Short Communication

New graph of binary mixture solvent strength in adsorption liquid chromatography

Veronika R. Meyer*

Institute of Organic Chemistry, University of Berne, Freiestrasse 3, CH-3012 Berne (Switzerland)

Mariana D. Palamareva

Department of Chemistry, University of Sofia, Sofia 1126 (Bulgaria)

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ABSTRACT

A graph that allows the determination of the composition of a binary solvent mixture if a given eluent strength is needed is presented. It is suited for adsorption (*i.e.* normal-phase) liquid chromatography on silica and includes the twelve binary mixtures possible with hexane, dichloromethane, *tert.*-butyl methyl ether, tetrahydrofuran, ethyl acetate and isopropanol.

INTRODUCTION

In 1974, Saunders presented a graph for the determination of binary eluent strength in adsorption liquid chromatography [1]. It found widespread use and was reprinted in many books about column liquid chromatography. Fig. 1 is a reproduction of this diagram; it is included here because it was important in the development of adsorption chromatography and because it is the model for the new graph described in this paper. It allows the quick determination of the eluent composition if a certain solvent strength is needed. The graph was inspired by an earlier figure by Neher [2].

The uppermost bar in the drawing represents the solvent strength parameter ε^0 after Snyder [3] (in this volume, the concept of solvent strength is developed in Chapter 8, pp. 185–240). In most tables of the eluotropic series, ε^0 values are given for alumina, but the graph is for silica with $\varepsilon^0(\text{silica}) = 0.77\ \varepsilon^0(\text{alumina})$. The other horizontal lines represent the volume per cent composition of the following solvent mixtures, from top to bottom: isopropyl chloride in pentane, dichloromethane in pentane, diethyl ether in pentane, acetonitrile in pentane, methanol in pentane, dichloromethane in isopropyl chloride, diethyl ether in isopropyl chloride, acetonitrile in isopropyl chloride, methanol in isopropyl chloride, diethyl ether in dichloromethane, acetonitrile in dichloromethane, methanol in dichloromethane, acetonitrile in diethyl ether, methanol in di-
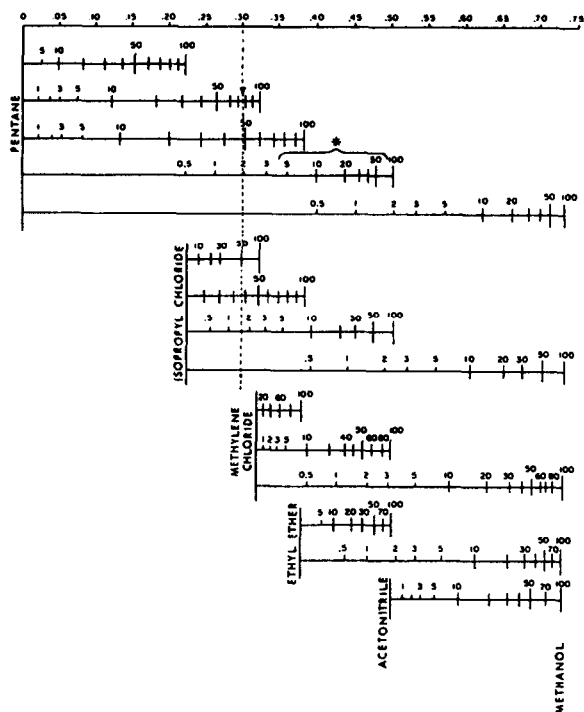
* Corresponding author.

Fig. 1. Graph of mixed solvent strengths ε^0 on silica by Saunders (reprinted with permission from ref. 1, copyright American Chemical Society 1974). It considers the solvents pentane, isopropyl chloride, dichloromethane (methylene chloride), diethyl ether (ethyl ether), acetonitrile and methanol. The asterisk marks the region where pentane and acetonitrile are not miscible; Saunders recommends adding some carbon tetrachloride. The dashed vertical line was added for explanatory purposes: to obtain a mixture with $\varepsilon^0 = 0.30$ it is possible to use, for example, 2% acetonitrile in pentane or 50% dichloromethane in isopropyl chloride.

ethyl ether, and methanol in acetonitrile.

In the paper [1] it is not explained how the graph was calculated, but this is clear from Snyder's book [3]. There the following equation can be found (eqns. 8–10 on p. 208 of that volume):

$$\varepsilon_{ab} = \varepsilon_a + \frac{\log(N_b 10^{\alpha n_b(\varepsilon_b - \varepsilon_a)} + 1 - N_b)}{\alpha n_b}$$

where ε_a is the eluent strength of the weaker solvent (=solvent a), N_b is the mole fraction of

the stronger solvent (=solvent b), α is the activity of the adsorbent surface ($\alpha = 1$ if the adsorbent is higher active; $\alpha = 0$ in the case of full deactivation), n_b is the reduced (*i.e.* relative) cross-section of a molecule of the stronger solvent (dimensionless) and ε_b is the eluent strength of the stronger solvent.

