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Note

Use of modified molecular connectivity indices to predict retention indices of monosubstituted alkyl, alkoxy, alkylthio, phenoxy and (phenylthio)pyrazines

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We have estimated that the retention index (I) of a pyrazine derivative can be represented as the sum of the increments for substituent groups and the retention index of pyrazine[1].

The concept of molecular connectivity (χ) was introduced by Randić[2] and extensively developed by Kier and Hall[3,4] through the topological branching index. It has previously been demonstrated that a good correlation exists between chromatographic parameters, such as I and χ, for a series of similar compounds[5,6].

The present paper deals with our investigation of the relationship between connectivity indices and retention indices of monosubstituted pyrazines on OV-101 and CW-20M columns.

EXPERIMENTAL

Pyrazine and methyl- and ethylpyrazine were commercially available (Pyrazine Specialties). All other monoalkylpyrazines (4–14, Table I) were prepared as described in the literature[7]. Alkoxy- and (alkylthio)pyrazines (15, 16, 18 and 19) were prepared by the reaction of chloropyrazine with the appropriate sodium alkoxide or sodium thioalkoxide[8]. Phenoxy- and (phenylthio)pyrazine (17 and 20) were prepared from chloropyrazine by reaction with sodium phenoxide and sodium thiophenoxide, respectively[9].

The first-order connectivity index ($^1\chi$) was calculated according to the Kier and Hall's[3] equation:

$$^1\chi = \Sigma(\delta i \cdot \delta j)^{-\frac{1}{2}} \quad (1)$$

where δi and δj are the number of non-hydrogen bonds of the bonded carbon atoms i and j.

The gas chromatographic conditions were as described in the previous paper[1].

TABLE I

RETENTION INDICES FOR MONOSUBSTITUTED PYRAZINES ON CW-20M AND OV-101

$D = I^{st.ph.}_{obsd.} - I^{st.ph.}_{calcd.}$

No.	*R*	$I^{OV}_{obsd.}$	$I^{OV}_{calcd.}$	*D*	$I^{CW}_{obsd.}$	$I^{CW}_{calcd.}$	*D*
1	H	710	710	0	1179	1179	0
2	CH_3	801	801	0	1235	1235	0
3	C_2H_5	894	890	−4	1300	1299	−1
4	C_3H_7	986	989	3	1374	1388	14
5	C_4H_9	1088	1088	0	1474	1476	2
6	C_5H_{11}	1192	1188	−4	1575	1565	−10
7	C_6H_{13}	1293	1288	−5	1668	1653	−15
8	$CH(CH_3)_2$	949	954	5	1316	1335	19
9	$CH_2CH(CH_3)_2$	1043	1050	7	1406	1424	18
10	$(CH_2)_2CH(CH_3)_2$	1157	1150	−7	1530	1512	−18
11	$CH_2CH(CH_3)C_2H_5$	1151	1146	−5	1527	1522	−5
12	$CH_2CH(CH_3)C_3H_7$	1240	1245	5	1606	1610	4
13	$CH(CH_3)C_2H_5$	1040	1037	−3	1394	1388	−6
14	$CH(CH_3)C_3H_7$	1133	1136	3	1471	1476	5
15	OCH_3	877	864	−13	1306	1281	−25
16	OC_2H_5	959	968	9	1348	1372	24
17	OC_6H_5	1415	1427	12	2104	2123	19
18	SCH_3	1076	1088	12	1600	1607	7
19	SC_2H_5	1148	1151	3	1635	1642	7
20	SC_6H_5	1606	1594	−12	2400	2392	−8

RESULTS AND DISCUSSION

The relationship between the $^1\chi$ values and the observed retention indices of the homologous series of monosubstituted pyrazines on the OV-101 column ($I^{OV}_{obsd.}$; see Table I) was observed, to be linear (Fig. 1).

Fig. 2 shows that an approximately linear relationship exists between the retention indices for *n*-alkanes (C_nH_{2n+2}, n = 7–24) and their $^1\chi$ values. This relationship is approximated by eqn. 2:

$$I = 202.6\ ^1\chi \tag{2}$$

In this case, the relationship between the I and δ value may be given by eqn. 3:

$$I = 202.6\Sigma(\delta i \cdot \delta j)^{-\frac{1}{2}} \tag{3}$$

In order to determine the retention indices for various monosubstituted pyrazines from their structures, the $\delta^{st.ph.}$ values on a stationary phase were determined from the $I^{st.ph.}_{obsd.}$ values and eqn. 3.

First of all, when the $I^{st.ph.}_{obsd.}$ values of benzene ($I^{OV}_{obsd.}$ = 655, $I^{CW}_{obsd.}$ = 954) are substituted in eqn. 3, the δ^{OV} and δ^{CW} values for =C– (benzene, pyrazine) are determined to be 1.855 and 1.274, respectively. Then, substituting the $\delta^{st.ph.}$ values for

