Peculiar features of sorption of positional isomers of formyl-, acetyl-, and aminopyridines in capillary gas-liquid chromatography

*M. B. Terenina, I. L. Zhuravleva, and R. V. Golovnya**

N. M. Emanuel' Institute of Biochemical Physics, Russian Academy of Sciences, 28 ul. Vavilova, 117813 Moscow, Russian Federation.
Fax: 007 (095) 135 5085

The GLC retention parameters of α-, β-, and γ-isomers of formyl-, acetyl-, and aminopyridines were determined on two columns with stationary phases of different polarities. The contributions of formyl, acetyl, methyl, and amino groups located in the α-, β-, and γ-positions of the ring to the retention indices were calculated. The contributions of these groups to the retention were found to depend on their positions with respect to the N atom of the ring and are the smallest for α-substituents. The difference between pyridines containing electron-withdrawing substituents and those containing electron-donating substituents is manifested as different orders of elution of α-, β-, and γ-derivatives. The distinctions between the GLC behaviors of pyridines, benzenes, and furans with the same substituents were identified.

Key words: capillary gas-liquid chromatography, retention indices; substituted pyridines, positional isomers.

Interest in compounds of the pyridine series is due to the fact that many of them exhibit physiological activity, are constituents of drugs and pesticides, and have been found among the components of the odor of foodstuffs. Among compounds of the pyridine series, alkyl-substituted derivatives[1—5] and some derivatives with functional groups[6] have been studied by gas chromatography. The retention parameters of these compounds were found to depend on the positions of substituents in the ring.

In the present work, we studied characteristic features of sorption of substituted pyridines containing electron-withdrawing and electron-donating substituents, in order to estimate quantitatively the contribution of a substituent to the retention index as a function of its position in the ring and its remoteness from the N atom.

Experimental

Pyridine and isomeric methyl-, formyl-, acetyl-, and aminopyridines were used as investigation objects (Table 1). Two glass capillary columns (50 m × 0.3 mm) filled with OV-101 and PEG-40M (see Ref. 7) were used. The thickness of the stationary phase film d_f was 0.4 mm. Analyses were carried out under isothermal conditions at 110 and 150 °C on a Carlo Erba-5300 chromatograph of the "Mega" series (Italy) with a flame ionization detector. The temperature of the detector was 250 °C, and the injector temperature was 200 °C. The carrier-gas (He) flow was split at the inlet of the column in a ratio of 1 : 30.

Solutions containing 8—15 mL of each substance in 1 mL of a solvent (diethyl ether for formyl and acetyl derivatives or benzene for aminopyridines) were prepared for the analysis. To determine retention indices, solutions of C_6—C_{23} *n*-alkanes in pentane were used. The volume of an injected sample was 0.1—0.3 mL. The retention indices calculated from six or seven measurements are listed in Table 1.

Results and Discussion

Pyridine derivatives containing CHO, Ac, NH_2, and Me substituents in various positions of the ring (see Table 1) were analyzed on two columns packed with phases of different polarities. The effect of the sorbent polarity was evaluated from the difference between the retention indices (ΔI) determined for these two columns.

To estimate quantitatively the effects of substituents on the sorption, we calculated the contributions (δI) of substituents to the retention indices (Table 2). Pyridine and picolines were used as the initial compounds for the determination of the contributions; they were chromatographed under the same conditions. It can be seen from the data listed in Table 2 that the δI value for a substituent depends on its character and its position in the ring and on the polarity of the stationary phase. Unlike the contributions of alkyl groups,[1,2,6] the contributions of polar substituents in the pyridine ring to the retention indices increase as the polarity of the phase increases, which is due to the strong donor-acceptor interaction between them.

Whereas the retention indices of dialkyl-substituted pyridines can be predicted using additive schemes from

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Table 1. Boiling points, dipole moments (μ), retention indices (I), and differences between the retention indices (ΔI/iu) for substituted pyridines and benzenes on capillary columns of different polarities at 150 °C

Compound	B.p./°C[8] (p/Torr)	μ/D[9]	I/iu		ΔI/iu
			OV-101	PEG-40M	
Benzene	79.1	0	677*	925	248
Benzaldehyde	179.0	2.75	976*	1533	557
Acetophenone	202.0	2.97	1077*	1655	578
Pyridine	115.0	2.11	756*	1195	439
			762	1195	433
2-Formylpyridine	181.0	3.35	968*	1570	602
3-Formylpyridine	96 (15)	2.37	1044*	1717	643
4-Formylpyridine	78 (12)	1.74	1025*	1668	643
2-Acetylpyridine	188.5	2.85	999*	1608	609
3-Acetylpyridine	220.0	2.53	1128*	1833	705
4-Acetylpyridine	212.0	2.41	1112*	1800	688
2-Aminopyridine	204.0—210.0	2.04	1058	1892	834
3-Aminopyridine	248.0	3.12	1182	2156	974
4-Aminopyridine	273.0	3.95	1270	2278	1008
2,6-Diaminopyridine	115.0	1.46	1377	—	—
2-(Aminomethyl)pyridine	84 (12)	2.25	1075	1748	673
2-Amino-4-methylpyridine	230.0	2.27	1153	2001	848
2-Amino-5-methylpyridine	227.0	2.02	1148	1984	836
3-Methylpyridine	144.0.	2.30	877	1310	433
4-Methylpyridine	145.0	2.57	877	1316	439

* Compounds were analyzed at 110 °C.

