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Role of the Na^+ ion on phenol derivatives/hydroxypropyl-β-cyclodextrin complex formation on porous graphitic carbon phase

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Abstract

The reversed-phase liquid chromatography retention of phenol derivatives was investigated over a concentration range of sodium chloride ($0–10^{-2}$ *M*) and hydroxypropyl-β-cyclodextrin (HP-β-CD) ($0–35\times10^{-3}$ *M*) using a porous graphitic carbon (PGC) stationary phase and a methanol/water mixture (50:50 (v/v)) as the mobile phase. A theoretical treatment was developed to investigate the effect of the sodium chloride and hydroxypropyl-β-cyclodextrin on the equilibrium between the solutes with the PGC surface and the aqueous medium, respectively. The thermodynamic parameter variations were calculated using van't Hoff plots. It was expected that the sodium ion acted on the solute–PGC association process by modifying the surface tension of both the bulk solvent and the PGC surface. The phenol derivative/HP-β-cyclodextrin complexation was shown to be entropically controlled for all the solutes except for the one which contained the $-NO_2$ group in its structure, i.e. the nitro phenol derivative. A comparison of the compensation temperature of the solute–PGC association process when sodium chloride and HP-β-CD concentration changed in the mobile phase led to the conclusion that these two modifiers acted via a variation in the hydrophobic effect.

Keywords: Porous graphitic carbon; Sodium ion

1. Introduction

Cyclodextrins (CDs) are a series of torus-shaped oligosaccharides composed of 6 to 12 α-1,4 linked D-glucopyranose units per molecule. The most widely used CDs are α-, β-, γ-, and δ-cyclodextrin containing six, seven, eight and nine glucose monomers, respectively [1]. The rigidity of the CD structure and its relatively non-polar central cavity [2] are characteristics that enable the formation of inclusion complexes with various solutes. These reversible ''host–guest'' inclusion complexes, can change the physico-chemical properties of the guest molecule. Therefore, cyclodextrins are used in many application fields to take full advantage of the encapsulation of the solute: β-CD is used as a drug carrier to improve solubility [3], stability [4] and the

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dissolution rate of therapeutics [1]. CDs can protect [5] flavors against evaporation, atmospheric oxidation and light or heat-induced transformations. A major application of cyclodextrins is used in chromatography to obtain the separation of solutes having very close structures. They are chiral selectors when they are bonded to the stationary phase [6–8] or used as mobile phase additives in reversed-phase liquid chromatography [9–11].

The addition of cyclodextrins to the mobile phase modifies the solute retention according to its size, its functional group position or the strength and the stoichiometry of its complex with cyclodextrin. Mohseni et al. [11] reported retention data and apparent complex dissociation constants of several compound classes on a C_{18} column with methanol- or ethanol–water mobile phases containing various concentrations of β-cyclodextrin. They also measured changes in enthalpy and entropy with and without cyclodextrins in order to explore the thermodynamic aspects of the separation process. Nowakowski et al. [12] demonstrated, using thermodynamic data and molecular modeling, that the calculation of inclusion equilibrium constants was dependent on the stationary phase–mobile phase system.

