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POSSIBILITIES OF CYCLIZATION OF SIDE ALKYL CHAINS OF N-ALKYLPHENOLS AND N-ALKYLBENZENES IN THE ENVIRONMENT OF A STATIONARY PHASE

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ABSTRACT

During separations in both polar and nonpolar stationary phases of gas chromatographic columns, side alkyl chains of n-alkylphenols and n-alkylbenzenes become cyclized. In the aromatic–quasi-alicyclic molecules that are thereby formed, the effect of van der Waals forces is thus increased. The increase involves not only intramolecularly but also intermolecularly acting effects and becomes significantly evident when propyl and higher substituents as butyl, pentyl and hexyl constitute the side alkyl chains. As a result, boiling points considerably increase (non-linearly) in the case of n-alkylphenols and n-alkylbenzenes with total number of carbons in the molecule higher than 9. This leads to divergence in the retention characteristics of the above-mentioned compounds, which can be observed in the dependence of relative retention times on the number of carbons. Cyclization of side alkyl chains in a stationary phase is a quite new phenomenon.

KEYWORDS: alkylphenols, alkylbenzenes, non-covalent interactions, van der Waals forces, retention times

1. INTRODUCTION

Gas chromatographic measurements of relative retention times ($R_{t,rel}$) of n-alkylphenols and n-alkylbenzenes C_7–C_{12} on capillary columns with both polar and nonpolar stationary phases at temperatures of 125–140 °C showed that these retention times increase non-linearly with the number of carbon atoms in a molecule (z) (Fig. 1) (Buryan and Macák, 1982). Two linear areas in the consecutive intervals C_7–C_9 and C_9–C_{12}, with the slopes of each line being different, were proved in the relation $\log R_{t,rel} = az + b$ (where a and b are constants), although only one line was expected to be found. The complete dependence was thus of a divergent character with break (Fig. 1). This dependence was under the mentioned conditions also found in the case of n-alkylphenol methylethers (Buryan and Macák, 1982).

In classic considerations on the dependence of retention times on the number of carbons in different homologous series of gas chromatographically separated substances, purely linear dependence without any divergence is always considered, be it for isotherm or non-isotherm separations (Purnell, 1962; Leibnitz and Struppe, 1966; Hartus and Habgood, 1966).

However, the divergence detected in the dependence $\log R_{t,rel} = az + b$ suggests, that the behavior of molecules of the compounds in question during separations in stationary phases is more

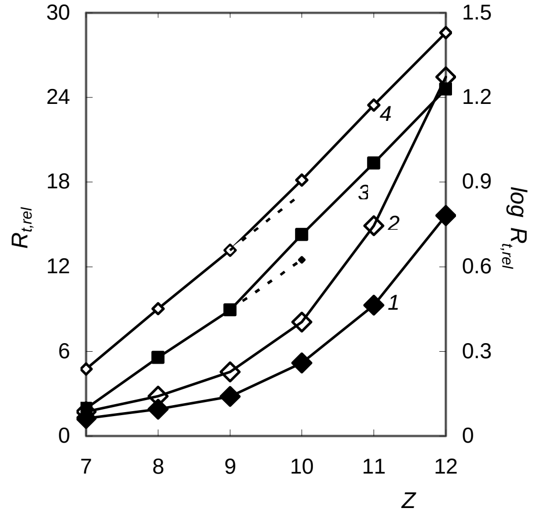

Fig. 1 Non-linear dependence of the relative retention time ($R_{t,rel}$) (lines *1* and *2*) and divergence dependence of $\log R_{t,rel}$ (lines *3* and *4*) on the number of carbons in the molecule (z) for the stationary phase of Apiezon K at a temperature of 130 °C in the case of n-alkylphenols. Full points – ortho n-alkylphenols, empty points – para n-alkylphenols. Similar dependences were found also in the case of n-alkylbenzenes. Based on Buryan and Macák, 1982, adjusted.

complicated than has been assumed by the classic considerations. The relation $log\ R_{t,rel} = a + bz$ should be expected to be purely linear as a result of the growing number of carbon atoms in the molecule (Simpson, 1970) and the corresponding increase of $R_{t,rel}$ or more precisely $log\ R_{t,rel}$ with boiling points (T_b) of the given homologs ($log\ R_{t,rel} = a + bT_b$). The mentioned purely linear relation was frequently applied when identifying unknown substances using data acquired through gas chromatographic separations, but the validity of this usage is questionable.

In the study (Buryan and Macák, 1982), the relative retention times were expressed as a logarithm of the ratio of the retention time of the given n-alkylphenol substituted in the positions ortho, meta and para and phenol, and in the case of n-alkylbenzenes as a logarithm of the ratio of the retention time of n-alkylbenzene and benzene. The mentioned divergence (break) in the increase of retention characteristics was always observed at C_9.

In our work, the following possibilities were considered as an explanation of this phenomenon.

- *Cyclization.* In a high density stationary phase, the longer alkyl side chains of n-alkylphenols and n-alkylbenzenes are subject to cyclization as a result of the resistance force of this phase affecting molecules of the compounds during their thermal and diffusion motion. Consequently, common conventional aromatic-aliphatic molecules become new molecules with quasi-alicyclic parts. It is likely that in comparison with the conventionally conceived molecules, the resulting aromatic–quasi-alicyclic molecules are characterized by rather different, possibly even completely different non-covalent interactions between the molecules (chiefly van der Waals interactions), which then affect the retention characteristics.
- *Association.* The molecules of the compounds in question are of an aromatic-aliphatic character. Such molecules tend, in a dense environment (e.g. in organic gels), to form molecular aggregates, as was discovered during the research on the formation of coal structures (Straka et al., 2002; Straka, 2003). A similar phenomenon may occur in the environment of a dense stationary phase. The molecules in question may associate, which would lead to a change in retention characteristics. The association could also increase with the growing length of the side alkyl chain and might strongly manifest itself in the case of molecules containing more than 9 carbons.
- *Non-covalent interactions with a stationary phase.* With the increasing number of carbons in the molecule of n-alkylphenols and n-alkylbenzenes, intermolecular interactions between compounds in question and the stationary phase might change non-linearly with the growing number of carbons in the molecule. These interactions may manifest themselves differently in polar and nonpolar phases.

