The influence of molecular conformation of N-alkylsubstituted six-membered cyclic amines and alkylcyclohexanes on the thermodynamic characteristics of sorption in gas chromatography

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The standard partial molar free energies, enthalpies, and entropies of sorption of the methylene units in the homologous series of alkylcyclohexanes and N-alkylsubstituted six-membered heterocycles (piperidines, morpholines, and thiomorpholines) were determined on a capillary column with the methylsiloxane OV-101 stationary phase at 70—150 °C. A characteristic feature of all series under study is an abnormally high increase in the values of thermodynamic parameters of sorption on going from the methyl to the ethyl homolog. This peculiarity is believed to be associated with the presence of the *gauche* butane or *gauche* methylethylamine fragments in the ethyl homolog. These *gauche* fragments have an increased sorption activity under conditions of gas chromatography in comparison with the corresponding *trans* form.
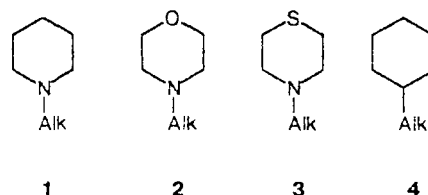
Key words: capillary gas chromatography; N-n-alkylsubstituted piperidines, morpholines, thiomorpholines, and n-alkylcyclohexanes; homologous series; conformation of homologs; thermodynamic parameters of sorption of the methylene units.

In the homologous series of compounds, the dependence of the standard partial molar free energy of sorption on the length of the n-alkyl group is nonlinear, which manifests itself in different energies of sorption of the methylene units $\Delta G_n^0(CH_2)$ and their contributions to the retention indices $\Delta I_n(CH_2)$.[1—8] For most series of compounds containing functional groups, the $\Delta G_1^0(CH_2)$ value (*i.e.*, the increase in the free energy of sorption on going from the methyl to the ethyl homolog) is appreciably lower than the $\Delta G_2^0(CH_2)$ value obtained by comparison of the energies of sorption of the ethyl and propyl members of the series. For the following homologs only small smooth changes in the $\Delta G_n^0(CH_2)$ values are observed.[1] For several homologous series, the $\Delta G_n^0(CH_2)$ and $\Delta I_n(CH_2)$ values change in a zigzag pattern, which is particularly pronounced for the initial members of the series.[2—4] Thus, in the opinion of the authors of Refs. 2 and 3, the abnormally high values of $\Delta G_1^0(CH_2)$ and a minimum on the curve of the dependence of $-\Delta G_n^0(CH_2)$ on n (at n = 2) in several series of carbonyl containing compounds suggest an intramolecular interaction between the methyl and carbonyl group in the first homolog. For the homologous series containing an unsaturated system, the "propyl effect" caused by interaction between the methyl group of the propyl homolog and the π-electrons of multiple bonds or of benzene ring has been found.[5,6]

In the case of N-alkylsubstituted six-membered cyclic amines (piperidines, morpholines and thiomorpho-

lines) and n-alkylcyclohexanes, the dependence of the free energy of sorption of homologs ΔG^0 on the length of the alkyl chain was shown to deviate from linearity for the first members of the series.[7]

To investigate plausible reasons for similarity and distinctions in the gas chromatographic behavior of the six-membered carbo- and heterocycles, in the present work the standard partial molar free energies of sorption of the methylene units $\Delta G_n^0(CH_2)$ for the members of homologous series of N-n-alkylpiperidines (1), N-n-alkylmorpholines (2), N-n-alkylthiomorpholines (3), and n-alkylcyclohexanes (4) have been determined in the temperature interval from 70 to 150 °C and the partial molar enthalpies and entropies of sorption ($\Delta H_n^0(CH_2)$ and $\Delta S_n^0(CH_2)$, respectively) have been calculated.