More recently, Guillaume and coworkers [13] showed that the main parameter governing retention of imidazole derivatives on an RP-18 column with hydro-organic mobile phases containing β-cyclodextrins was the distribution of the solute in the mobile phase rather than the interactions with the stationary phase. Although many studies of β-CD inclusion complexes have been carried out in RP-HPLC with hydrocarbonaceous stationary phases, only a few publications have reported the separation of solutes with cyclodextrins in the mobile phase using a porous graphitic carbon (PGC) column [14]. This type of column packing has shown the remarkable ability to separate isomers or closely related compounds [15,16]. Furthermore, PGC has a high chemical and physical stability, allowing repeated use without loss of performance and reproducibility [17,18]. It is an extremely strong adsorbent due to the existence of large dispersion forces between the solute and the rigid planar graphite surface. PGC exhibits high retention for polar solutes mainly caused by specific interactions with the π electronic structure of the graphite, the retention mechanism is still under discussion [15,19,20]. A study of the temperature effects on the retention of natural cyclodextrins on PGC with methanol–water mobile phases has been reported [20], demonstrating the existence of a double-retention mechanism for solutes on a PGC stationary phase. However, earlier studies have not specifically modeled the influence of the sodium chloride as a mobile phase modifier on both the solute retention and its complexation with a cyclodextrin molecule in the reversed-phase mode with a PGC stationary phase. In order to explore the mechanistic aspect on both the solute retention and its complexation with a cyclodextrin molecule on a PGC surface, the elution mechanism of five phenol derivatives on PGC, with methanol–water mobile phases containing various concentrations of hydroxypropyl-β-cyclodextrin (HP-β-CD) and sodium chloride was studied. The thermodynamic parameters of: (i) the transfer of the solute from the mobile to the PGC surface and (ii) the complexation reaction of the solute with HP-β-CD were determined. Enthalpy–entropy compensation was investigated in order to determine the main parameter controlling retention.

2. Material and methods

2.1. Apparatus

HPLC was carried out with an Hitachi L7100 pump (Merck, Nogent sur Marne, France), a Rheodyne (Interchim, Montluçon, France) 7125 injection valve fitted with a 20-μl sample loop, and a Hitachi L4500 diode-array detector. The porous graphitic column used was a Shandon (100 mm×4.6 mm I.D., 5.7 μm particle size) model Hypercarb S column (Shandon, Eragny/Oise, France). The column temperature was controlled by means of an Interchim TM 701 oven. The mobile phase flow-rate was 1 ml/min and the detection wavelength 254 nm.

2.2. Solvents and samples

Methanol was used without further purification (Merck, Nogent sur Marne, France). Sodium chloride was supplied by Prolabo (Paris, France). Water was

obtained from an Elgastat water purification system (Odil, Talant, France) fitted with a reverse-osmosis cartridge. All the phenol derivatives were obtained from Sigma–Aldrich (Saint Quentin, France). The chemical structures of these compounds are given in Figure 1. Fresh samples were prepared daily at a concentration of 20 mg/l. The column void volume was determined by injecting pure bidistilled water with a methanol mobile phase. The mobile phase was 50:50 (v/v) water–methanol; the sodium chloride and HP-β-CD concentrations were varied from 0 to 10^{-2} *M* and 0 to 35×10^{-3} *M*, respectively; 20 μl of each solute was chromatographed and its retention time was measured.

2.3. Temperature studies

Compound retention factors were determined over the temperature range 20–55 °C. The chromatographic system was left to equilibrate at each temperature for at least 1 h before each experiment. To study this equilibration the retention time of 4-ethoxyphenol was measured after 22, 23 24 h. The maximum relative difference between retention times of this compound was never more than 0.7%, meaning that after 1 h the chromatographic system was sufficiently equilibrated for use. All the solutes were injected three times at each temperature and for each salt and HP-β-CD concentration.

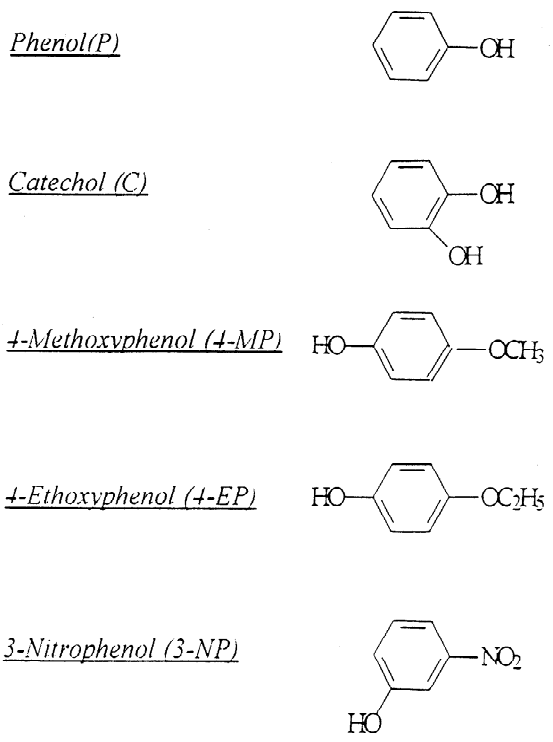

Fig. 1. Phenol derivative structures.