The mentioned phenomena can be evaluated and compared using methods of computational chemistry. In order to assess cyclization, association and different interactions, energies of covalent bonds and non-covalent interactions (mainly van der Waals) can be computed. For the purpose of this assessment, molecular conformations which are realistic and energetically advantageous or possible and are in correlation with the ascertained chromatographic data can also be estimated.

On the basis of experience with the evaluation of aromatic, aromatic-aliphatic, aromatic-alicyclic and phenolic structures in terms of energy using the methods of molecular and quantum mechanics (Carlson, 1991), two methods of molecular mechanics were selected for the calculations (see below).

The aim of the presented work is to explain the divergence (break) in the logarithmic dependence of relative retention time on the number of carbons in the molecule in the case of n-alkylphenols and n-alkylbenzenes by utilisation of computational methods of molecular mechanics and to clarify the behavior of these compounds in the environment of a stationary phase of a capillary column. Further, to describe a cyclization of side alkyl chains in a stationary phase as a new phenomenon.

2. CALCULATIONS

For considerations the retention data obtained on a nonpolar stationary phase of Apiezion K and a polar stationary phase of trixylenylphosphate-phosphoric acid (95:5) at temperature of 130°C (Buryan and Macák, 1982) were taken into account.

For calculations the molecular mechanics methods were chosen and two force fields, MM+ and AMBER (Becker and Allinger, 1982; Allinger and Yuh, 1982; Howard et al., 1994), were used. The reason is that these methods use an analytical and relatively simple potential energy functions for describing the interactions between a set of atoms, further, they are empirical and accurate and very suitable for small organic molecules. Important is that atom types, not atoms, are the fundamental basis for calculating interactions. In these methods the interaction potential describes both bonding and non-bonding interactions. In the potentials the following energetic terms were calculated:

- bond stretching (E_{bond}), which is associated with deformation of a bond from its standard equilibrium length,
- bond angle bending (E_{angle}), which is associated with the deformation of an angle from its normal value,
- stretch-bend ($E_{stretch\text{-}bend}$); bond stretch and angle bending cross term, which includes coupling between bond stretching and angle bending,

- dihedrals ($E_{dihedral}$); torsional energy, which is associated with the tendency of dihedral angles to have a certain *n*-fold symmetry and to have minimum energy,
- van der Waals ($E_{vdWaals}$), which describes the repulsive forces keeping two non-bonded atoms apart at close range and attractive forces drawing them together at long range,
- electrostatic (E_{elst}), which describes the classical non-bonded electrostatic interactions, particularly dipole-dipole interactions.

These energetic terms were calculated both by MM+ and AMBER methods, except $E_{stretch\text{-}bend}$, which was calculated only by means of the MM+.

The mentioned potential energies of covalent bonds and non-covalent interactions were calculated for common (conventional) n-alkylphenols and n-alkylbenzenes and also for models of cyclized forms of these compounds. The conceptions of the cyclized forms were formulated on the basis of the study of distribution of electron densities (atomic charges in a molecule) in common and cyclized molecules. As expected, in n-alkylphenol molecules, a high electron density was detected on the oxygen of the hydroxyl group and a very low electron density on the hydrogens of the terminal methyl group. The closing of the cyclanic ring was thus easily implemented by a hydrogen bridge as shown in Fig. 2 *a*. The conception of the cyclized form of alkylbenzenes was more complicated. The electron density on the alkyl carbon in the α position with respect to the benzene ring was discovered to be considerably higher in the case of the cyclized form than on the other carbons and, especially, on hydrogen atoms of the methyl group in an alkyl chain. The closing of the cyclanic ring was thus implemented by an interaction of methyl hydrogen with the ascribed charge +δ and the benzene ring with the ascribed charge -δ (Fig. 2 *b*). The basic conceptions of cyclized forms and models of these forms, for the sake of calculations demonstrated on n-propylphenol and n-propylbenzene, are also shown in Figs. 2 *c, d*, namely for the case of ortho n-propylphenol and alicyclic n-propylbenzene. In the latter case, the cyclization occurs until it reaches the position neighboring the position of a propyl substituent (i.e. n-propylbenzene is cyclized to the position ortho with respect to the propyl). The cyclization here is realized on the terminal methyl group (-CH_3 cyclization).

Besides the -CH_3 case, cyclization was also considered and calculated for the group -CH_2- neighboring CH_3- (i.e. in the position α with respect to CH_3-, Fig. 3, -CH_2-α cyclization) and for the group -CH_2- in the position β with respect to the group CH_3- (Fig. 4, -CH_2-β cyclization). These cyclizations were considered for molecules from methyl- up to

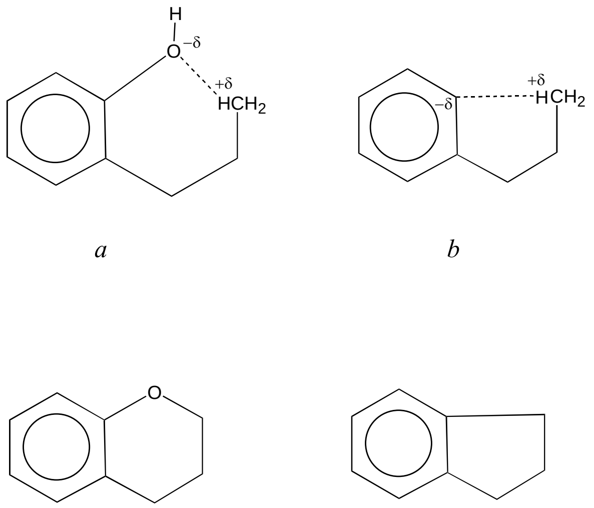

Fig. 2 Conceptions of cyclized forms in the case of ortho n-propylphenol (*a*) and alicyclic propylbenzene (*b*), in the latter of which the cyclization takes place until the position is reached neighboring the position of the propyl substituent. The cyclization is realized on the terminal methyl group (-CH_3 cyclization). These conceptions are depicted by the models for energy calculations (*c*) and (*d*).

