Gas chromatographic determination of the free energy of sorption of methylene units of *N*-alkylsubstituted six-membered cyclic amines

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The free energy of sorption of methylene units, $\Delta G(CH_2)$, for the homologous series of *N*-alkylsubstituted morpholines, thiomorpholines, piperidines and 2-methyl-, 3-methyl-, 4-methyl- and 2,6-dimethylpiperidines was determined. It was shown that the dependence of these values on the number of CH_2 units in the carbon chain is not linear. Universal equations for calculating the values of the energy contribution depending on the number of CH_2 units in the carbon chain were obtained. Abnormally high values of free energy of sorption of the first CH_2 unit were found in all series studied and reasons for the anomaly are discussed.

Key words: capillary gas chromatography; *N*-alkylsubstituted piperidines; morpholines; thiomorpholines; free energy of sorption of CH_2 units.

Previous investigations of the gas chromatographic (GC) behavior of a large number of homologous series of mono and bifunctional aliphatic compounds demonstrated the nonequivalence of the energy contributions of different methylene units $\Delta G(CH_2)$ to the overall differential molar free energy of sorption of the homologs.[1,2] For most of the series the $\Delta G(CH_2)$ values vary significantly for the first five members, and the first methylene unit has the lowest value.[1] Only for some mono and dicarbonyl-containing homologous series were the values of $\Delta G(CH_2)$ of the first methylene unit bigger than those of the second.[2,3]

In the present work the dependence of the partial molar free energy of sorption of methylene units on the molecular mass of the homologs for seven homologous series of *N*-*n*-alkyl-substituted piperidines, morpholines, and thiomorpholines was investigated.

Experimental

A series of *N*-*n*-alkylmorpholines (**1**), *N*-*n*-alkylthiomorpholines (**2**), *N*-*n*-alkylpiperidines (**3**), *N*-*n*-alkyl-2-methyl (**4**), *N*-*n*-alkyl-3-methyl (**5**), *N*-*n*-alkyl-4-methyl (**6**), and *N*-*n*-alkyl-2,6-dimethylpiperidines (**7**) with a number of homologs up to 6—7 were analyzed (Table 1). Chromatographic analysis was performed on a Carlo Erba gas chromatograph model 5300 Mega series at 110 °C on glass capillary columns coated with OV-101/KF(40 m × 0.27 mm) and PEG-40M/KF(40 m × 0.22 mm) (stationary phase thickness d_f = 0.4 μm), prepared as in Ref. 4. The injector temperature was 150 °C, detector temperature 200 °C, split ratio 1:30, sample volume was 0.1—0.3 μL of a 1—2 % pentane solution of investigated substances. The values of the partial molar free energy of sorption of the methylene units, $\Delta G(CH_2)$, were determined by the equation:

$$\Delta G(CH_2) = -RT \ln(t'_{m+1}/t'_m), \quad (1)$$

where R = 8.31 J mol^{-1} K^{-1}; T — analysis temperature, K; t'_{m+1} and t'_m — corrected retention times of neighboring homologs of *N*-alkylsubstituted heterocyclic compounds.

Results and Discussion

The values of $\Delta G(CH_2)$ calculated by Eq. (1) are listed in Table 1. The retention indices of all of the compounds and the coefficients of the universal equation linking the retention index with the homolog number were obtained earlier.[5,6] The data listed in Table 1 show that an increase in phase polarity is accompanied by a decrease in values of $\Delta G(CH_2)$, as for all earlier studied homologous series of organic compounds.[1] The introduction of a second sulfur heteroatom into the piperidine ring exerts a very weak influence on $\Delta G(CH_2)$ of *N*-alylthiomorpholines both on polar and nonpolar phases. The values of $\Delta G(CH_2)$ for *N*-*n*-alkylpiperidines and *N*-*n*-alkylthiomorpholines have a practically similar trend, changing from −1.62 to −1.90 kJ mol^{-1} on OV-101/KF, and from −1.15 to −1.64 kJ mol^{-1} on PEG-40M/KF. The introduction of an oxygen atom into the piperidine ring leads to an increase in the energy contributions of the first methylene units. Thus, the values of $\Delta G(CH_2)$ for the first methylene unit of *N*-*n*-alkylmorpholines on OV-101/KF and PEG-40M/KF are respectively −1.70 and −1.35 kJ mol^{-1}. Therefore the pre-