2.4. Theory

Much information on the retention mechanism, in a HPLC system, may be gained by examining the temperature dependence of analyte elution. The Gibbs free energy of the solute molecule transfer ΔG° from the mobile to the PGC surface could be linked to its equilibrium constant *K* with the following equation [21]:

$$\ln K = \frac{-\Delta G^{\circ}}{RT} \quad (1)$$

where *R* is the gas constant and *T* is the absolute temperature. Since $k' = \varphi K$, where k' is the solute retention factor and φ the phase ratio of the column (volume of the stationary phase divided by the volume of the mobile phase). In any case, the choice of φ must be in agreement with the definition of *K*. For reversed-phase chromatography, Melander and Horvath [22] suggested the expression of φ per surface area of the adsorbent (m^2). Davydov et al. [23] divided the mass of material (g) in the column by the column dead volume (cm^3), as is usual in adsorption chromatography. The volume of the mobile phase was determined from the weight differences of the column when filled with solvents of different densities (methanol and chloroform) [24]. Since the technical data on the hypercarb column were available, φ could be calculated. When the dead volume of the column and the technical data were taken into account φ was calculated as 0.51. Eq. (1) can be rewritten as:

$$\ln k' = \frac{-\Delta H^{\circ}}{RT} + \frac{\Delta S^{\circ}}{R} + \ln \varphi \quad (2)$$

where ΔH° and ΔS° are the enthalpy and entropy of transfer of the solute from the mobile to the PGC surface. With an invariant retention mechanism over the temperature range being studied, the enthalpy of transfer ΔH° remained constant and a plot of $\ln k'$ in

relation to $1/T$, which is commonly described as a van't Hoff plot [25], leads to a straight line with an enthalpic slope and an entropic origin. When HP-β-CD is added to the mobile phase, the solute retention factor k' is affected as described by Eq. (3) [11]:

$$\frac{1}{k'} = \frac{1}{k'_o} + \frac{K_f}{k'_o}[(CD)_m] \quad (3)$$

where k'_o is the retention factor without cyclodextrin, $[(CD)_m]$ is the equilibrium concentration of HP-β-CD in the mobile phase and K_f is the apparent formation constant of the inclusion complex. As previously demonstrated [20], free cyclodextrins are not retained in the solvent range with the PGC surface. As a consequence, interactions between complexed solutes and the stationary phase can be neglected in the theoretical treatment of the retention mechanism. Inclusion formation enthalpy and entropy (ΔH^o_f and ΔS^o_f) between the solute molecule and the cyclodextrin in the mobile phase are determined by plotting the logarithm of the apparent complex formation K_f versus the temperature reciprocal:

$$\ln K_f = \frac{-\Delta H^o_f}{RT} + \frac{\Delta S^o_f}{R} \quad (4)$$

A further thermodynamic approach to the analysis of physicochemical data is enthalpy–entropy compensation [21]. The enthalpy–entropy compensation method is an extra-thermodynamic approach to analyze physico-chemical data. This investigation tool has been previously used in chromatographic procedures to analyze and compare the retention mechanism for the group of compounds [26–29]. The enthalpy–entropy compensation can be described by the following equation:

$$\Delta H^o = \beta \Delta S^o + \Delta G^o_\beta \quad (5)$$

where ΔG^o_β is the free Gibbs energy of a physicochemical interaction at a compensation temperature β, ΔH^o and ΔS^o are the corresponding standard enthalpy and entropy, respectively. According to Eq. (5), when enthalpy–entropy compensation is observed for a group of compounds in a particular chemical transformation (or interaction in the case of chromatographic retention), all of the compounds have the same free energy change ΔG^o at temperature β. For example, if enthalpy–entropy compensation is observed in liquid chromatography for a group of compounds, all the compounds will have the same net retention at the compensation temperature β, although their temperature dependences may differ. Eq. (5) shows that if a plot of ΔH^o against ΔS^o is linear for a family of compounds then the solutes are retained by an essentially identical interaction mechanism.