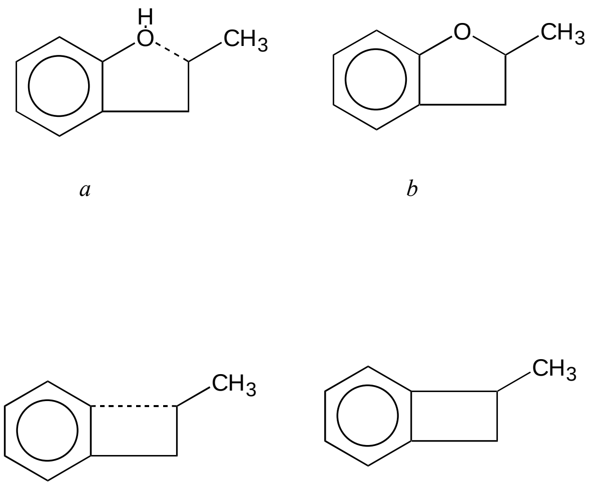

Fig. 3 The cyclization of -CH_2-α. Conceptions and models of cyclized forms for energy calculations in the case of ortho n-propylphenol (*a, b*) and alicyclic propylbenzene (*c, d*), in the latter of which the cyclization occurs until the position is reached neighboring the position of the propyl substituent. The cyclization is realized on the group -CH_2- neighboring with CH_3- (i.e. in the positron α with respect to -CH_3, -CH_2-α cyclization).

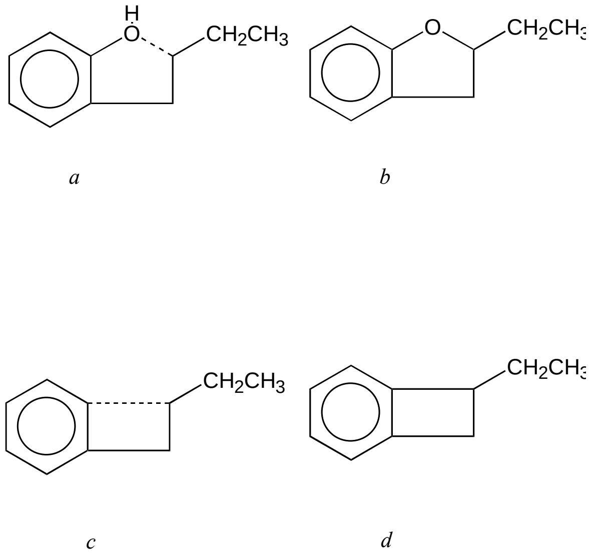

Fig. 4 The cyclization of -CH_2-β. Conceptions and models of cyclized forms for energy calculations in the case of ortho n-propylphenol (*a, b*) and alicyclic propylbenzene (*c, d*), in the latter of which the cyclization occurs until the position is reached neighboring the position of the propyl substituent. The cyclization is realized on the group -CH_2- vicinal to CH_3- (i.e. in the position β with respect to -CH_3, -CH_2-β cyclization).

hexylphenol and from methyl- up to hexylbenzene. With n-alkylphenols and n-alkylbenzenes the cyclization was considered and calculated for the positions ortho, meta and para; the mentioned energy terms were calculated for 252 cases altogether. The calculated energies of covalent bonds and non-covalent interactions for common and model cyclic forms were compared, and it was ascertained that energy changes are related to the determined retention times.

The program HyperChem also enables to perform measurements of the distances between atoms of defined molecules. This possibility was utilized for the measurement and comparison of the maximum sizes of common and cyclized molecules of the examined compounds. The part of the program, Atomic Charges, was also used for the study of distribution of electron densities in the molecules of the observed compounds.

3. RESULTS AND DISCUSSION

With regard to the temperature of the chromatographic column (125–140 °C), a possibility of side-chain cyclization was considered first. This possibility was based on the conception that in high-density stationary phase, the longer side alkyl chains of n-alkylphenols and n-alkylbenzenes are subject to deformation as a result of resistance of this phase affecting molecules of these compounds in motion. Conventional aromatic-aliphatic molecules are thus transformed into aromatic–quasi-alicyclic molecules. Cyclization is then accompanied by decrease in the effective size of molecules, which is significant for C_9 and larger molecules. Aromatic–quasi-alicyclic molecules of a smaller size are more easily mixed with the dense stationary phase, and the formed system is, in comparison with a system with common aromatic-aliphatic molecules, more homogenous and thus thermodynamically more stable. The reduction of the maximum size (D_{max}) of molecules during the cyclization of the side chain is shown in Table 1. The change in size of molecules moving through a chromatographic column is then accompanied by changes in intermolecular interactions and subsequently in change in relative retention time.

Table 1 Reduction of the maximum molecular size (D_{max}) during the cyclization of the side chain (comparison of D_{max} values for common and cyclized forms of n-alkylphenols).

Molecule	D_{max} (nm) Position of substituent		
	ortho	meta	para
Common:			
Methylphenol	0.56	0.59	0.67
Ethylphenol	0.72	0.72	0.80
n-Propylphenol	0.82	0.83	0.91
n-Butylphenol	0.93	0.95	1.04
n-Pentylphenol	1.06	1.08	1.15
n-Hexylphenol	1.19	1.21	1.28
Cyclized on -CH_3:			
Methylphenol	0.58	0.49	0.47
Ethylphenol	0.65	0.55	0.48
Propylphenol	0.72	0.61	0.57
Butylphenol	0.72	0.66	0.54
Pentylphenol	0.80	0.70	0.61
Hexylphenol	0.78	0.71	0.73

Table 2 Potential energies of covalent bonds and non-covalent interactions in ortho n-alkylphenols (common, cyclized on CH_3-, cyclized as -CH_2-α and -CH_2-β). Calculated by the MM+ program. Energetic terms: E_{bond}–bond stretching, E_{angle}–bond angle bending, $E_{stretch\text{-}bend}$–stretch-bend (bond stretch and angle bending cross term), $E_{dihedral}$–torsional energy, $E_{vdWaals}$–van der Waals interactions, E_{elst}–the classical non-bonded electrostatic interactions (particularly dipole-dipole interactions). For D_{max} see Table 1.