1   2   3   4

Experimental

GC analysis was performed on a Carlo Erba 5300 Mega Series chromatograph equipped with a flame ionization detector on a capillary column (50 m × 0.3 mm) coated with the

Table 1. Partial molar free energies of sorption of the methylene units $\Delta G_n^0(CH_2)$ in the homologous series of N-alkylpiperidines (1), N-alkylmorpholines (2), N-alkylthiomorpholines (3), and alkylcyclohexanes (4) on a capillary column coated with OV-101 stationary phase at different temperatures of analysis

Homolo-gous series	Compa-red homologs	n	$-\Delta G_n^0(CH_2)$/kJ mol^{-1}			
			70 °C	90 °C	110 °C	130 °C
1	Et/Me	1	1.810±0.022	1.692±0.024	1.610±0.032	1.515±0.044
	Pr/Et	2	1.743±0.003	1.655±0.003	1.570±0.015	1.481±0.026
	Bu/Pr	3	2.043±0.006	1.935±0.011	1.853±0.008	1.753±0.025
	Pent/Bu	4	2.083±0.008	1.974±0.007	1.870±0.005	1.764±0.012
2	Et/Me	1	1.963±0.007	1.860±0.022	1.771±0.018	1.678±0.024
	Pr/Et	2	1.841±0.005	1.741±0.005	1.646±0.011	1.566±0.020
	Bu/Pr	3	2.102±0.012	1.985±0.007	1.883±0.010	1.784±0.011
	Pent/Bu	4	2.150±0.018	2.009±0.015	1.903±0.008	1.798±0.008
3	Et/Me	1	*1.486±0.012	1.754±0.008	1.637±0.014	1.568±0.010
	Pr/Et	2	*1.442±0.014	1.677±0.009	1.581±0.014	1.513±0.009
	Bu/Pr	3	*1.658±0.010	1.959±0.016	1.837±0.013	1.752±0.003
	Pent/Bu	4	*1.682±0.006	1.987±0.024	1.863±0.009	1.773±0.005
4	Et/Me	1	2.367±0.011	2.270±0.009	2.147±0.033	2.039±0.029
	Pr/Et	2	2.055±0.008	1.949±0.013	1.837±0.015	1.741±0.021
	Bu/Pr	3	2.138±0.004	2.040±0.010	1.909±0.017	1.817±0.012
	Pent/Bu	4		2.043±0.002	1.913±0.008	1.811±0.005

* Determined at 150 °C.

OV-101 (film thickness, $d_f = 0.4$ μm) stationary phase. The chromatograms were obtained under isothermal conditions at four temperatures in the range from 90 to 150 °C for the series of N-n-alkylthiomorpholines and from 70 to 130 °C for other series with an increment of 20 °C. Helium was used as the carrier gas with the inlet split ratio of 1 : 30. The volumes of the samples of 1—2% solutions of homologs in n-pentane were 0.1—0.4 μL.

The standard partial molar free energies of sorption of the methylene units $\Delta G_n^0(CH_2)$ were determined from the corrected retention times of neighboring homologs t'_{m+1} and t'_m using the formula

$$\Delta G_n^0(CH_2) = -2.3RT \lg(t'_{m+1}/t'_m), \qquad (1)$$

where R is the universal gas constant; T is the temperature of the analysis, K; m and $m + 1$ are the numbers of the homologs being compared; index $n = 1$ was assigned to the $\Delta G_n^0(CH_2)$ value calculated from t' values for the first pair of homologs (Et—Me), while $n = 2$ was assigned to the $\Delta G_n^0(CH_2)$ value calculated from t' values for the second pair (Pr—Et), etc. The hold-up time of the column was determined from the retention time of methane injected simultaneously with the compounds analyzed. The resulting average values of $\Delta G_n^0(CH_2)$ and the errors of their determination are given in Table 1.

The partial molar enthalpies and entropies of sorption of the methylene units $\Delta H_n^0(CH_2)$ and $\Delta S_n^0(CH_2)$ were determined from the $\Delta G_n^0(CH_2)$ values at four temperatures of analysis using the relation

$$\Delta G_n^0(CH_2) = \Delta H_n^0(CH_2) - T \cdot \Delta S_n^0(CH_2). \qquad (2)$$

Results and Discussion

The $\Delta G_n^0(CH_2)$ values, calculated using formula (1) (Table 1), reflect changes in the standard partial molar free energies of sorption for the six-membered cyclic

compounds studied on going from one homolog to another, beginning with the methyl one. These values are the overall thermodynamic characteristics of the changes in the sorbate molecules caused by lengthening the n-alkyl chain by one CH_2 group. If one correlates the calculated values of thermodynamic quantities with certain methylene units of the n-alkyl chain, the values with indices "1" should be assigned to the second unit, those with indices "2" should be assigned to the third one, etc., counting from the cycle.