In order to express the free energy change, ΔG^o_T at a given temperature, T, the Gibbs–Helmotz relationship:

$$\Delta G^o = \Delta H^o - T\Delta S^o \quad (6)$$

can be written with the use of Eq. (5) as:

$$\Delta G^o_T = \Delta H^o\left(1 - \frac{T}{\beta}\right) + \frac{T\Delta G^o_\beta}{\beta} \quad (7)$$

Eq. (7) shows that a plot ΔG^o_T for different compounds at a constant temperature T, is a linear function of the corresponding ΔH^o, and a compensation temperature β can be evaluated from the slope. Similarity of the values for the compensation temperature suggests that the solutes are retained by essentially identical interaction mechanisms, and the compensation study is therefore a useful tool for comparing the retention mechanism for different compounds. However, the results obtained with this method can be misleading, due to the cumulative errors associated with the determination of enthalpy [30,31]. According to Krug et al. analysis [32], similar mechanisms could be mapped through thermodynamic studies if the correlation between ΔG^o and ΔH^o was used at the harmonic temperature T_{hm} (the arithmetic mean of the independent variable, $1/T$, the inverse experimental temperature, $\langle 1/T \rangle$).

3. Results and discussion

3.1. Solute transfer from the mobile phase to the PGC surface

The asymmetry factor of all peaks calculated from measurements made at 50% of the total peak height

was in the range $1.00 < A_s < 1 \times 10$. From the solute retention times determined at the maxima of the chromatographic peaks, the retention factor k' of the five solute molecules under study was determined with the PGC surface in the entire range of temperature i.e. from 20 to 55 °C. A first series of experiments was carried out for which the hydroxypropyl-β-cyclodextrin (HP-β-CD) concentration in the mobile phase was nil and the NaCl concentration varied from 0 to 10^{-2} *M* and a second series for which the HP-β-CD concentration in the mobile phase varied from 0 to 35×10^{-3} *M* and the NaCl concentration was nil (Table 1). For all solutes, when the temperature increased there was a decrease in the retention factor whatever the mobile phase used, as expected for a reversed-phase system [33]. Linear van't Hoff plots were obtained with correlation coefficients *r* higher than 0.998 for all fits. This behavior demonstrated that the invariant retention mechanism in the full range of temperatures was observed. The thermodynamic data of the solute transfer from the mobile to the PGC surface were determined according to Eq. (2). All the phenol derivatives exhibited a similar variation for the thermodynamic data with NaCl or HP-β-CD concentration. For example, Figs. 2A,B and 3A,B show the variation in ΔH^o and ΔS^o in relation to the NaCl and HP-β-CD concentration, respectively for 4-ethoxyphenol. Negative enthalpies indicated that it was energetically more favorable for the solute to be in the PGC surface. Negative entropies showed an increase in the order of the chromatographic system when the solutes were transferred from the mobile to the PGC surface. This transfer was enthalpically driven (magnitude of ΔH^o was always greater than that of $T\Delta S^o$) and can be described by the replacement of weak solute/solvent interactions by strong solute PGC/surface Van der

Table 1
Values of ln k' of the five solutes at 50 °C for A (NaCl) and B (CD)

Solute denomination	A	B
P	−0.03	−1.03
C	0.11	−0.89
4-MP	1.16	−0.13
4-EP	2.08	0.41
3-NP	2.67	1.17

Concentration = 5×10^{-3} *M* (standard deviations < 0.004).