n-Alkylphenols	E_{bond}	E_{angle}	$E_{stretch\text{-}bend}$ (kJ/mol)	$E_{dihedral}$	$E_{vdWaals}$	E_{elst}	D_{max} (nm)
Phenol	4.57	9.43	-0.443	-23.32	12.11	0	0.56
Common:							
Methylphenol	6.90	9.68	-0.589	-31.35	17.12	0.205	0.56
Ethylphenol	8.80	9.68	-0.577	-31.94	41.25	0.920	0.72
n-Propylphenol	10.70	9.68	-0.577	-31.94	44.24	0.920	0.82
n-Butylphenol	12.60	9.68	-0.573	-31.94	47.23	0.920	0.93
n-Pentylphenol	14.50	9.68	-0.568	-31.94	50.40	0.920	1.62
n-Hexylphenol	16.40	9.69	-0.568	-31.94	53.58	0.920	1.93
Cyclized on CH_3:							
Methylphenol	37.06	232.19	-1.986	-16.79	11.39	0.004	0.58
Ethylphenol	12.93	24.32	0.180	-16.75	12.09	0.786	0.65
Propylphenol	11.09	4.56	-0.042	-23.86	27.61	0.334	0.72
Butylphenol	12.81	4.82	-0.004	2.26	49.25	0.146	0.72
Pentylphenol	14.53	4.22	-0.004	8.44	210.20	0.247	0.79
Hexylphenol	16.67	4.18	-0.230	4.29	-	0.096	0.78
Cyclized as -CH_2-α:							
Ethylphenol	12.93	24.32	0.180	-16.75	12.09	0.786	0.65
Propylphenol	14.83	24.14	0.155	-17.14	14.22	0.786	0.72
Butylphenol	16.73	24.15	0.159	-15.67	33.18	0.786	0.82
Pentylphenol	18.63	24.15	0.159	-15.68	38.08	0.786	0.88
Hexylphenol	20.53	24.15	0.163	-15.68	40.93	0.786	0.94
Cyclized as -CH_2-β:							
Propylphenol	14.83	24.14	0.155	-17.14	14.22	0.786	0.72
Butylphenol	12.83	4.37	-0.050	-23.86	29.67	0.334	0.81
Pentylphenol	14.71	4.36	-0.046	-21.73	41.34	0.334	0.89
Hexylphenol	16.64	4.37	-0.046	-21.76	44.21	0.334	0.99

Calculation results for the energies of covalent bonds and non-covalent interactions for ortho n-alkylphenols (common, cyclized through CH_3-, cyclized as -CH_2-α and -CH_2-β) and n-alkylbenzenes both common and cyclized into the position ortho with respect to the substituent (again cyclization through CH_3-, as -CH_2-α and -CH_2-β are summarized in Tables 2, 3 and 4. From these tables it is evident that cyclization hardly brings any important changes in covalent bonds (only small changes in electrostatic interactions and some expected changes in the E_{angle} term). However, substantial changes in van der Waals interactions between nonbonded atoms inside molecules took place. Changes in van der Waals forces inside the cyclized molecules must also be reflected in changes of these forces between molecules. The dependence of van der Waals forces on the number of carbons (z), demonstrated in Figs. 5 and 6, is of the same (divergent) character as the detected dependence *1* of logarithms of retention times on z (Fig. 1). This finding is in accordance with the fact that the same dependences were detected both in cases of polar and nonpolar phases and also in the cases of alkylphenols and alkylbenzenes, because retention data and their changes are in the given case related with intermolecular forces rather than with the structure of the considered compounds.

The same results have been obtained in the case of ortho, meta and para n-alkylphenols cyclized on the group -CH_3 and even in the case of n-alkylbenzenes, cyclized on the group -CH_3 as well to ortho, meta and para positions with respect to the substituent. Another example is shown in Fig. 7. Therefore, attention was focused on systematic calculations of the energies of van der Waals interactions. Numerical values of these energies show strength of van der Waals forces and results are summarized in Tables 5 and 6. From the data in these tables it is evident that in all the cases the divergence in the size of these interactions occurs at $z = 9$ (to be more specific when phenol or benzene are substituted by n-propyl). However, this result was ascertained only for alkylphenols and alkylbenzenes

Table 3 Potential energies of covalent bonds and non-covalent interactions in meta n-alkylphenols (common, cyclized on CH_3-, cyclized as -CH_2-α and -CH_2-β). Calculated by the MM+ program. For symbols see Table 2.

n-Alkylphenols	E_{bond}	E_{angle}	$E_{stretch\text{-}bend}$ (kJ/mol)	$E_{dihedral}$	$E_{vdWaals}$	E_{elst}	D_{max} (nm)
Phenol	4.57	9.43	-0.443	-23.32	12.11	0	0.56
Common:							
Methylphenol	6.90	9.68	-0.589	-26.33	14.57	0.113	0.59
Ethylphenol	8.80	9.68	-0.577	-26.92	39.44	0.113	0.72
n-Propylphenol	10.70	9.68	-0.577	-26.92	42.49	0.113	0.83
n-Butylphenol	12.60	9.68	-0.573	-26.92	45.48	0.113	0.95
n-Pentylphenol	14.50	9.68	-0.568	-26.92	48.66	0.113	1.08
n-Hexylphenol	16.40	9.69	-0.568	-26.92	51.84	0.113	1.21
Cyclized on CH_3:							
Methylphenol	10.26	38.69	-0.961	389.88	32.45	0.002	0.49
Ethylphenol	13.81	36.63	-3.064	369.97	95.81	0.493	0.55
Propylphenol	29.75	64.02	3.703	243.10	385.13	0.159	0.61
Butylphenol	31.13	59.18	1.726	-1.34	3173.33	0.054	0.66
Pentylphenol	19.09	29.00	0.581	-13.30	2941.51	0.042	0.69
Hexylphenol	16.64	4.66	-0.038	-10.80	8006.79	0.054	0.71
Cyclized as -CH_2-α:							
Ethylphenol	13.81	36.63	-3.064	369.97	95.81	0.493	0.55
Propylphenol	15.72	36.38	-0.380	371.00	140.79	0.493	0.66
Butylphenol	17.62	36.38	-0.376	373.11	1252.08	0.493	0.66
Pentylphenol	19.52	36.38	-0.376	373.11	1250.91	0.493	0.77
Hexylphenol	21.42	36.38	-0.372	373.11	1252.79	0.493	0.81
Cyclized as -CH_2-β:							
Propylphenol	29.75	64.02	3.703	243.10	385.13	0.159	0.61
Butylphenol	31.66	63.70	3.478	243.36	388.27	0.159	0.71
Pentylphenol	33.56	63.71	3.478	245.48	397.56	0.159	0.75
Hexylphenol	35.45	63.71	3.482	245.48	400.36	0.159	0.85