For three reasons we found it appropriate to calculate and draw a new graph:

(1) Whereas the ε^0 values of pure pentane (=0 by definition), isopropyl chloride (0.22), dichloromethane (0.32), acetonitrile (0.50) and methanol (0.73) are in accordance with the values given by Snyder [3] (p. 195) if corrected by the silica factor of 0.77, the value for diethyl ether as given in the graph is wrong. ε^0(alumina) is 0.38, therefore ε^0(silica) is 0.29. In error the alumina value of 0.38 was used for the drawing. However, this is a historical remark as some of the ε^0 values have undergone revision in the meantime.

(2) The choice of solvents does not represent the most used eluents by today's experience.

(3) The weakest point of the graph is that it does not include an important concept in adsorption chromatographic theory which has been developed in the meantime, that is solvent localization [4,5]. The localization parameter, m, is a measure of the ability of the solvent molecule to interact with the adsorbent which is used as stationary phase. In the case of silica, the adsorptive sites responsible for retention are its silanol groups. Molecules that can interact with these sites by means of their polar functional group, such as ethers, esters, alcohols, nitriles and amines, will prefer a specific position with respect to a nearby silanol group. Silica surrounded with such a localizing solvent or sample is covered with a well-defined layer of molecules. In contrast to this, a non-localizing solvent or sample such as dichloromethane or benzene will interact with silica to a much weaker extent and the coverage is random. It is obvious that even a small amount of a strongly localizing solvent, such as an alcohol, will have a distinct influence on sample retention.

THE NEW GRAPH

Choice of solvents

For the calculation of a new graph the following six solvents were chosen.

Hexane. As pentane, the solvent has $\varepsilon^0 = 0$, but it is cheaper (as a mixture of isomers) and has a suitable boiling point of 69°C, whereas pentane with a boiling point of 36°C is less convenient (but can be useful for special purposes).

Dichloromethane. Of the medium polar solvents, this is a weak one because it is non-localizing. In the course of the optimization of a separation it offers a distinct selectivity as it is the representative eluent with dipole properties [6]. Despite its interesting and useful properties it should be avoided whenever possible because it is toxic and environmentally harmful.

tert.-Butyl methyl ether (tBME). This solvent has now replaced diethyl ether in many applications because it does not form peroxides and offers the same boiling point advantage as in the case of hexane *vs.* pentane: 55°C for tBME and 35°C for diethyl ether [7]. It is the representative eluent with proton-accepting properties [6] and is localizing.

Tetrahydrofuran (THF). Although it is not cheap, THF is often used. It offers the same strength as tBME and is localizing but it is much weaker a proton acceptor [6].

Ethyl acetate. This solvent also has the same strength as tBME and THF. Its polarity properties are quite similar to THF [6]. Its drawback is the missing UV transparency; it cannot be used below 260 nm.

Isopropanol (IPA). This is a strong (polar and localizing) solvent that is fully miscible with hexane.

In any case all six solvents are fully miscible with each other. Acetonitrile and methanol are not miscible with hexane and for this reason they are not included in the graph. In compositions with hexane, acetonitrile and methanol, as well as water, play an important role as modifiers to deactivate the adsorbent surface [8] but not as mobile phase strength adjusters. For toxicological and ecological reasons chloroform was not considered, although it is the representative solvent as proton donor [6].

Calculations

The calculation of solvent strength ε^0 according to Snyder's theory [4,5] is demanding because it involves iterative mathematics and for this reason cannot be done without an appropriate program run on a personal computer. This program is described in detail in a previous paper [9].

The parameters used for the calculations here are listed in Table I. The program failed to calculate ε^0 values of mixtures of hexane con-

TABLE I

SOLVENT PARAMETERS USED FOR THE CALCULATIONS

d/M_r = solvent density (g/ml) divided by molecular mass; n = reduced molar cross-section; ε' = elution strength on silica when the molar fraction of the solvent in the mobile phase approaches 0; ε'' = elution strength on silica when the molar fraction of the solvent in the mobile phase approaches 1; $f_1(C)/n$ = parameter describing the influence of strong solvent concentration on elution strength.