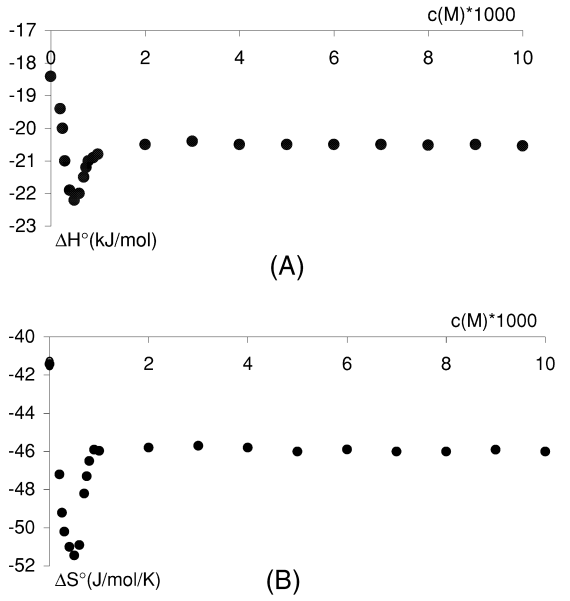

Fig. 2. Influence of NaCl concentration on (A) ΔH^o (kJ/mol) and (B) ΔS^o (J/mol per K) for 4-ethoxyphenol.

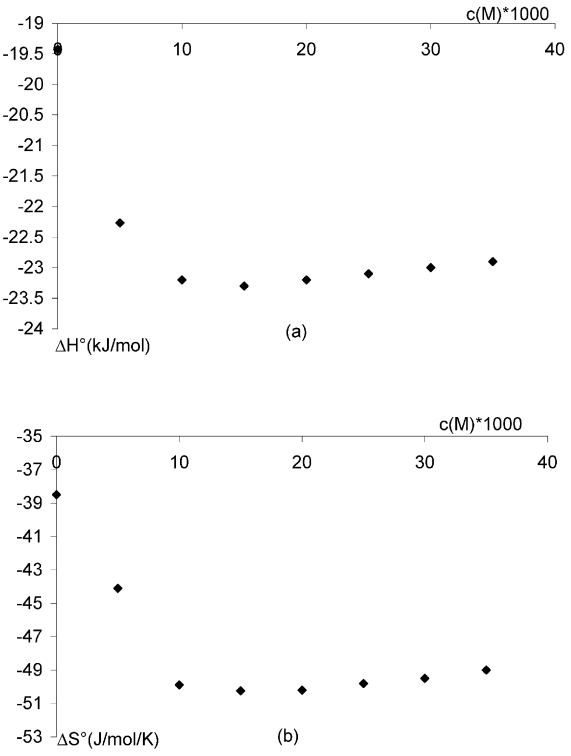

Fig. 3. Influence of HP-β-CD concentration on (A) ΔH^o (kJ/mol) and (B) ΔS^o (J/mol per K) for 4-ethoxyphenol.

Waals interactions. This is consistent with results reported in the literature from various chromatographic separations [34–36]. On PGC, the elution order of the five phenol derivatives with all mobile phases used was constant:

Phenol (P) < catechol (C)
< 4-methoxyphenol (4-MP)
< 4-ethoxyphenol (4-EP)
< 3-nitrophenol (3-NP)

On PGC, retention of family of compounds was related to size, polarity, and deformability of the molecules. Phenol was eluted first, followed by catechol which contained a second –OH group in its ring. This specific effect called ''polar retention effect on graphite'' [18] appeared to be additive to the normal hydrophobic and dispersive effects found with conventional reversed-phase materials. These results were corroborated by the fact that the highest values of ΔH^{o} and ΔS^{o} were observed for phenol. Indeed, phenol had the lowest interactions with the graphite surface. Among the phenol derivatives, 3-NP exhibited the lowest thermodynamic data. Indeed, the substitution of the –OH group for catechol with a $-NO_2$ substituent had the strongest Van der Waals and polar interactions with the PGC surface. This was associated with the decrease in the entropy state classically attributed in RP-HPLC to the release of the water molecules surrounding the solute when it is transferred towards the PGC surface [37–39].