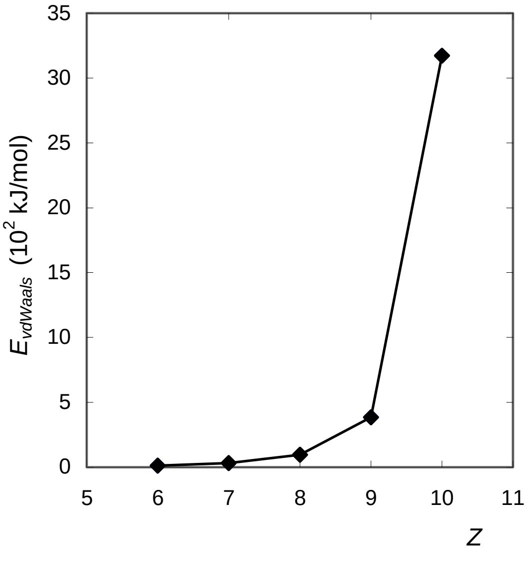

Fig. 5 The dependence of the van der Waals energies (and consequently forces) in effect on the number of carbons in the cyclized molecules of meta n-alkylphenols (MM+ method, -CH_3 cyclization).

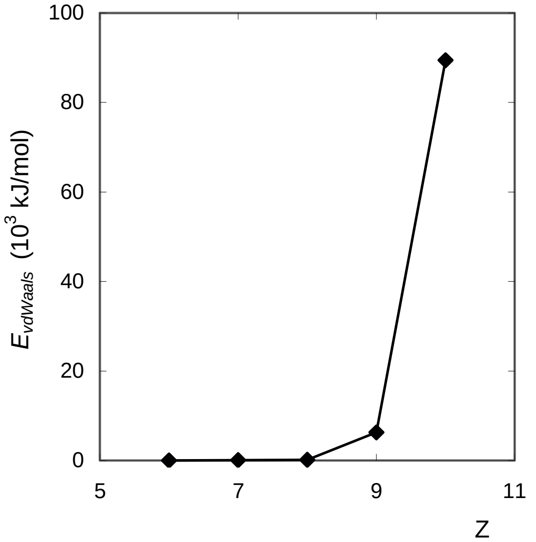

Fig. 6 The dependence of the van der Waals energies (and consequently forces) in effect on the number of carbons in the cyclized molecules of para n-alkylphenols (AMBER method, -CH_3 cyclization).

Table 4 Potential energies of covalent bonds and non-covalent interactions in n-alkylbenzenes cyclized into the position meta with respect to the substituent (common, cyclized on CH_3-, cyclized as -CH_2-α and -CH_2-β). Calculated by the MM+ program. For symbols see Table 2.

n-Alkylbenzenes	E_{bond}	E_{angle}	$E_{stretch\text{-}bend}$ (kJ/mol)	$E_{dihedral}$	$E_{vdWaals}$	E_{elst}	D_{max} (nm)
Benzene	4.573	9.434	-0.443	-23.324	12.114	0	-
Common:							
Methybenzene	7.060	0.247	-0.142	-26.334	14.852	0	0.59
Ethylbenzene	8.958	0.247	-0.130	-26.919	39.727	0	0.72
n-Propylbenzene	10.860	0.247	-0.130	-26.919	42.778	0	0.82
n-Butylbenzene	12.757	0.247	-0.125	-26.919	45.771	0	0.95
n-Pentylbenzene	14.659	0.247	-0.125	-26.919	48.956	0	1.06
n-Hexylbenzene	16.561	0.247	-0.125	-26.919	52.137	0	1.19
Cyclized on CH_3:							
Methylbenzene	7.829	123.134	-3.582	194.742	41.503	0	0.47
Ethylbenzene	10.266	29.465	-2.274	292.847	34.230	0.560	0.51
Propylbenzene	12.858	21.611	-1.058	305.633	54.081	0.242	0.57
Butylbenzene	27.337	50.051	2.479	185.379	257.722	0.159	0.62
Pentylbenzene	30.443	49.667	0.982	-2.504	3102.939	0.134	0.66
Hexylbenzene	17.217	5.304	-0.117	-0.573	-	0.125	0.69
Cyclized as –CH2-α:							
Ethylbenzene	10.266	29.465	-2.274	292.847	34.230	0.560	0.51
Propylbenzene	12.344	29.565	-2.182	294.372	51.493	0.560	0.62
Butylbenzene	14.241	29.565	-2.182	297.114	456.540	0.560	0.72
Pentylbenzene	16.143	29.565	-2.178	297.114	457.585	0.560	0.81
Hexylbenzene	18.045	29.565	-2.174	297.114	458.588	0.560	0.95
Cyclized as –CH2-β:							
Propylbenzene	12.858	21.611	-1.058	305.633	54.081	0.242	0.57
Butylbenzene	14.755	21.657	-1.058	308.701	55.765	0.242	0.65
Pentylbenzene	16.657	21.657	-1.053	311.523	78.927	0.242	0.75
Hexylbenzene	18.555	21.657	-1.049	311.523	81.619	0.242	0.84

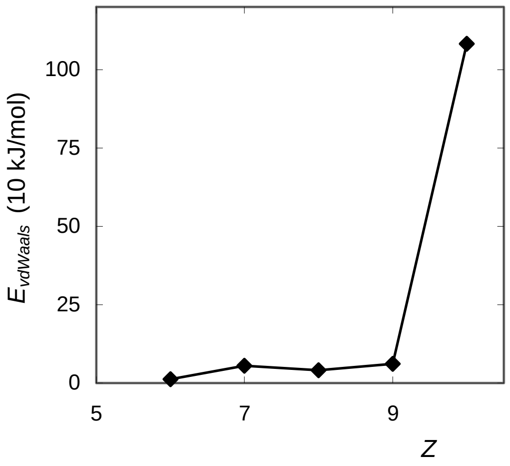

Fig. 7 The dependence of the van der Waals forces in effect on the number of carbons in the molecules of n-alkylbenzenes cyclized into the position meta with respect to the substituent (the AMBER method, -CH_3 cyclization).

cyclized on the terminal methyl group. In the case of -CH_2-α and -CH_2-β cyclizations, the detected $E_{vdWaals}$ values were similar to common n-alkylphenols and n-alkylbenzenes or no relevant dependences on z were found.

