Sorption characteristics of *N*-alkylimidazoles under conditions of capillary chromatography

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The retention indices for *N*-*n*-alkyl (C_1—C_5) substituted imidazoles with Me, Et, Pr, and Bu groups in different positions of the cycle were determined. Two capillary columns with OV-101/KF and PEG-40M/KF were used. The two nitrogen atoms of the imidazole molecule were shown to have different effects on the contributions of the alkyl groups to the retention indices. The maximum and minimum contributions are observed for the substituents at the 5 and 4 positions of the imidazole cycle, respectively. An increase in a size of the C_mH_{2m+1} substituent attached to the N(1) atom has a notable effect only on the contributions of the alkyl groups at the 2 and 5 positions. The retention indices values for a homologous series with an *n*-alkyl group attached to the N or C(2) atom were described by a universal type equation. The obtained equations can be used for predicting the retention indices of new homologs and identification of *N*-alkylimidazoles in complex mixtures.

Key words: capillary gas chromatography, homologous series, alkyl substituted *N*-alkylimidazoles, retention indices, equations, contributions of alkyl groups at the C and N atoms.

Alkyl substituted imidazoles are used as medicines[1] and can be components of food volatiles.[2,3] There are only a few reports on gas chromatographic analysis of imidazoles.[4,5] *N*-alkyl substituted and unsubstituted imidazoles have been separated on a packed column with OV-17 (see Ref. 4). Earlier,[5] we proposed schemes for predicting the retention indices of *N*-alkylimidazoles under conditions of capillary chromatography.

In the present work, the specific features of the sorption of a homologous series of *N*-alkyl substituted imidazoles containing Me-, Et-, Pr-, and Bu substituents in the cycle were investigated in order to elucidate the effects of the N atoms and the size of the substituent on the retention indices.

Experimental

Analyses were carried out on a Pye Unicam-104 chromatograph modified for working with capillary columns. A flame-ionization detector was used at a detector temperature of 200 °C and an injector temperature of 220 °C. We used two glass capillary columns: one with OV-101/KF (50 m×0.3 mm), with the thickness of the layer of the stationary phase d_f = 0.4 μm, and one with PEG-40M/KF (30 m×0.3 mm, d_f = 0.2 μm). Analyses were done at 150 and 180 °C, respectively. The columns were prepared according to the known procedure.[6] The samples of the compounds under study were injected as 0.1-0.2 μL of a 1 % solution in benzene. The retention indices of *N*-alkylimidazoles were determined with respect to *n*-alkanes C_9—C_{15}. The mean values of the indices (*I*) obtained from 5—7 measurements are given in Table 1. The reproducibility of the retention indices was ±1 i.u.

Results and Discussion

Of the six homologous series of *N*-alkylsubstituted imidazoles (see Table 1), the *N*-alkyl-2-ethyl- and *N*-alkyl-2-butylimidazoles series, as well as *N*-propyl-2-propylimidazole were studied in this work for the first time. In the case of the other compounds, the *I* values obtained on the columns with OV-101/KF at 110 °C and with PEG-40M/KF at 170 °C were reported earlier.[5] To obtain comparable results, the retention indices were determined for all of the compounds included in Table 1 on a column with OV-101/KF at 150 °C and on a column with PEG-40M/KF at 180 °C.

There are three pairs of 1,2-dialkyl substituted isomeric imidazoles among the compounds given in Table 1, *viz.*, 1) *N*-methyl-2-ethyl- and *N*-ethyl-2-methyl-, 2) *N*-ethyl-2-butyl- and *N*-butyl-2-ethyl-, 3) *N*-methyl-2-butyl- and *N*-butyl-2-methyimidazoles. On the apolar column, the retention indices of the first and second isomer pairs are too close each other (see Table 1) for separation. Due to the longer alkyl chain, the retention indices of the third isomer pair differ more significantly, which allows them to be separated on an apolar column with OV-101/KF (see Table 1). On a polar column with PEG-40M/KF the isomer pairs cannot be separated.

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Table 1. Retention indices of alkyl substituted *N*-*n*-alkylimidazoles on capillary columns of different polarity

Imidazole	OV-101/KF, 150 °C	PEG-40M/KF, 180 °C
N-methyl-2-methyl-	1012	1757
N-ethyl-2-methyl-	1069	1774
N-propyl-2-methyl-	1153	1831
N-butyl-2-methyl-	1248	1918
N-methyl-2-ethyl-	1068	1773
N-ethyl-2-ethyl-	1125	1784
N-propyl-2-ethyl-	1206	1836
N-butyl-2-ethyl-	1296	1920
N-pentyl-2-ethyl-	1390	2007
N-methyl-2-butyl-	1238	1920
N-ethyl-2-butyl-	1291	1925
N-propyl-2-butyl-	1368	1970
N-butyl-2-butyl-	1457	2049
N-pentyl-2-butyl-	1549	2133
N-methyl-	944	1717
N-ethyl-	1012	1752
N-propyl-	1093	1810
N-butyl-	1187	1902
N-pentyl-	1281	1997
N-methyl-4-methyl-	991	1729
N-ethyl-4-methyl-	1062	1764
N-propyl-4-methyl-	1138	1811
N-butyl-4-methyl-	1235	1902
N-pentyl-4-methyl-	1329	1999
N-methyl-5-methyl-	1090	1885
N-ethyl-5-methyl-	1148	1901
N-propyl-5-methyl-	1217	1951
N-butyl-5-methyl-	1313	2038
N-pentyl-5-methyl-	1406	2134
N-propyl-2-propyl-	1277	1881