3.2. Role of the Na^+ ion on the solute–PGC surface association/the HP-β-CD concentration in the mobile phase was nil

In order to gain further insight into the interaction model on PGC, the enthalpy–entropy compensation described in Eq. (7) was applied. A $\Delta G^{o}_{Thm} - \Delta H^{o}$ plot determined at T_{hm} and at different NaCl concentration was made for the five phenol derivatives. The correlation coefficient for the linear fit was equal to 0.989. This degree of correlation can be considered adequate to verify enthalpy–entropy compensation, indicating that the interaction mechanism was independent of the NaCl concentration and the phenol derivative structures.

The solute transfer thermodynamic data can be expressed by:

$$\Delta H^{o} = H^{o}_{PGC} - H^{o}_{m} \quad (8)$$

$$\Delta S^{o} = S^{o}_{PGC} - S^{o}_{m} \quad (9)$$

where H^{o}_{PGC}, H^{o}_{m}, S^{o}_{PGC}, S^{o}_{m}, are, respectively enthalpy and entropy of transfer of the solute associated with the PGC surface and the bulk solvent (m). It has been known for several years that increasing the ionic strength of a bulk solvent increases its surface tension [40]. Therefore, if the salt concentration increased, the surface tension of: (i) the bulk solvent and (ii) the PGC surface increased. When the NaCl concentration in the mobile phase increased to 5×10^{-4} *M*, the effect (ii) was dominant and the solute molar enthalpy and entropy associated with the PGC surface i.e. H^{o}_{PGC} and S^{o}_{PGC} decreased strongly leading to a decrease in the solute transfer thermodynamic data ΔH^{o}, ΔS^{o} (Eqs. (8) and (9)) (Fig. 2A,B). Over 5×10^{-4} *M*, the effect (i) was dominant H^{o}_{m}, S^{o}_{m} decreased and thus ΔH^{o}, ΔS^{o} values increased (Eqs. (8) and (9)) (Fig. 2A,B). If an RP18 stationary phase was used instead of a PGC, the effect (ii) would always be hidden. The PGC enables the differentiation of these two effects and gives a more realistic visualization of the retention process of the phenol derivatives with the PGC stationary phase. Over 10^{-3} *M*, the solute retention was constant due to its maximum association with the PGC surface and, thus, no or weak changes in the thermodynamic parameters were observed (Fig. 2A,B).

3.3. HP-β-CD-phenol derivatives complexation process/the NaCl concentration in the mobile phase was nil

The apparent formation constant K_f of phenol derivatives/HP-β-CD inclusion complexes was calculated according to Eq. (3). The correlation coefficients obtained were over 0.997. These complex formation constants were calculated for different temperatures. Table 2 presents K_f values at five temperatures. For phenol, catechol, and 4-methoxyphenol, the K_f values remained relatively constant when the temperature increased demonstrating an unusual behavior when compared with the literature

Table 2
Values of the complexation constants K_f of the five solutes at four different temperatures (20, 30, 40, 50, 55 °C)

Solute denomination	20 °C	30 °C	40 °C	50 °C	55 °C
P	3.8	3.7	3.7	3.7	3.7
C	3.6	3.5	3.6	3.5	3.5
4-MP	8.5	8.5	8.5	8.5	8.4
4-EP	14.0	13.1	12.4	11.7	11.3
3-NP	7.7	7.1	6.5	6.1	5.8

Standard deviations <0.1.