An increase in van der Waals interactions inside the cyclized molecules (i.e. intramolecularly) must also be reflected in an increase of forces between molecules (i.e. intermolecularly). More intense effect of attraction forces between molecules should then manifest itself through a corresponding increase of boiling temperatures of the C_9-compounds and higher in both types of molecules in question. The increase of intermolecular forces caused by cyclization was confirmed by comparison of boiling points of normal and cyclic hydrocarbons C_3–C_8. The results are shown in Table 7 (the values of boiling points were taken from the compendium (Spravotschnik Chimika, 1951) and verified against the compendium (Večeřa et al., 1975)). From the values shown in Table 7 it is evident that boiling points of cyclic hydrocarbons increase with the number of carbons z in the molecule non-linearly, divergently, similarly to van der Waals forces

Table 5 Energies of van der Waals interactions ($E_{vdWaals}$, kJ/mol) in the molecules of n-alkylphenols and n-alkylbenzenes. Calculated by the MM+ program. Positions *„ortho", „meta", „para"* at n-alkylbenzenes mean cyclization into the positions with respect to the substituent.

n-Alkylphenols	ortho	meta	para	n-Alkylbenzenes	*„ortho"*	*„meta"*	*„para"*
Common:				*Common:*			
Methylphenol	17.117	14.57	14.6	Methylbenzene	14.852	14.85	14.85
Ethylphenol	41.248	39.44	39.47	Ethylbenzene	39.727	39.73	39.73
n-Propylphenol	44.237	42.49	42.51	n-Propylbenzene	42.778	42.78	42.78
n-Butylphenol	47.226	45.48	45.51	n-Butylbenzene	45.771	45.77	45.77
n-Pentylphenol	50.402	48.66	48.69	n-Pentylbenzene	48.956	48.96	48.96
n-Hexylphenol	53.583	51.84	51.87	n-Hexylbenzene	52.137	52.14	52.14
Cyclized on CH_3:				*Cyclized on CH_3:*			
Methylphenol	11.395	32.45	44.96	Methylbenzene	10.396	41.5	23.99
Ethylphenol	12.089	95.81	109.4	Ethylbenzene	11.227	34.23	46.87
Propylphenol	27.609	385.1	411.3	Propylbenzene	14.254	54.08	67.42
Butylphenol	49.249	3173.0	1037	Butylbenzene	27.642	257.7	339.3
Pentylphenol	210.2	2942		Pentylbenzene	64.514	3103	832.2
Hexylphenol	-	8007	1132	Hexylbenzene	476.77	-	905.6
			-				
Cyclized as -CH_2-α:				*Cyclized as -CH_2-α:*			
Ethylphenol	12.089	95.81	109.4	Ethylbenzene	11.227	34.23	46.87
Propylphenol	14.22	140.8	735.8	Propylbenzene	11.608	51.49	54.72
Butylphenol	33.177	1252	129.3	Butylbenzene	21.916	456.5	216
Pentylphenol	38.076	1251	132.1	Pentylbenzene	24.658	457.6	218.1
Hexylphenol	40.931	1251	135	Hexylbenzene	27.362	458.6	220
Cyclized as -CH_2-β:				*Cyclized as -CH_2-β:*			
Propylphenol	14.22	385.1	411.3	Propylbenzene	11.608	54.08	67.42
Butylphenol	29.665	388.3	479.1	Butylbenzene	16.386	55.77	70.17
Pentylphenol	41.34	397.6	3399	Pentylbenzene	27.312	78.93	132.4
Hexylphenol	44.208	400.4	3395	Hexylbenzene	29.783	81.62	134.9

and, consequently, relative retention times. Due to obvious importance of the dependence of the T_b values on z in the case of normal and cyclic hydrocarbons, this dependence is graphically depicted in Fig. 8 as a difference of boiling points (ΔT_b) of these hydrocarbons in dependence on z.

If a change in the relative retention time as a result of cyclization is caused by a change in the size of the molecule moving in a chromatographic column and a change in both intramolecular and intermolecular van der Waals forces, then the related cyclization of alkyl chain could really be, in the case of n-alkylphenols, accompanied by formation of a hydrogen bridge between the oxygen in the phenolic group -OH and a hydrogen of the terminal group -CH_3 of the alkyl; in other words, in the case of n-alkylphenols, the tendency to form hydrogen bridges resulting in a heterocyclic ring with six or more members being formed including also one C-C bond of the aromatic ring of phenol as shown in Fig. 2 could actually be considered. Similarly, in the case of alkylbenzenes, a tendency to integrate could exist between the benzene ring (-δ) and a hydrogen of the terminal group of the -CH_3 alkyl (+δ), resulting in a formation of a five-membered or more-membered

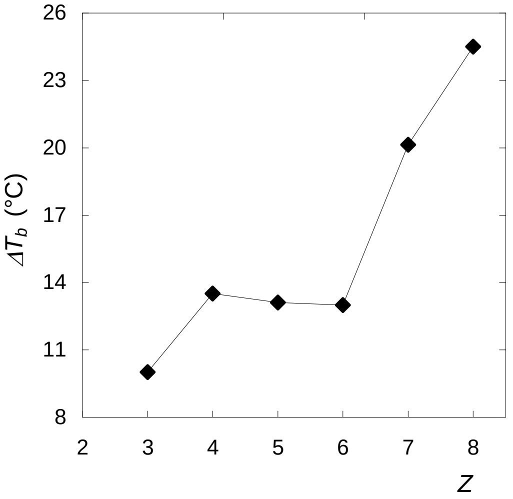

Fig. 8 The difference of the boiling points (ΔT_b) of normal and cyclic hydrocarbons C_3–C_8 in dependence on z.