The data of Table 1 indicate that the dependences of $-\Delta G_n^0(CH_2)$ on n have an unusual character at any temperature of analysis in the interval from 70 to 150 °C. The $-\Delta G_n^0(CH_2)$ values are abnormally high at $n = 1$ and are minimal at $n = 2$, whereas for most homologous series of organic compounds the minimum value is observed at $n = 1$.[1] As an example, the dependences of $-\Delta G_n^0(CH_2)$ on n for cyclic amines and alkylcyclohexanes studied at 110 °C are compared in Fig. 1. The observed similarity of dependences *1—4* (Fig. 1) suggests that the reason for the unusual character of changes in the contributions of the methylene units to the energy of sorption of homologs of carbo- and heterocycles is the same for both groups of compounds and is associated with specific features of the spatial structure of their molecules. The similarity of conformations of the studied cyclic compounds was repeatedly emphasized: both cyclohexane and six-membered nitrogen-containing heterocycles exist in a "chair" shape with somewhat different geometric parameters.[9,10]

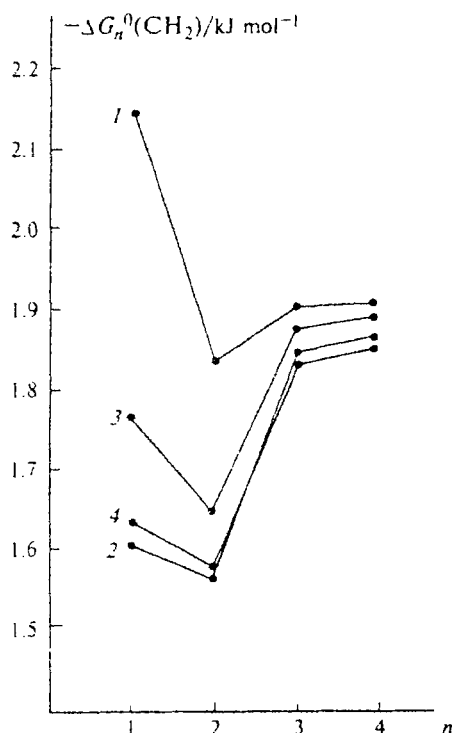The alkyl groups in monosubstituted six-membered cyclic amines and cyclohexanes are known to have

Fig. 1. Dependence of the standard partial molar free energies of sorption of the methylene units $-\Delta G_n^0(CH_2)$ on n in the homologous series of alkylcyclohexane (*1*), *N*-alkylpiperidine (*2*), *N*-alkylmorpholine (*3*), and *N*-alkylthiomorpholine (*4*); n is the number of the pair of homologs being compared (see Table 1).

predominantly equatorial orientation[9−11] in the gas phase as well as in organic solvents.[11] The equatorial orientation of the substituents might be assumed to be predominant under GLC conditions if the nonpolar OV-101 stationary phase is used. The percent ratios of the equatorial (*e*) and axial (*a*) conformers, that we calculated from the energies of conformational transitions in an aprotic solvent,[10,11] are 90 : 10 for methylcyclohexane, 91 : 9 for ethylcyclohexane, and 98 : 2 for methylpiperidine at 110 °C. The appearance of an *e*-methyl substituent in the cyclohexane molecule results in the appearance of two additional *trans* butane fragments, while two *trans* methylethylamine fragments arise in the piperidine molecule. These *trans* fragments remain after the transition from the methyl to the ethyl homolog; however, two new butane (and, accordingly, methylethylamine) fragments appear. Each of them contains a carbon atom in the α- or α'-position of the ring, a cyclic carbon or nitrogen atom, and carbon atoms of the ethyl group. The *gauche* forms inevitably appear in these fragments. Thus, for instance, the content of the *N*-ethylpiperidine conformer with one *gauche* methylethylamine fragment is 76%, whereas it is 24% in the case of two fragments. The content of conformers was

estimated from the data of Ref. 12 at 110 °C. The above mentioned *gauche* fragments, characteristic of the ethyl member of the series, remain in the propyl and higher homologs.

The appearance of *gauche* butane and methylethylamine fragments in the molecules of the homologs in question affects their sorption activity. The increased internal strain in these fragments (compared with that in *trans* ones) is caused by nonvalent intramolecular van der Waals interactions between the terminal units. The presence of *gauche* fragments increases the retention of compounds under GLC conditions.[13−16] The influence of the *gauche* butane fragment on the increase in the boiling point[10] and in the retention parameters[13,15] is most clearly demonstrated for dimethylcyclohexanes in which stable stereoisomers are capable of individual existence.[10] An analogous role of the methylethylamine fragment in the retention becomes evident if the values of the retention indices of the dimethylpiperidines we obtained previously[16] are compared.

