 1100/1200 thermostated autosampler and ChemStation for LC systems Rev. B.04.03 software. Mobile phase preparation and mixing were performed using a quaternary pump with multichannel gradient valves. Chromatographic conditions were as follows: flow rate 0.8 ml min^{-1}, column temperature 25 °C, injection volume 1 μl and detection wavelength 230/270 nm.

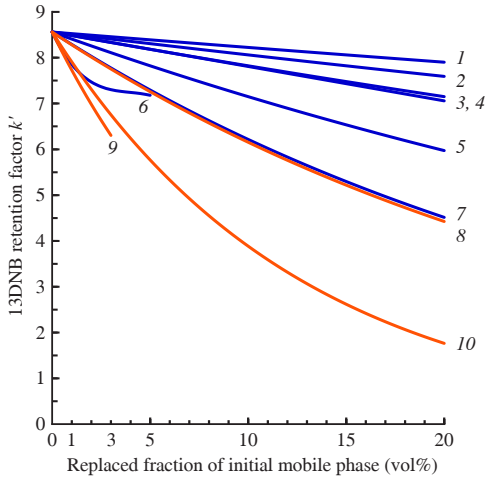


Figure 1 Dependence of the 13DNB retention factor k' on the type of replacement solvent and the amount of the initial mobile phase isopropanol–*n*-hexane (40 : 60, vol/vol) replaced with (*1*) isobutanol, (*2*) isopropanol, (*3*) *n*-butanol, (*4*) *n*-propanol, (*5*) ethanol, (*6*) water, (*7*) methanol, (*8*) methyl *tert*-butyl ether, (*9*) 1,4-dioxane and (*10*) tetrahydrofuran.

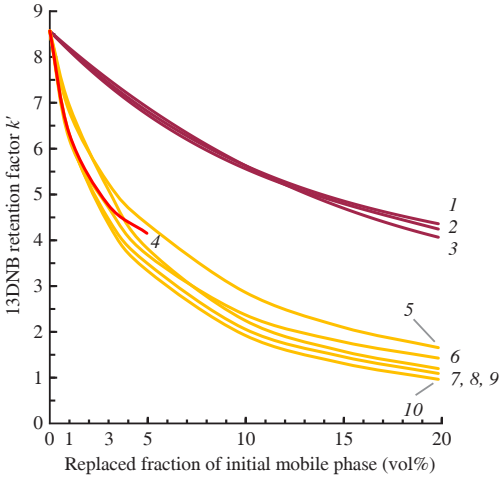


Figure 3 Dependence of the 13DNB retention factor k' on the type of replacement solvent and the amount of the initial mobile phase isopropanol–*n*-hexane (40 : 60, vol/vol) replaced with (*1*) benzene, (*2*) toluene, (*3*) xylene, (*4*) propylene carbonate, (*5*) acetone, (*6*) acetonitrile, (*7*) dimethyl sulfoxide, (*8*) *N*,*N*-dimethylacetamide, (*9*) *N*,*N*-dimethylformamide and (*10*) *N*-methyl-2-pyrrolidone.

moles (Figure S1, see Online Supplementary Materials). The elution strength of carboxylic acids and esters decreases with increasing alkyl chain length (Figure 2).

Dipolar solvents have the highest elution strength (Figure 3). The curved shape of the dependence for some solvents, especially for dipolar ones, is related to the solvent concentration at which solvent molecules are adsorbed on the selector surface and modify it. The elution strength of aromatic solvents (see Figure 3) increases with the number of electron-donor substituents if the volume fraction of the solvent is converted into the number of moles (see Figure S1).

In general, the strength of solvents in the eluotropic series of parallel-displaced π–π interaction chromatography increases with the growth of the dipole moment of the solvent, the electron density of the lone pair of the electronegative atom (esters > carboxylic acids, ethers > protic) and the electron density of aromatic compounds (xylene > toluene > benzene). The established eluotropic series of solvents allows choosing a solvent to regulate the strength of parallel-displaced π-interactions and, as a result, the selectivity of the chromatographic separation of aromatic substances.

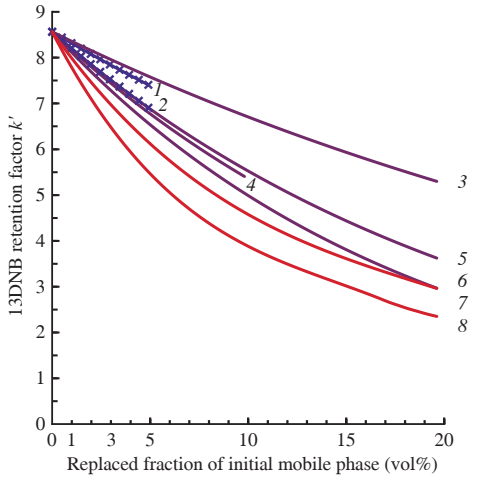


Figure 2 Dependence of the 13DNB retention factor k' on the type of replacement solvent and the amount of the initial mobile phase isopropanol–*n*-hexane (40 : 60, vol/vol) replaced with (*1*) pentanoic acid, (*2*) propionic acid, (*3*) chloroform, (*4*) dichloromethane, (*5*) 1,2-dichloropropane, (*6*) 1,2-dichloroethane, (*7*) butyl acetate and (*8*) ethyl acetate.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.71267/mencom.7576.