Table 6 Energies of van der Waals interactions ($E_{vdWaals}$, kJ/mol) in the molecules of n-alkylphenols and n-alkylbenzenes. Calculated by the AMBER program. Positions *„ortho”, „meta”, „para”* at n-alkylbenzenes mean cyclization into the positions with respect to the substituent.

n-Alkylphenols	ortho	meta	para	n-Alkylbenzenes	*„ortho”*	*„meta“*	*„para“*
Common:				*Common:*			
Methylphenol	17.54	13.53	13.58	Methylbenzene	13.90	13.90	13.90
Ethylphenol	36.17	35.04	35.09	Ethylbenzene	35.43	35.43	35.43
n-Propylphenol	36.54	35.48	35.53	n-Propylbenzene	35.87	35.87	35.87
n-Butylphenol	37.13	36.07	36.13	n-Butylbenzene	36.48	36.48	36.48
n-Pentylphenol	37.90	36.86	36.91	n-Pentylbenzene	37.26	37.26	37.26
n-Hexylphenol	38.71	37.67	37.72	n-Hexylbenzene	38.07	38.07	38.07
Cyclized on CH_3:				*Cyclized on CH_3:*			
Methylphenol	14.93	43.83	65.28	Methylbenzene	12.92	55.41	24.34
Ethylphenol	11.05	141.61	175.12	Ethylbenzene	14.35	40.43	53.46
Propylphenol	19.08	2975.8	6246.6	Propylbenzene	11.52	61.62	74.65
Butylphenol	38.38	$4*10^{6}$	$9*10^{4}$	Butylbenzene	16.90	1082.8	4182.5
Pentylphenol	703.1	$4*10^{6}$	-	Pentylbenzene	61.29	$6*10^{6}$	35913
Hexylphenol	-	$4*10^{10}$	-	Hexylbenzene	-	-	-
Cyclized as -CH_2-α:				*Cyclized as -CH_2-α:*			
Ethylphenol	11.05	141.61	175.12	Ethylbenzene	14.35	40.43	53.46
Propylphenol	11.42	249.91	17755	Propylbenzene	13.74	65.87	60.95
Butylphenol	37.26	31143	195.47	Butylbenzene	21.82	5888.8	777.48
Pentylphenol	41.70	31142	195.82	Pentylbenzene	22.05	5887.9	777.15
Hexylphenol	42.22	31142	196.36	Hexylbenzene	22.44	5887.1	777.06
Cyclized as -CH_2-β:				*Cyclized as -CH_2-β:*			
Propylphenol	19.08	2976	6247	Propylbenzene	11.52	61.62	74.65
Butylphenol	19.35	2977	6387	Butylbenzene	11.85	61.63	75.59
Pentylphenol	28.03	2982	$8*10^{6}$	Pentylbenzene	20.19	94.76	194.70
Hexylphenol	28.44	2983	$8*10^{6}$	Hexylbenzene	20.24	95.01	194.76

Table 7 Boiling points of normal and cyclic hydrocarbons C_3–C_8 and energies of intramolecular van der Waals interactions.

Alkane	T_b (°C)	$E_{vdWaals}$ (MM+) (kJ/mol)	$E_{vdWaals}$ (AMBER) (kJ/mol)
n-Propane	-44.5	8.469	1.835
n-Butane	-0.5	11.867	2.796
n-Pentane	36.15	15.132	3.666
n-Hexane	68	18.363	4.514
n-Heptane	98.34	21.577	5.355
n-Octane	125.5	24.787	6.191
Cyclopropane	-33.5	0.134	0.067
Cyclobutane	13	11.265	1.233
Cyclopentane	49.262	14.768	2.399
Cyclohexane	81	22.121	5.338
Cycloheptane	118.48	204.757	721.522
Cyclooctane	150	501.123	7839.966

ring**,** including also one C-C bond of the aromatic ring of benzene (Fig. 2).

The question of association. The molecules of the compounds in question are of an aromatic-aliphatic character. As already mentioned above, in the environment of a dense stationary phase, molecular aggregates may be formed. The molecules in question can thus associate in the separation zone, which would lead to a change in retention characteristics. It is likely to be that the association

Table 8 Energies of van der Waals interactions in the association of two molecules of a common n-alkylphenols and n-alkylbenzenes in comparison with those of two non-associated (isolated) molecules. Calculated by the AMBER method.

Compound	$E_{vdWaals}$(associate) (kJ/mol)	$E_{vdWaals}$(2 isolated molecules) (kJ/mol)
Phenol	$2.189*10^{10}$	24.512
ortho n-Methylphenol – ortho n-Hexylphenol	$2.427*10^{10}$–$8.945*10^{13}$	35.087–77.414
para n-Methylphenol – para n-Hexylphenol	$2.943*10^{9}$–$4.193*10^{12}$	27.162–75.441
Benzene	$2.291*10^{15}$	25.076

would increase with the increasing length of the side n-alkyl chain increasing and would strongly be manifested in the case of molecules with a number of carbons higher than 9. Therefore, the close association was investigated both in the case of n-alkylphenols and n-alkylbenzenyes for the system of two molecules. This was done by calculating the energies of van der Waals interactions ($E_{vdWaals}$) using the above-mentioned methods after the two common molecules (i.e. without the side chains being cyclized) were conformed until the state of the energy minimum was reached. The calculated energies were then compared with the energies of van der Waals interactions in two non-associated (isolated) molecules. The data summary is in Table 8.

From the data in Table 8 it can be seen that intensive nonbonding physical interactions occur in the association of two molecules of n-alkylphenol or n-alkylbenzene. These interactions can determine the elution/retention behavior of molecules when they are moving through the chromatographic column. However, unlike in the case of cyclized forms no dependence of the $E_{vdWaals}$ values on the length of the n-alkyl chain was detected. Moreover, if we take into consideration that the measurements were taken at temperatures 125–140 °C, the close association of the molecules is unlikely.