[11]. The van't Hoff plots ($\ln K_f$ vs. $1/T$) were assessed for 4-ethoxyphenol and 4-nitrophenol. Linear graphs were observed (r^2 over 0.989) and the resulting thermodynamic parameters are given in Table 3. The water molecules surrounding the phenol derivatives were more constrained than those in the bulk solvent (hydration shell of high energy water). When the complex formation occurred the phenol derivatives were transferred from this well structured water environment to the less ordered HP-β-CD cavity. Consequently, for phenol, catechol and 4MP the solute complexation process was accompanied by a large positive entropy and a strong decrease in the Van der Waals interactions and hydrogen bonding (Table 3). The minimum value obtained for the positive entropy was for 4-EP ($\cong 5.3$ J/mol per K). The corresponding enthalpy value was -4.8 kJ/mol. This negative value was due to the favorable Van der Waals interactions that 4-EP, the highest hydrophobic compound in the phenol derivatives, could established with the hydrophobic HP-β-CD cavity. For phenol, catechol, and 4MP, the solute complexation mechanism with HP-β-CD was entropically driven as opposed to the classical results generally observed in the literature with an RP18 stationary phase. The inclusion process can be compared to a classical transfer of a hydrocarbonaceous molecule from water to an apolar liquid phase. For 4-EP, the complexation process was also entropically governed (i.e. both enthalpically and entropically controlled) and thus the most favorable, which was in good agreement with the highest K_f value determined for this compound (at $T=20$ °C, $K_f=14$, Table 2). For 3-NP, the $-NO_2$ group greatly increased the dipolar–dipolar interactions between the solute and the HP-β-CD cavity and thus decreased its degree of freedom in this cavity leading to the lowest value of $\Delta H_f^o = -6.3$ kJ/mol and $\Delta S_f^o = -4.4$ J/mol per K values. For 3-NP, the solute complexation process was enthalpically controlled. The previous experiments were carried out at $T=20$ °C with a mobile phase containing, respectively 2.0×10^{-4} *M*, 2.5×10^{-4} *M*, 3.0×10^{-4} *M*, 4.0×10^{-4} *M*, 5.0×10^{-4} *M*, and, 7.0×10^{-4} *M*, 8.0×10^{-4} *M*, 9.0×10^{-4} *M*, and 10^{-3} *M* of sodium chloride. The HP-β-CD concentration range dissolved in the mobile phase was always $0–35\times10^{-3}$ *M*. The apparent formation constants K_f of the phenol derivatives/HP-β-CD inclusion complexes were determined for these conditions. The correlation coefficients obtained were over 0.996. All the phenol derivatives exhibited a similar variation for the K_f with the NaCl concentration in the mobile phase. For example, Figure 4 represents the variation of the K_f values with the NaCl concentration in the mobile phase for 4-ethoxyphenol. From 0 to 5×10^{-4} *M*, the K_f values varied slightly and over 5×10^{-4} *M* increased more strongly. This variation confirmed the previous results presented above, i.e. the ion Na^+ increased the hydrophobic effect in the mobile phase and thus the complex formation (Fig. 2A,B) especially when NaCl was over 5.00×10^{-4} *M*. These results showed the positive role of the salting out agent Na^+ as a co-promoter of complexation.

Table 3
Values of formation enthalpy ΔH^o (kJ/mol) and entropy ΔS^o (J/mol per K) of the five complexes between the phenol derivatives with HP-β-CD

Solute denomination	ΔH_f^o (kJ/mol)	ΔS_f^o (J/mol per K)
P	–	+37.6
C	–	+38.3
4-MP	–	+17.4
4-EP	−4.8	+5.3
3-NP	−6.3	−4.4

Standard deviations <0.2; –, ΔH^o values were not defined.

3.4. Role of HP-β-CD on the solute–PGC surface association/the NaCl concentration in the mobile phase was nil

An enthalpy–entropy compensation study, determined always at T_{hm} (Eq. (7)) was performed to investigate the solute–PGC surface association process. The linear variation ($r^2=0.989$) verified the enthalpy–entropy compensation indicating that the