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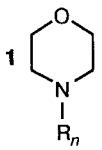
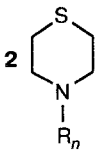
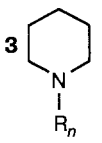
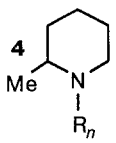
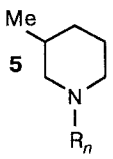
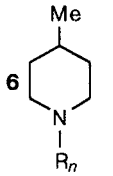
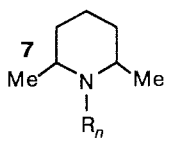
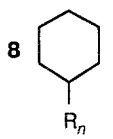
Table 1. The partial molar free energy of methylene units ($\Delta G(CH_2)$/kJ mol^{-1}) and error of determination (s/kJ mol^{-1}) for homologous series of cyclic amines and *n*-alkylcyclohexanes on glass capillary columns with OV-101/KF and PEG-40M/KF at 110 °C

Homologous series	Number of CH_2-units	OV-101/KF		PEG-40M/KF	
		$-\Delta G(CH_2)$	s	$-\Delta G(CH_2)$	s
 **1**	1	1.70	0.03	1.35	0.02
	2	1.61	0.02	1.10	0.01
	3	1.86	0.01	1.61	0.01
	4	1.90	0.01	1.66	0.01
	5	1.90	0.01	1.64	0.01
 **2**	1	1.64	0.02	1.15	0.01
	2	1.58	0.01	1.00	0.01
	3	1.85	0.01	1.56	0.01
	4	1.88	0.01	1.62	0.01
	5	1.90	0.01	1.62	0.01
 **3**	1	1.62	0.02	1.15	0.01
	2	1.56	0.01	1.02	0.01
	3	1.84	0.01	1.59	0.01
	4	1.88	0.01	1.64	0.01
	5	1.90	0.01	1.64	0.01
 **4**	1	1.64	0.02	1.18	0.02
	2	1.54	0.01	1.04	0.01
	3	1.82	0.01	1.60	0.01
	4	1.82	0.01	1.61	0.01
	5	1.86	0.01	1.66	0.02
	6	1.88	0.01	1.66	0.02
 **5**	1	1.53	0.03	1.08	0.02
	2	1.53	0.02	1.03	0.01
	3	1.80	0.01	1.57	0.02
	4	1.84	0.01	1.63	0.01
	5	1.89	0.01	1.65	0.01
	6	1.88	0.01	1.69	0.02
 **6**	1	1.56	0.01	1.20	0.02
	2	1.55	0.01	1.04	0.01
	3	1.83	0.01	1.56	0.01
	4	1.85	0.01	1.65	0.01
	5	1.88	0.01	1.65	0.01
	6	1.89	0.01	1.68	0.01
 **7**	1	1.62	0.01	1.31	0.01
	2	1.52	0.01	1.10	0.01
	3	1.81	0.01	1.58	0.01
	4	1.81	0.01	1.58	0.01
	5	1.88	0.01	1.65	0.01
	6	1.88	0.01	1.67	0.01
 **8**	1	2.15	0.03	—	—
	2	1.84	0.01	—	—
	3	1.91	0.01	—	—
	4	1.91	0.01	—	—
	5	1.92	0.01	—	—

sence in the heterocycle molecule of a second heteroatom more electronegative than sulfur, *i.e.*, an oxygen atom exerts a stronger influence on $\Delta G(CH_2)$ of the investigated compounds. The presence of methyl groups in the piperidine ring (homologous series **4**—**7**) exerts only a slight influence on the values of $\Delta G(CH_2)$ either on polar or nonpolar phases.

For most of the homologous series of organic compounds the minimum values of $\Delta G(CH_2)$ are observed for the first methylene units.[1] In this case the contribution of the first methylene unit is comparable to or even slightly higher than that for the second unit, especially on a polar column packed with PEG-40M/KF (see Table 1). The usual monotonic increase in the contribution of $\Delta G(CH_2)$ to the sorption energy of the homolog with the increase in chain length is then observed, beginning with the second CH_2 unit. The inequality of the $\Delta G(CH_2)$ contributions is reflected in the nonadditive nature of the alteration of the retention indices of the investigated homologs.[5,6] It should be noted that increased values of the contributions of the first CH_2 units to the sorption energy and the homolog retention indices have been observed for carbonyl compounds: homologous series of *n*-alkyl methyl ketones, *n*-alkyl butyl ketones, and methyl mono and dicarboxylates.[2,3]