The question of non-covalent interaction with the stationary phase. As has been already suggested, in the case of both the examined n-alkylphenols and n-alkylbenzenes, an increase in the number of carbons in the molecule may be accompanied by a change in the intermolecular interaction between a non-conventional compound and the stationary phase. A consequence of the non-linear changes in these interactions would also be a non-linear progression of retention times. However, these interactions would have to change differently in the case of polar and nonpolar stationary phases, with the dependence of the elution/retention times on the number of carbons consequently being of a completely different character for each type of the phase. Nevertheless, this was not observed. As shown in Fig. 9, the character of the dependences is the same, measured in the case of alkylbenzenes for both the polar and nonpolar phases. It seems that not even non-covalent interactions with the stationary phase are the cause of the observed progression of retention times.

Therefore, it is the cyclized form of the considered compounds that is preferred. The preference for the cyclized form arises also from the fact that cyclanic-aromatic ethers with five- and six-membered cyclanic rings with oxygen and an interconnected aromatic ring (Fig. 2) (which are thermodynamically stable compounds) are formed. (In the case of para methylphenol, higher values of some

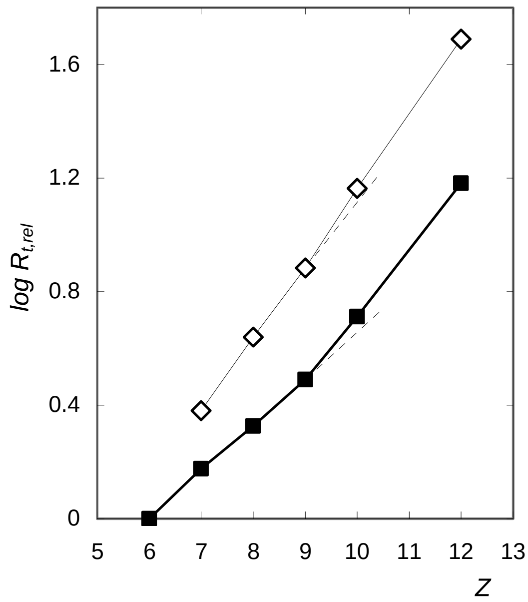

Fig. 9 Dependences of *log* $R_{t,rel}$ on *z* in the case of n-alkylbenzenes in a nonpolar (Apiezon K) and polar (trixylenylphosphate-phosphoric acid (95:5)) phases at temperature of 130 °C. Full points – nonpolar phase, empty points – polar phase. Similar dependences were found also in the case of n-alkylphenols. Based on (Buryan and Macák, 1982), adjusted.

covalent energies were calculated due to higher strain of bonds, however, no values on principle eliminating a hypothetical cyclization were found).

From the thermodynamical aspect, it is the affinity of the low-molecular compounds that is important in the given context in question with the stationary high-molecular phase when they are being mixed with this phase. The degree of affinity is the change in Gibbs energy of mixing when the molecules of alkylphenol or alkylbenzene are blended with high-molecular chains of the stationary phase (ΔG_{mix}) at constant temperature and pressure:

$$\Delta G_{mix} = \Delta H_{mix} - T\,\Delta S_{mix} < 0 \qquad (1)$$

where ΔH_{mix} is the enthalpy of mixing, ΔS_{mix} the entropy of mixing and T the temperature of the GC separation (K). The more negative ΔG_{mix} is, the better the mixing of the compounds will be (in question with the stationary phase). Since the entropy of the system always increases when the components are mixed, and the entropic term of the equation (1) is thus always negative ($-T\,\Delta S_{mix} < 0$), the mixing/solubility depends mainly on the value ΔH_{mix}. The thermodynamic condition of the solubility of a low-molecular element in the stationary phase, or the mixing of the two substances is then:

$$\Delta H_{mix} < T\,\Delta S_{mix.} \qquad (2)$$

The blending will thus be the best in the case $\Delta H_{mix} = 0$, when also the solubility of one component in the other will be maximal as well. However, this is an ideal case. Parameters of solubility δ were introduced for practical purposes, numerically characterizing solubility of low-molecular and high-molecular substances (Hildebrand and Scott, 1959). A low-molecular substance a solubility parameter of which will be identical to the solubility parameter of the high-molecular substance will achieve maximal dissolution during the mixing, because $\Delta H_{mix} = 0$ in this case. Since cyclization increases the δ in the case of hydrocarbons, e.g. in the case of hexane-cyclohexane from 15.1 (hexan) to 16.8 (cyklohexan) (Brandrup and Immergut, 1975), the mixing is improved, because the parameter for high-molecular stationary phases (Mleziva, 1993) is approximately 16–18. Cyclization thus facilitates the mixing of alkylphenols or alkylbenzenes with high-molecular stationary phases, because the thermodynamic condition for mixing is better fulfilled.

On the whole, the data obtained can serve both an analytical methodology for the analysis of aromatics and phenolics, which is still topical (Naczk and Shahidi, 2004), and a deeper insight into the problem of van der Waals forces/non-covalent interactions which is also actual (Hobza et al., 2006).

4. CONCLUSION

Side alkyl chains of n-alkylphenols become cyclized in both polar and nonpolar stationary phases of capillary columns, with a possible formation of hydrogen bridges between the oxygen of the phenolic -OH group and a hydrogen of the methyl group of the side alkyl chain. In the case of n-alkylbenzenes, cyclization is made possible due to the interaction between the benzene ring and a hydrogen of the terminal methyl group of the alkyl. In the case of the formed aromatic–quasi-alicyclic molecules, the effect of van der Waals forces thus increases not only intramolecularly but also intermolecularly, with a consequent increase in boiling points, mainly in the case of n-alkylphenols and n-alkylbenzenes with the number of carbons in a molecule higher than 9. This results in a divergence in the retention characteristics of the mentioned compounds observed in the dependence of the logarithm of the relative retention time on the total number of carbons in the molecule. Cyclization of side alkyl chains in a dense stationary phase is a quite new phenomenon.

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