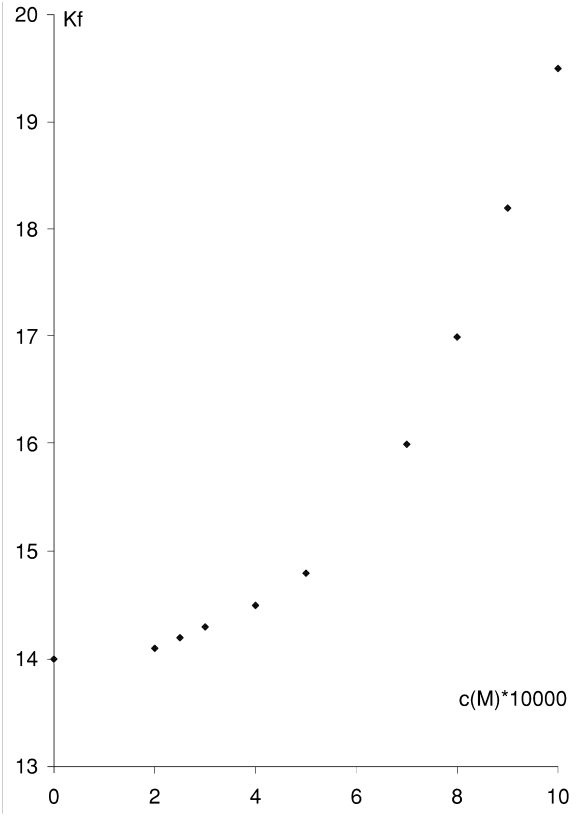

Fig. 4. Influence of NaCl concentration on the complexation constant K_f (at $T=20\,^{\circ}C$) of 4-ethoxyphenol.

interaction mechanism was independent of the HP-β-CD concentration in the mobile phase and the phenol derivative structures. Consequently, the interaction mechanism with the PGC surface appeared to be identical for both the free and complexed solute. This revealed that the complex was principally formed in the mobile phase and then transferred from the eluent to the PGC surface. Thus, the eventual adsorption of the HP-β-CD on the PGC and the possible complexation of phenol derivatives with the HP-β-CD seemed to be negligible as expected in the model. Moreover, the HP-β-CD was eluted in the void volume when it was injected into the chromatographic system using the same mobile phase without the modifier. The variations of the solute thermodynamic data (i.e. solute transfer from the mobile to the PGC surface) with HP-β-CD were similar for all the phenol derivatives. Compensation temperatures determined for NaCl and HP-β-CD were different, but very close ($\cong 440\,^{\circ}C$ and $\cong 320\,^{\circ}C$). This observation indicated that these two modifiers played an equivalent role in the global retention process and, thus could act on the retention mechanism via an identical physico-chemical process, i.e. the hydrophobic effect which is greatly improved on a PGC surface. When the HP-β-CD concentration increased in the mobile phase to 10^{-2} *M*, ΔH^{o} and the ΔS^{o} values decreased (Fig. 3A,B). This decrease in the thermodynamic data could, thus, be interpreted as a decrease in the hydrophobic effect as the enthalpy of the free phenol derivative inside the mobile phase increased: the solute hydration shell was destructured due to the solute inclusion in the HP-β-CD and the hydrogen bonds between the water molecules were broken. As the HP-β-CD concentration was $\geq 10^{-2}$ *M*, the retention was constant or presented a weak variation due to the full complexation of the solute and therefore there were no or only weak changes in the thermodynamic parameters (Fig. 3A,B). In summary, retention of phenol derivatives was investigated on a porous graphite carbon surface with various NaCl salt and HP-β-CD concentrations in the mobile phase in relation to column temperature. Results of the thermodynamic study showed that the sodium ion acted on the solute–PGC association process by modifying the surface tension of both the bulk solvent and the PGC surface. The phenol derivative/HP-β-CD complexation was shown to be entropically controlled for all the solutes except the one which contained the group $-NO_2$ in its structure. Enthalpy–entropy compensation revealed that NaCl and HP-β-CD governed the solute–PGC surface association with an equivalent influence. Compared with C_{18}, the PGC surface appears to be a best visualization tool for the inclusion complex formation and solute retention and could lead to new applications in supra molecular chemistry.

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