The contribution of the alkyl substituent (δI^{Alk}) for the five homologous series was calculated with Eq. (1):

$$\delta I^{Alk} = I(AlkIm) - I(Im), \quad (1)$$

where I(AlkIm) and I(Im) are the retention indices of *N*-alkylimidazoles that do and do not contain alkyl substituents in the cycle, respectively.

The calculated δI^{Alk} values are given in Table 2. The Me substituent at position 2 is in the α-position to two nitrogen atoms, and its contribution to the retention, δI^{Me}, is 68 on the apolar column. Meanwhile, the contribution of the Me substituent at position 5, *i.e.*, in the α-position to one alkyl substituted N atom, is abruptly increased (δI^{Me} = 146 i. u.), due to the asymmetrical distribution of the electron density on the C(2) and C(5) atoms of the cycle.

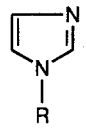
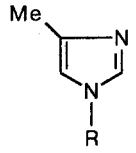
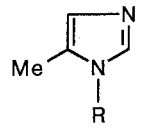
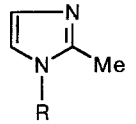
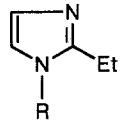
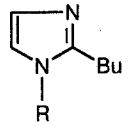
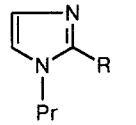
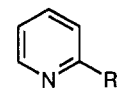
The δI^{Alk} value for the 2- and 5-alkyl substituted compounds is maximum for the first homolog. Increasing the weight of the alkyl group attached to the N atom gradually decreases the contribution of δI^{Me} in positions 2 and 5 and does not significantly affect the contribution of the substituent in position 4. Thus, the length of the alkyl substituent bonded directly to the N atom in the imidazole cycle affects the energy of the disperse interaction of only the alkyl substituents in the α- and α′-positions to this N atom.

On the polar phase PEG-40M/KF, the contributions of the C_1—C_4 alkyl substituents also differ considerably and depend on their position in the cycle. For example, the δI^{Alk} value varies from 0 to 168 i.u. for the methyl substituent. The contribution of the Me(5) group in the α′-position with respect to the N-alkyl group of the cycle is greater on the polar sorbent (PEG) than on the non-polar sorbent. In the case of a polar sorbent, it is difficult to reveal the physical meaning of these contri-

Table 2. Contributions of the alkyl substituents (δI^{Alk}/i.u.) to the values of the retention indices of the substituted *N*-alkylimidazoles on capillary columns of different polarity

N-alkyl group	Alk (position in the cycle)	δI^{Alk} OV-101/KF, 150 °C	δI^{Alk} PEG-40M/KF, 180 °C
Me	Me (2)	68	40
Et		57	22
Pr		60	21
Bu		61	16
Me	Et (2)	124	56
Et		113	32
Pr		113	26
Bu		109	18
Pent		109	10
Pr	Pr (2)	184	71
Me	Bu (2)	294	203
Et		279	173
Pr		275	160
Bu		270	147
Pent		268	136
Me	Me (4)	47	12
Et		50	12
Pr		45	1
Bu		48	0
Pent		48	2
Me	Me (5)	146	168
Et		136	149
Pr		124	141
Bu		126	136
Pent		125	137

Table 3. Contributions of the methylene units, $\delta I(CH_2)$, for a homologous series of *N*-alkyl substituted imidazoles on capillary columns of different polarity

Homologous series ($R = C_mH_{2m+1}$)		$\delta I(CH_2)$/i.u.							
		OV-101/KF, 150 °C				PEG-40M/KF, 180 °C			
		1	2	3	4	1	2	3	4
1 	$m = 1 \div 5$	68	81	94	94	35	58	92	95
2 	$m = 1 \div 5$	71	76	97	94	35	47	91	97
3 	$m = 1 \div 5$	58	69	96	93	16	50	87	96
4 	$m = 1 \div 4$	57	84	95	—	17	57	87	—
5 	$m = 1 \div 5$	57	81	90	94	11	52	84	87
6 	$m = 1 \div 5$	53	77	89	92	5	45	79	84
7 	$m = 1 \div 4$	53	71	91	—	5	45	89	—
8* 	$m = 1 \div 4$	84	90	100	—				

* The temperature of the analysis was 110 °C.