Table 2. Contributions of substituents (δI) to the magnitudes of retention indices on capillary columns of different polarities

Compounds being compared	Substituent	δI/iu	
		OV-101	PEG-40M
Heptanal—hexane[10]	CHO	299	607
Benzaldehyde—benzene	CHO	299	608
2-Formylpyridine—pyridine	α-CHO	212	375
3-Formylpyridine—pyridine	β-CHO	288	522
4-Formylpyridine—pyridine	γ-CHO	269	473
Nonan-2-one—heptane[10]	Ac	393	720
Acetophenone—benzene	Ac	400	730
2-Acetylpyridine—pyridine	α-Ac	243	413
3-Acetylpyridine—pyridine	β-Ac	372	638
4-Acetylpyridine—pyridine	γ-Ac	356	605
Aniline—benzene[11]	NH_2	—	763
2-Aminopyridine—pyridine	α-NH_2	296	697
3-Aminopyridine—pyridine	β-NH_2	420	961
4-Aminopyridine—pyridine	γ-NH_2	508	1083
2,6-Diaminopyridine—2-aminopyridine	α-NH_2 (α′-NH_2)	319	—
2-Amino-5-methylpyridine—3-methylpyridine	α-NH_2 (β′-Me)	271	674
2-Amino-4-methylpyridine—4-methylpyridine	α-NH_2 (γ-Me)	276	685
Toluene—benzene[10]	Me	100	100
2-Methylpyridine—pyridine[2]	α-Me	66	30
3-Methylpyridine—pyridine	β-Me	115	115
4-Methylpyridine—pyridine	γ-Me	115	121
2-Amino-5-methylpyridine—2-aminopyridine	β-Me (α′-NH_2)	90	92
2-Amino-4-methylpyridine—2-aminopyridine	γ-Me (α-NH_2)	95	109

the contributions of the alkyl groups, determined for the corresponding monosubstituted derivatives,[3,5] in the case of compounds under consideration, the additive schemes do not work. The calculated retention indices of 2,6-diamino-, 2-amino-4-methyl-, and 2-amino-5-methylpyridines differ by 20—25 index units (iu) from those obtained experimentally for a column packed with a nonpolar stationary phase. This indicates that the

electron density of the ring and of the substituents has been substantially redistributed in the molecules of functional pyridine derivatives.

For comparison, we calculated the contributions δI of the CHO, Ac, NH_2, and Me groups in benzene derivatives and in aliphatic compounds (see Table 2). It was found that the contributions of the CHO and Ac groups to the retention indices of substituted pyridines are smaller than the corresponding values for benzaldehyde, acetophenone, and aliphatic compounds (see Table 2). Substituents located in the α-position with respect to the heteroatom experience an especially strong effect. Whereas the contribution of the formyl group in benzaldehyde is 299 iu for chromatography on OV-101 or 608 iu for PEG-40M, the same values for 2-formylpyridine are 212 and 375 iu, respectively. The contribution of an α-acetyl group in pyridine decreases with respect to its contribution in acetophenone to an even greater degree (see Table 2). Thus, as in the case of alkylpyridines, we have observed a negative α-effect,[2] which is manifested as a decrease in the contribution of a substituent located in the α-position with respect to the heteroatom compared to the contribution of the corresponding functional group in benzene. Unlike the contributions of β- and γ-alkyl substituents in alkylpyridines, which are identical in the case of a column with a nonpolar stationary phase and are very close for a column with a polar phase[3] (see Table 2), the contributions of β- and γ-formyl and acetyl groups in pyridine are markedly different both on polar (by 49 iu for CHO) and on nonpolar (by 19 iu for CHO) phases. In addition, the contributions of β-substituents are higher than those of γ-substituents, whereas in the case of β- and γ-Me groups, the opposite dependence is observed (see Table 2, PEG-40M). The higher contributions of β-carbonyl-containing groups account for stronger retention of β-formyl- and β-acetylpyridines compared to that of γ-isomers. The fact that the order of elution of β- and γ-substituted carbonyl-containing pyridines differs from that for alkylpyridines is probably due to the electron-withdrawing effect of the substituents. It has been shown[6] that in the series of pyridine derivatives containing an electron-withdrawing amide group, the β-isomer is also retained most strongly. Possibly, electron-withdrawing groups in the β-position decrease the electron density on the N atom of the ring to a lesser degree than similar α- and γ-substituents and thus increase the ability of the molecule to be involved in van der Waals interactions with the stationary phase.