The appearance of the *gauche* fragments in the molecules of homologs beginning with ethyl one affects the character of dependences of the standard partial molar enthalpies and entropies of sorption of the methylene unit ($-\Delta H_n^0(CH_2)$ and $-\Delta S_n^0(CH_2)$, respectively) on n. These parameters also have a minimum at $n = 2$ (Fig. 2), *i.e.*, the appearance of an additional conformational factor affects both the nonadditive increase in the heat of interaction of the substances with the stationary phase and the change in the entropy component of the free energy of sorption. A similar character of changes in the entropy of sorption of the methylene units in carbo- and heterocycles indicates that the similarity of conformations of compounds studied mostly affects the change in the number of degrees of freedom in the process of sorption.
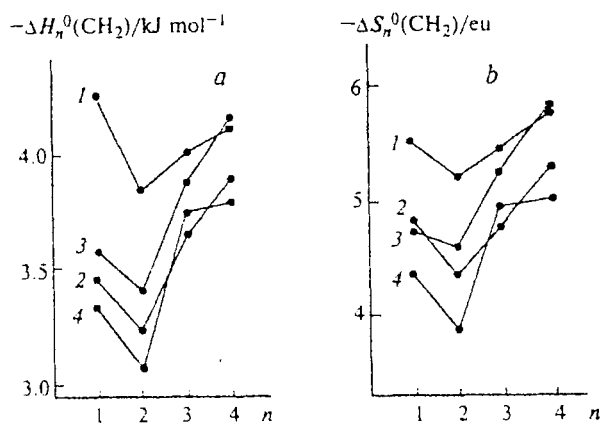

Fig. 2. Dependences of the standard partial molar enthalpies (*a*) and entropies (*b*) of sorption of the methylene units on n in the homologous series of carbo- and heterocycles. Designations see in Fig. 1.

At the same time, along with the analogy in the change in the thermodynamic parameters of sorption for carbo- and heterocycles, distinctions due to the presence of heteroatoms in the ring are also clearly seen (see Table 1 and Figs. 1 and 2). The result of the influence of the nitrogen atom cause the free energy of sorption $\Delta G_i^0(CH_2)$ in *N*-alkylsubstituted heterocycles to be appreciably lower than the average additive value of $-\Delta G_n^0(CH_2)$ which is characteristic of $n \geq 3$. At the same time the $\Delta G_i^0(CH_2)$ value for *n*-alkylcyclohexanes is abnormally high. The effect of the nitrogen atom rapidly decreases along the chain. As a result, the $\Delta G_n^0(CH_2)$ values for all studied series at $n \geq 3$ (Fig. 1 and Table 1) are close to each other at a given temperature irrespective of the presence, nature, and number of heteroatoms and also (as follows from Ref. 8) the presence of the methyl substituents in the cycle.

Thus, the abnormally high $-\Delta G_i^0(CH_2)$, $-\Delta H_i^0(CH_2)$, and $-\Delta S_i^0(CH_2)$ values (Table 1, Figs. 1 and 2) for the ethyl and methyl homologs are explained by the appearance of the most sorptionally active *gauche* fragment in the ethyl homolog. This fragment remains also in all other higher homologs. As a result, the curves of the dependence of $-\Delta G_n^0(CH_2)$ on *n* (Fig. 1) beginning with $n = 2$ adopt the shape characteristic of most homologous series of organic compounds containing functional groups.[1]

It can be assumed that an anomalous dependence of the retention parameters of the methylene unit on its number will be observed in the homologous series where (due to their spatial structure) lengthening the *n*-alkyl chain results in the appearance of additional *gauche* fragments. An analysis of the published data shows that the dependences of the increment of the retention index of the methylene unit $\Delta I_n(CH_2)$ on *n* in the series of alkylcyclopentanes, alkyl-1- and -3-cyclopentenes, alkyl-1-, -3- and -4-cyclohexenes,[5] as well as those of aliphatic hydrocarbons, where the *n*-alkyl chain is linked to the secondary or tertiary carbon atom,[17] also have an extremum with minimal values at $n = 2$.

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