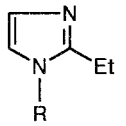
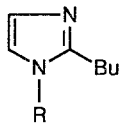
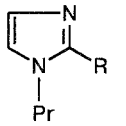
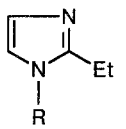
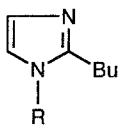
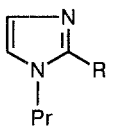
butions due to the absence of data on the distribution of electron density for the compounds that were used for calculating δI^{Alk}. The unusually great contributions of Me(5), which exceed those for this group on the non-polar column, attest to a combined effect, *viz.*, the electronic influence of the α′-alkyl group and an additional contribution due to the fact that the energy of the polar interaction between the substrate and the sorbent is higher than that of the unsubstituted *N*-alkylimidazole that was used for the calculation with Eq. (1).

Two types of homologous series are possible for *N*-alkylimidazoles, wherein the alkyl group is attached either to the "pyrrole" nitrogen atom ($N—C_mH_{2m+1}$) or to a carbon atom of the cycle ($C—C_mH_{2m+1}$). The results of calculating the homologous difference $\delta I(CH_2)$ in these series with Eq. (2) are given in Table 3. For comparison, the $\delta I(CH_2)$ values for α-*n*-alkylpyridines are also given. The $\delta I(CH_2)$ values reflect the variation of the disperse interaction with the sorbent of a column:

$$\delta I(CH_2) = I_{m+1} - I_m, \qquad (2)$$

were I_{m+1}, I_m are the retention indices of the neighboring homologs. In all of the *N*-alkylimidazole

Table 4. Coefficients of universal Eq. (3) for the calculation of the retention indices of the homologs of *N*-alkyl substituted imidazoles on capillary columns of different polarity

Homologous series (R=C_mH_{2m+1})		Coefficient of Eq. (3)				s*/i.u.
		α	β	γ	ε	
		OV-101/KF, 150 °C				
	m = 1÷5	977.5	89.80	−115.1	0.78	0.6
	m = 1÷5	1149.0	88.10	−127.1	0.99	0.4
	m = 1÷4	1062.3	89.20	−148.6	1.68	0.0
		PEG-40M/KF, 180 °C				
	m = 1÷5	1690.1	80.59	−268.2	2.57	0.1
	m = 1÷5	1840.9	76.43	−281.9	2.89	0.4
	m = 1÷4	1742.6	85.02	−327.8	3.69	0.0

* s is the standard deviation.

homologous series, the further a CH_2-unit from the N atom, the greater its contribution to the total value of the retention index of the homolog. The greatest contributions for the first methylene units are observed in the case of the *N*-alkyl substituted series that contain no substituents at the C(2) and C(5) atoms of the cycle (see Table 3, series 1 and 2). Regardless of the type (Me, Et, Bu) and position (2 or 5) of a substituent, the contribution of the first methylene unit is almost the same (53 and 58 i.u. on an apolar column and 5 and 17 i.u. on a polar column), which indicates only a weak effect of the α- and α′-alkyl groups on the energy of the disperse interaction between the column sorbent and the *N*-alkyl substituent (see Table 3, series 3—6).

The homologous difference of the methylene units in *N*-propyl-2-*n*-alkylimidazoles (Table 3, series 7) changes similarly to that of *N*-*n*-alkyl-2-butylimidazoles, which probably indicates that the influence of the "pyrrole" N atom on the C_mH_{2m+1} substituent bonded directly to the N atom or to the α-C atom of the cycle is the same. A comparison between the values of $\delta I(CH_2)$ in the C—R_m- and N—R_m-series of substituted imidazoles and those of the 2-*n*-alkylpyridines series reveals a significant difference in the contributions of the first methylene unit, probably due to the fact that the electron density on the "pyrrole" N atom is greater than that on the pyridine N atom.

It was shown earlier[7] that the variation of the retention indices for the homologous series is described by a universal equation:

$$I = \alpha + \beta m + \gamma \frac{\ln m}{m} + \frac{\varepsilon}{(m-2)^2 + 0.1}, \qquad (3)$$

where m is the homolog number; α, β, γ, and ε are coefficients that are constant for the analysis conditions and the homologous series under investigation.

As an example, we used Eq. (3) to describe the GC behavior of the homologous series of 2-ethyl-*N*-*n*-alkyl, 2-*n*-butyl-*N*-*n*-alkylimidazoles, and *N*-*n*-propyl-2-*n*-alkylimidazoles. The coefficients obtained for the homologs on columns with OV-101/KF and PEG-40M/KF and the accuracy of the calculations are given in Table 4.

These values can be used to identify the investigated compounds in mixtures and to predict the retention indices of other homologs.

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