Comparison of the characteristic features of sorption of pyridine derivatives and carbonyl-substituted sulfur-containing heterocyclic compounds[12] has shown that the contributions of the β-formyl and β-acetyl groups in pyridine (see Table 2) are close to those found for the corresponding β-groups in thiophene. For example, the contributions of β-CHO and β-Ac substituents to the retention indices of thiophenes on a nonpolar stationary phase are 288 and 382 iu, respectively.[12] The nature of the heteroatom, N or S, has an effect only if the substituent is located in the α-position with respect to it. In the case of pyridines, a negative α-effect is observed both for methyl and for carbonyl substituents (see Table 2), whereas in the case of thiophenes, this effect is negative only for Me but is positive for carbonyl groups,[12] *i.e.*, contributions of formyl and acetyl groups to the retention indices of thiophenes are higher in the case of α-substituted isomers than for β-isomers. A positive α-effect is also observed for pyridine derivatives with electron-withdrawing substituents such as an ester or cyano group.[6] These compounds are eluted in the following order: γ, β, and α (*i.e.*, α-cyanopyridine and methyl or ethyl α-pyridinecarboxylates are held most tightly). The redistribution of the electron density in the molecules of substituted pyridines, depending on the type of substituent and its position, has an effect on the GLC behavior of these compounds.

The GLC behavior of pyridine derivatives incorporating electron-donor substituents, *viz.*, amino groups, differs somewhat from that of carbonylpyridines. The positional isomers of aminopyridine are eluted in the normal order from both nonpolar and polar phases, *viz.*, α, β, and then γ, in conformity with their boiling points. The dipole moments of their molecules increase in the same order (see Table 1). The negative α-effect observed for alkyl-substituted pyridines is also manifested for these compounds, and to an even greater degree. Unlike the retention of alkyl derivatives for which the contributions of substituents in β- and γ-positions are virtually identical,[1,2] the retention of γ-aminopyridine is much greater than that of the β-isomer, especially in the case of the polar stationary phase. The contribution of the γ-amino group on PEG-40M is 1083 iu, which is larger than the contribution of the amino group in aniline (763 iu on PEG-20M).[11] γ-Aminopyridine has the largest dipole moment (see Table 1), and it is a stronger base than α- and β-aminopyridines or aniline.[13] The contribution of the α-NH_2 group changes somewhat if the molecule of the pyridine derivative contains other substituents (see Table 1). In the presence of the second α′-NH_2 group, it increases from 296 to 319 iu on OV-101, and when the molecule contains β- or γ-Me substituents, this contribution decreases to 271—276 iu for the same column. This attests to the mutual effect of the α-NH_2 and β- or γ-Me groups, which changes the ability of the molecule as a whole to be involved in the dispersion interaction with the stationary phase.

Table 1 also presents the differences (ΔI) between the retention indices determined for two columns. Since the retention indices on the column with the OV-101 nonpolar phase depend only slightly on the temperature of the analysis (*cf.* the I values for pyridine at 110 and 150 °C), the ΔI values obtained on both columns at 150 °C can be compared with the values obtained for OV-101 at 110 °C and for PEG-40M at 150 °C. It can

be seen from the data of Table 1 that the ΔI values for functional derivatives of pyridine are much higher than those for unsubstituted pyridine, picolines, and the corresponding benzene derivatives. For each group of compounds, the smallest ΔI values correspond to α-substituted isomers; the highest ΔI values are observed for amino derivatives, due to the ability of the amino group to be involved in the donor-acceptor interactions with PEG-40M. It is of interest that the increase in ΔI in the series of α-, β-, and γ-aminopyridines occurs in parallel with the increase in the dipole moments of the molecules. A different situation is observed in the case of carbonyl derivatives of pyridine: the ΔI values are the lowest in the case of α-isomers, which have the largest dipole moments.

The I, δI, and ΔI values that we found (see Tables 1 and 2) indicate that the GLC behavior of the positional isomers of functional derivatives of pyridine on columns with polar and nonpolar phases differs markedly from that of the corresponding alkyl derivatives. In the case of formyl-, acetyl-, and amino-substituted pyridines chromatographed on the methylsiloxane and poly(ethylene glycol) stationary phases, only a negative α-effect is observed. The GLC characteristics of the positional isomers of pyridine under consideration indicate that the heteroatom and the substituent participate actively in the electron density redistribution in the whole molecule, which has an effect on the intermolecular interaction with the stationary phase.

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