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Theoretical characterization of McReynolds' constants

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Abstract

The properties of McReynolds' constants were studied by a detailed statistical/chemometric analysis. The electronic structure, geometries and hydrophobicity of the McReynolds' test compounds (benzene, 1-butanol, 2-pentanone, 1-nitropropane, pyridine, 2-methyl-2-pentanol, 1-iodobutane, 2-octyne, 1,4-dioxane and *cis*-hidrindane) were calculated at the level of PM3 semiempirical quantum chemical method and empirical formulas. The predominant pattern was revealed using cluster and principal component analyses (CA and PCA). Dependence of McReynolds' constants on the calculated chemical descriptors was modeled by multiple linear regression (MLR) with stepwise selections, principal component regression (PCR) and partial least-square regression (PLSR). A novel statistical approach was developed for case-and-variable selection using the PCR and PLSR methods for characterizing and modeling the polarity of 25 gas chromatography (GC) stationary phases (phthalates, adipates, sebacates, phosphates, citrates and nitrils). Highest occupied molecular orbital energy, dipole moment, averaged isotropic polarizability and the apolar solvent accessible surface area; and energy of the lowest unoccupied molecular orbital and total solvent accessible surface area were suitable to describe the McReynolds' constants based on the results obtained using Q^2 and adjusted-Q^2. Six of the 10 test compounds were found to be sufficient for the description of the polarity of the columns studied.

Keywords: Polarity; McReynolds' constants; Stationary phases; Gas chromatography; Quantum chemical method; Principal component analysis; Principal component regression; Partial least-square regression; Case and variable selection

1. Introduction

It is a continuously arising question for chromatographers to find an easy-to-use method to characterize the stationary phase and solute interaction to forecast gas chromatographic retention behavior. Which stationary phase (column type) is suitable to separate possibly all or as many solutes in a complex mixture as possible? In this respect we have to know the polarity and selectivity of a column. The selectivity is the ability of the stationary phase to participate in specific intermolecular interactions. Depending on the extent of the interactions, some solutes may be dissolved better or to a smaller extent in a given stationary phase finally resulting in some separations [1].

The polarity concept was intended to use for the characterization of the interaction of the stationary phase and the solute on the basis of its structure. Basically, polarity means that the more polar is a stationary phase, the greater is the retention of a polar solute compared to a non-polar solute as e.g. an *n*-alkane, see e.g. in Ref. [2]. On this basis, the polarity is the sum of various intermolecular interactions (inductive, dispersive, orientation and H-bonding). In gas chromatography, the interactions do not depend only on the stationary phase, but also on the solute and its functional group. The polarity is a term difficult to define: e.g. dipole moment is often used as a symbol of polarity but in chromatographic interactions it cannot be used as a single measure. Some empirical measures for the polarity and/or selectivity parameters of the stationary phases are available: McReynolds' polarity (P) [3], Kovats coefficient (K_C) [4], retention polarity (R_P) [5], Snyder's selectivity parameters [6], Castello's ΔC [7] and ΔG_{CH2} [8]. The polarity/selectivity properties of thirty stationary phases were characterized by Heberger [9] by principal component analysis (PCA). Two groups of polarity scales were

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found. The first group (P, K_C, R_P and ΔC) and the second group (Snyder's selectivity parameters, Castello's ΔC) of the polarity scales can characterize the column mainly by their polarity and selectivity, respectively. The most influential properties are: (i) polarity, (ii) hydrogen donating and accepting ability and (iii) dipole interactions. The principal components of retention data for oxo compounds were correlated with the physical properties (molar refractivity (R_M), boiling point (T_{BP}), molar volume (V_m)) [10]. A predictive model was suggested by partial least-square regression (PLSR) method [11].

According to the thermodynamic concept the reluctance of the liquid phase to accept a hydrocarbon may be considered as a measure of polarity. The measure of this behavior is the partial molar Gibbs free energy of solution for a methylene group [8,12,13].

According to the most well-known and widely used Rohrschneider–McReynolds concept, the Kovats retention index difference of some specific test compound p on the column studied (I_p) and squalane (I_{sq}) provides a measure of polarity [3,14,15] (Eq. (1)). By definition the polarity of squalane is 0, because it was considered as an apolar (reference) phase:

$$\Delta I_x = I_p - I_{sq} \tag{1}$$

In the Rohrschneider concept the intermolecular forces are additive which are characterized by several factors both characteristic for the solute (a, b, c, d, e) and the stationary phase (x, y, z, u, s):

$$\Delta I_{i,j}(\text{calc.}) = a_i x_j + b_i y_j + c_i z_j + d_i u_j + e_i s_j \tag{2}$$