Solvent	$100d/M_r$	n	ε'	ε''	$f_1(C)/n$
Hexane	0.77	–	0	0	0
Dichloromethane	1.57	4.1	0.30	0.30	0
tert.-Butyl methyl ether	0.84	4.1	1.01	0.48	1.10
Tetrahydrofuran	1.23	5.0	0.73	0.48	1.30
Ethyl acetate	1.02	5.2	0.94	0.48	1.60
Isopropanol	1.34	4.4	1.80	0.60	4.10

taining less than 3% IPA, so these values were taken from a paper by Snyder and Glajch [10]. Indicating these extreme mixture ratios, the graph shows the drastic increase in solvent strength if a minute amount of a strong component is added to a weak eluent; however, the numeric value of ε^0 should not be taken for granted in this region.

The graph

Fig. 2 presents the new solvent strength graph for binary mixtures on silica. It is used in identical manner as the Saunders graph. The possible range of ε^0 values offered by a certain mixture is indicated by the horizontal bars. The numbers below these bars indicate the amount of stronger solvent in volume per cent that is needed to obtain the desired strength of the mixture. The use of the graph is illustrated by an example:
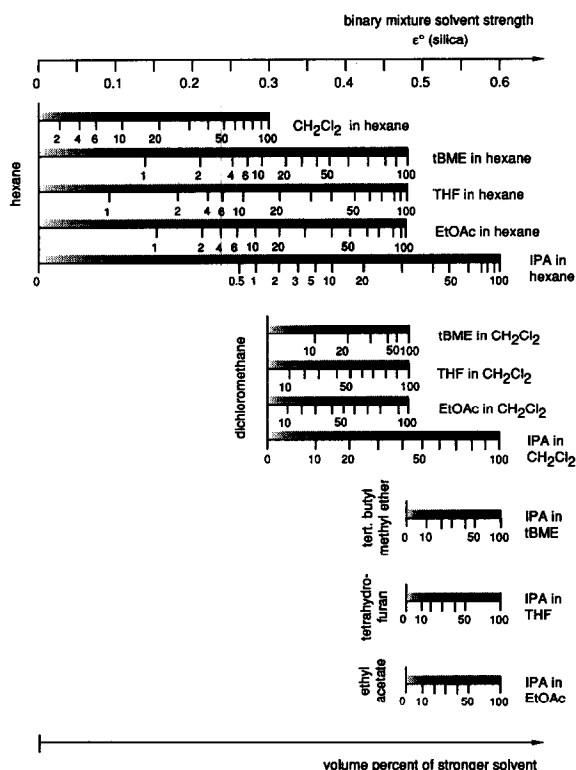

Fig. 2. Solvent strength graph for binary mixtures of hexane, dichloromethane, *tert.*-butyl methyl ether, tetrahydrofuran, ethyl acetate and isopropanol used in adsorption liquid chromatography on silica.

If a solvent strength of 0.4 is needed, this can be obtained by the following mixtures: approximately 60% *tert.*-butyl methyl ether in hexane; 45% tetrahydrofuran in hexane; 50% ethyl acetate in hexane; 15% isopropanol in hexane; 20% *tert.*-butyl methyl ether in dichloromethane; 45% tetrahydrofuran in dichloromethane; 50% ethyl acetate in dichloromethane; or 20% isopropanol in dichloromethane.

Although all of these eight mixtures have the same strength, their selectivity for a given separation problem can be rather different. "Selectivity" means that the strength, as determined by the capacity factor k' of a certain individual solute, is not constant but can vary. For the solution of complex separation problems it can be useful to try several of these mixtures, as separation factors, resolutions and even elution orders may change. Thus, it has been shown [4,5,11,12] that solvent selectivity varies depending on whether the strong (polar) solvent is non-localizing, localizing and basic or localizing and non-basic. Of the polar solvents shown in Fig. 2, dichloromethane is non-localizing. The solvents *tert.*-butyl methyl ether and THF are localizing and basic, and they should be similar in terms of selectivity (but different from dichloromethane). Ethyl acetate is a localizing, non-basic solvent whose selectivity is expected to be different from the other solvents of Fig. 2. Finally, isopropanol is a localizing, basic solvent. But it should differ somewhat in selectivity because of its proton-donating ability. Thus the solvents in Fig. 2 encompass a wide range of possible selectivity and they should be useful for optimizing band spacing and resolution. Unfortunately, it is still difficult to predict elution orders, and today's research interest is not directed towards this type of problem [13]. Nevertheless, the effect of ε and two other parameters of Snyder's theory on various separations has been studied in detail [14].

CONCLUSIONS

The graph presented in Fig. 2 can be useful for the determination of the composition of a binary mixture if a certain elution strength is needed in adsorption chromatography on silica. An alter-

native approach is the use of the microcomputer program permitting an easier choice of mobile phases containing two or more solvents [9,14].

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