References

1 E. A. Meyer, R. K. Castellano and F. Diederich, *Angew. Chem., Int. Ed.*, 2003, **42**, 1210; https://doi.org/10.1002/anie.200390319.
2 *Heterocyclic Supramolecules II*, eds. K. Matsumoto and N. Hayashi, Springer, Berlin, 2009; https://doi.org/10.1007/978-3-642-02041-4.
3 R. Thakuria, N. K. Nath and B. K. Saha, *Cryst. Growth Des.*, 2019, **19**, 523; https://doi.org/10.1021/acs.cgd.8b01630.
4 C. de Castro Ferreira, M. R. Gama, G. S. da Silva, W. Pereira Almeida, C. Hollingworth Collins and I. C. Sales Fontes Jardim, *J. Sep. Sci.*, 2018, **41**, 3855; https://doi.org/10.1002/jssc.201800522.
5 K. Mallik, L. Montero, S. W. Meckelmann and O. J. Schmitz, *J. Chromatogr. A*, 2024, **1717**, 464688; https://doi.org/10.1016/j.chroma.2024.464688.
6 H. Aral, T. Aral, K. S. Çelik, B. Ziyadanoğulları and R. Ziyadanoğulları, *Chromatographia*, 2014, **77**, 771; https://doi.org/10.1007/s10337-014-2678-9.
7 H. Aral, K. S. Çelik, R. Altındağ and T. Aral, *Talanta*, 2017, **174**, 703; https://doi.org/10.1016/j.talanta.2017.07.014.
8 T. Aral, H. Aral, B. Ziyadanoğulları and R. Ziyadanoğulları, *Talanta*, 2015, **131**, 64; https://doi.org/10.1016/j.talanta.2014.07.060.
9 Y. F. Wong, A. Makahleh, B. Saad, M. N. M. Ibrahim, A. A. Rahim and N. Brosse, *Talanta*, 2014, **130**, 299; https://doi.org/10.1016/j.talanta.2014.07.021.
10 B. Cervinkova, L. K. Krcmova, S. Klabackova, D. Solichova and P. Solich, *J. Sep. Sci.*, 2017, **40**, 3375; https://doi.org/10.1002/jssc.201700492.
11 N. A. Penner, P. N. Nesterenko, M. M. Ilyin, M. P. Tsyurupa and V. A. Davankov, *Chromatographia*, 1999, **50**, 611; https://doi.org/10.1007/bf02493669.
12 V. A. Davankov, C. S. Sychov, M. M. Ilyin and K. O. Sochilina, *J. Chromatogr. A*, 2003, **987**, 67; https://doi.org/10.1016/s0021-9673(02)01914-3.
13 C. S. Sychov, M. M. Ilyin, V. A. Davankov and K. O. Sochilina, *J. Chromatogr. A*, 2004, **1030**, 17; https://doi.org/10.1016/j.chroma.2003.10.098.
14 S. V. Prokopov, E. V. Tyrina, V. A. Davankov, M. M. Il’in and S. V. Kurbatova, *Russ. J. Phys. Chem. A*, 2013, **87**, 114; https://doi.org/10.1134/s0036024413010184.
15 K. S. Sychev, *PhD Thesis*, A. N. Nesmeyanov Institute of Organoelement Compounds of Russian Academy of Sciences, Moscow, 2004 (in Russian); https://www.dissercat.com/content/primenenie-sverkhsshitogo-polistirola-v-vysokoeffektivnoi-zhidkostnoi-khromatografii-i-tverd.

16 M. Yang, S. Fazio, D. Munch and P. Drumm, *J. Chromatogr. A*, 2005, **1097**, 124; https://doi.org/10.1016/j.chroma.2005.08.028.
17 K. Croes, A. Steffens, D. H. Marchand and L. R. Snyder, *J. Chromatogr. A*, 2005, **1098**, 123; https://doi.org/10.1016/j.chroma.2005.08.090.
18 E. V. Upyrenko and D. A. Kurgachev, *Mendeleev Commun.*, 2024, **34**, 450; https://doi.org/10.1016/j.mencom.2024.04.044.
19 P. Jandera, *Anal. Chim. Acta*, 2011, **692**, 1; https://doi.org/10.1016/j.aca.2011.02.047.
20 C. H. Lochmüller, R. R. Ryall and C. W. Amoss, *J. Chromatogr. A*, 1979, **178**, 298; https://doi.org/10.1016/s0021-9673(00)89719-8.
21 B. Šmídová, D. Šatínský, K. Dostálová and P. Solich, *Talanta*, 2017, **166**, 249; https://doi.org/10.1016/j.talanta.2017.01.061.
22 S. L. Richheimer, M. C. Kent and M. W. Bernart, *J. Chromatogr. A*, 1994, **677**, 75; https://doi.org/10.1016/0021-9673(94)80546-6.
23 N. Grebenstein and J. Frank, *J. Chromatogr. A*, 2012, **1243**, 39; https://doi.org/10.1016/j.chroma.2012.04.042.
24 R. Brindle and K. Albert, *J. Chromatogr. A*, 1997, **757**, 3; https://doi.org/10.1016/S0021-9673(96)00682-6.
25 Y. Zhang, Q. Li, B. Dai, S. Zhou, M. Zhang, H. Han and H. Qiu, *J. Chromatogr. A*, 2018, **1553**, 81; https://doi.org/10.1016/j.chroma.2018.04.025.
26 S. R. Needham and P. R. Brown, *J. Pharm. Biomed. Anal.*, 2000, **23**, 597; https://doi.org/10.1016/S0731-7085(00)00348-4.
27 P. G. Stevenson, S. Kayillo, G. R. Dennis and R. A. Shalliker, *J. Liq. Chromatogr. Relat. Technol.*, 2007, **31**, 324; https://doi.org/10.1080/10826070701780607.
28 R. Li, Y. Zhang, C. C. Lee, L. Liu and Y. Huang, *J. Sep. Sci.*, 2011, **34**, 1508; https://doi.org/10.1002/jssc.201100130.

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