For the *n*-alkylcyclohexanes[7,8] having a molecular conformation analogous to that of the investigated six-membered cyclic amines[9] the increased contribution of the first methylene unit to values of the retention indices was also noted. We determined the values of $\Delta G(CH_2)$ for *n*-alkylcyclohexanes on unpolar column with OV-101/KF (see Table 1). The data listed in Table 1 show that the dispersion interaction capacity of a CH_2-unit of *n*-alkylcyclohexanes with OV-101/KF is 25 % higher than that of *N*-alkylpiperidines, which is possibly explained by the influence of the nitrogen atom directly bonded with growing alkyl group. In the case of *n*-alkylcyclohexanes the $\Delta G(CH_2)$ value for the first methylene unit is significantly higher than that for the investigated *N*-*n*-alkylheterocyclic compounds and is equal to -2.15 kJ mol^{-1}. It is believed that the increase in $\Delta G(CH_2)$ for the first methylene unit of carbonyl compounds is caused by the intramolecular interaction of the hydrogen atoms of the CH_3 units of the first homolog with the carbonyl group resulting in abnormally weak retention of the first methyl homolog.[2,3] In our case the cause of the anomaly is not fully clear. The influence of the nitrogen atom on the contributions of the CH_2 units of alkyl substituents directly bonded with it is doubtless. At the same time the comparison of the

data listed in Table 1 with earlier described results[8,9] and our experimental data on the chromatographic behavior of *n*-alkylcyclohexanes (see Table 1) allows one to propose that the abnormal behavior of homologous series of tertiary cyclic amines is caused not only by redistribution of the electron density at the cyclic nitrogen atom but also by conformational factors.

Although the values of $\Delta G(CH_2)$ for the 4th—6th methylene units of *N*-alkylheterocycles are close or are equal to each other for all the investigated series on both of the columns, still they do not reach the $\Delta G(CH_2)$ values for *n*-alkanes C_8—C_{14}, with the same retention times, which are equal to -1.93 kJ mol^{-1} on OV-101/KF and -1.74 kJ mol^{-1} on PEG-40M/KF, or the respective values for alkylcyclohexanes.

The data listed in Table 1 show that for all of the investigated series of heterocyclic amines and *n*-alkylcyclohexanes the energy contributions of the CH_2 units to the absorption energy of the homologs are not uniform for each of the series. The $\Delta G(CH_2)$ values depend on the chain length of the alkyl substituent according to a universal equation, which was proposed earlier in order to describe the retention of homologs:[10]

$$\Delta G(CH_2) = \alpha + \beta m + \gamma(\ln m)/m + \xi/[(m-2)^2 + 0.1], \quad (2)$$

where m is the number of CH_2 units. The coefficients of Eq. (2) for all of the investigated homologous series are listed in Table 2. The standard deviation (s) of the $\Delta G(CH_2)$ values calculated according to Eq. (2) is within the limits of experimental error of $\Delta G(CH_2)$ determination and does not exceed 0.03 kJ mol^{-1}. These equations can be used for *a priori* calculations of $\Delta G(CH_2)$ values for homologs absent from Table 1.

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Table 2. Coefficients of Eq. (2) for the calculation of $\Delta G(CH_2)$ values (in kJ mol^{-1}) for homologous series of cyclic amines and *n*-alkylcyclohexanes on glass capillary columns with OV-101/KF and PEG-40M/KF at 110 °C

Homologous series	$-\alpha$	$-\beta$	$-\gamma$	$-\zeta$	s*
		OV-101/KF			
1	1.706	0.0174	0.35	−0.0253	0.005
2	1.639	0.0244	0.44	−0.0259	0.001
3	1.615	0.0291	0.44	−0.0267	0.001
4	1.641	0.0230	0.33	−0.0259	0.011
5	1.518	0.0348	0.56	−0.0252	0.011
6	1.556	0.0273	0.58	−0.0260	0.005
7	1.615	0.0287	0.33	−0.0265	0.016
8	2.171	−0.0121	−0.60	−0.0101	0.003
		PEG-40M/KF			
1	1.392	0.0080	0.69	−0.0545	0.008
2	1.173	0.0286	0.98	−0.0569	0.005
3	1.177	0.0254	1.07	−0.0579	0.002
4	1.199	0.0303	0.94	−0.0546	0.014
5	1.078	0.0486	1.07	−0.0515	0.004
6	1.208	0.0397	0.80	−0.0524	0.011
7	1.318	0.0337	0.50	−0.0456	0.018

* s — standard deviation of $\Delta G(CH_2)$ in kJ mol^{-1}.

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