$\Delta I_{i,j}$(calc.) is the difference in Kovats indices between the phase of interest and squalane. x_j, y_j, z_j, u_j and s_j are calculated for each phase from the difference in Kovats indices of benzene, ethanol, methyl ethyl ketone, nitromethane and pyridine, respectively. a_i, b_i, c_i, d_i, and e_i are empirical coefficients, which can be calculated from retention data for each solute using various liquid phases. In the simplest case a_i, b_i, c_i, d_i, and e_i equal to 1s (or only one equals to 1, and the other is 0), however, if we know $\Delta I_{i,j}$(calc.) in advance the profiles (a, b, c, …, and x, y, z, …) can be estimated by factor analysis (FA) [16].

Rohrschneider originally used five compounds, but later McReynolds analyzed 68 compounds on 25 columns and selected the 10 compounds characterizing the columns the best [3]: benzene, 1-butanol, 2-pentanone, nitropropane, pyridine, 2-methyl-2-pentanol, 1-iodobutane, 2-octyne, 1,4-dioxane and *cis*-hidrindane. The most informative of these, benzene, 1-butanol, 2-pentanone, nitropropane and pyridine, are either the same compounds Rohrschneider used or homologs of Rohrschneider's compounds.

The criterion of selecting the test compounds was the ability to participate in various types of interactions with the different stationary phases through inductive, donor–acceptor forces or H-bonding (H+ donor and acceptor). While 2-methyl-2-pentanol and 1-iodobutane were found to increase the precision of prediction, such influence of 2-octyne, 1,4-dioxane and *cis*-hidrindane could be negligible. McReynolds' relative polarity scale was characterized for more than 200 liquid phases.

Although the polarity is often used for predicting retention data, several other factors may influence absorption [17]. A number of quantitative structure-retention relationship (QSRR) studies were performed on different series of compounds and good correlations were found between I_R (Kovats retention index) and the theoretically calculated data for molecules with different functional groups (azo compounds [18], alkenes and azo compounds [19], dialkyl hydrazones [20], alkenes [21], alkylbenzenes [22], phenol derivatives [23], primary, secondary and tertiary amines [24], etc.). Generally, the elution data related to one or only few columns were used. In the QSRR studies the correlation between the Kovats retention indices and molecular descriptors obtained by various methods (experimental, empirical results or theoretical methods) were studied in order to obtain linear multivariate functions for the prediction of the retention properties of the compounds (see e.g. [26]). There can be found some criticism on using quantum chemical descriptors [27], but their application is supported by their success [19–21, 24,25].

In this study, we investigate the correlation between the McReynolds' polarity scale [3] and the structural/physical properties of McReynolds' test compounds used for characterizing the columns. We analyze, what structural descriptor(s) (HOMO: energy of the highest occupied molecular orbital) $\{1\}$, LUMO: energy of the lowest unoccupied molecular orbital $\{2\}$, dipole moment (μ) $\{3\}$, isotropic average polarizability at 0 eV electric field (α) $\{4\}$, volume of the molecule (V) $\{5\}$, logarithm of the octanol–water partition coefficient ($\log P$) $\{6\}$ and total, polar and apolar solvent accessible surface area (SASA, pSASA and apSASA, respectively)) $\{7,8,9\}$ of McReynolds' test molecules ([1] benzene, [2] 1-butanol, [3] 2-pentanone, [4] 1-nitropropane, [5] pyridine, [6] 2-methyl-2-pentanol, [7] 1-iodobutane, [8] 2-octyne, [9] 1,4-dioxane, [10] *cis*-hidrindane) have the greatest influence on the McReynolds' numbers. The calculations were performed by the PM3 semiempirical quantum chemical and chemometric methods (cluster analysis (CA), principal component analysis (PCA), multiple linear regression (MLR), principal component regression (PCR) and partial least-square regression (PLSR)). A recently developed, novel chemometric method: case/variable selection by principal component and partial least-square regression (CVS–PCR and CVS–PLSR) — for building descriptive models was also applied.

2. Calculations

The structural descriptors, HOMO, LUMO, μ and α were calculated for the 10 McReynolds' test molecules with full geometry optimization by the PM3 semiempirical quantum chemical method implemented in MOPAC93 [28]. The gradient norms were always less then 0.01 kcal/mol/Å. The force matrix was positive definite for the small molecules supported that we found conformational minima. At some simple molecules 2–5 conformers were calculated and the thermodynamically most stable structure was always accepted. The SASA, pSASA, apSASA (radius of probe solvent molecule was set to 0.14 nm), V and $\log P$ were calculated by VEGA [29].