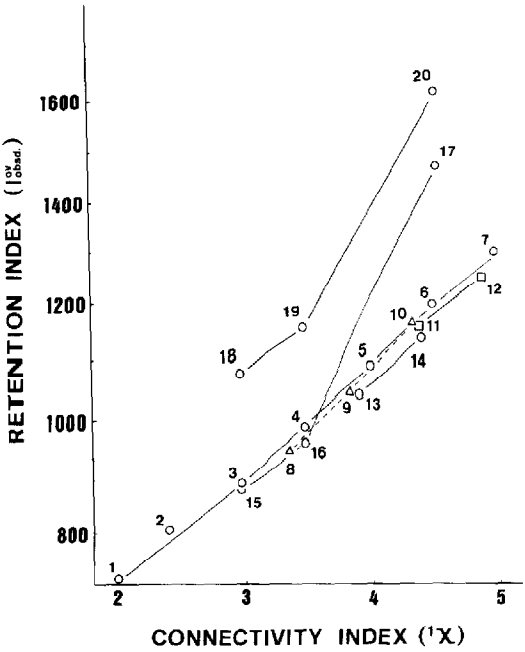

Fig. 1. Correlation of the observed retention indices for monosubstituted pyrazines on OV-101 column ($I^{OV}_{obsd.}$) with the first-order molecular connectivity indices ($^1\chi$).

$=C-$ (pyrazine, benzene) and the $I^{st.ph.}_{obsd.}$ value of pyrazine in eqn. 3 yields the $\delta^{st.ph.}$ value for $=N-$ (pyrazine). The $\delta^{st.ph.}$ values obtained in this way are shown in Table II along with δ values.

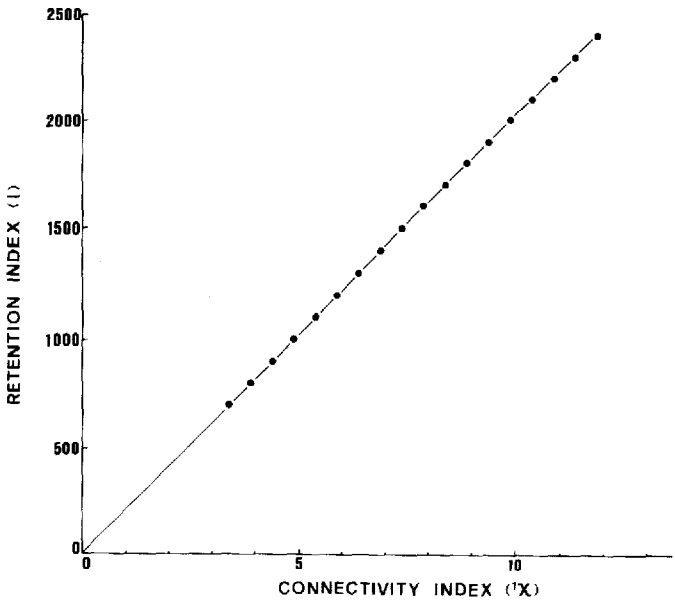

TABLE II

DELTA VALUES (δ, δ^{OV} AND δ^{CW}) FOR VARIOUS ATOMS

Group		δ	δ^{OV}	δ^{CW}
$-CH_3$		1	1.019	1.143
$-CH_3$	Substituted at pyrazine ring	1	0.776	0.799
$-CH_2-$		2	2.038	2.286
$-\overset{\vert}{C}H-$	*Iso-*	3	3.255	4.210
$-\overset{\vert}{C}H-$	*Sec-*	3	4.001	6.625
$-\overset{\vert}{C}H-$	Others	3	3.575	4.201
$=C-$	Pyrazine and benzene	3	1.855	1.274
$=\overset{\vert}{C}-R$	Substituted pyrazine and benzene	4	2.855	2.274
$=N-$	Pyrazine	3	1.462	0.695
$-O-$		2	2.581	2.730
$-S-$		2	0.574	0.385

Replacing the δ values in eqn. 3 by their corresponding $\delta^{st.ph.}$ values, we obtained the following expression:

$$I^{st.ph.} = 202.6\Sigma(\delta^{st.ph.} \cdot \delta^{st.ph.})^{-\frac{1}{2}} \quad (4)$$

It can be seen from eqn. 4 that as the $\delta^{st.ph.}$ value becomes smaller, the $I^{st.ph.}$ value becomes larger. The δ^{OV} value for the saturated alkyl groups (CH_3, $-CH_2-$ and $-\overset{\vert}{C}H-$) are smaller than the corresponding δ^{CW} values. The saturated alkyl groups contribute more to the retention indices on the OV-101 column than to those on the CW-20M column. That is to say, the non-polar solutes interact more strongly with a non-polar stationary phase than with a polar phase.

The $\delta^{st.ph.}$ values for a methyl group which is substituted at a pyrazine ring are smaller than those for other methyl groups. Such results are due to the hyperconjugation effect of the methyl group at the pyrazine ring.

The $\delta^{st.ph.}$ values for $-\overset{\vert}{C}H-$ groups follow the order *iso* < others < *sec*. Since the $I^{st.ph.}$ values depend on the intermolecular forces, a smaller surface area yields a larger $\delta^{st.ph.}$ value.

The δ^{CW} values for the polar groups, carbon atoms containing a double bond, nitrogen atoms and sulphur atoms are smaller than the corresponding δ^{OV} values, except for the oxygen atom. The results are explained on the basis of the stronger attractive forces between polar groups and a polar phase (CW-20M) than those between polar groups and a non-polar phase (OV-101).

The $\delta^{st.ph.}$ value for the $-S-$ group is much smaller than that for the $-O-$ group. The results are compatible with the fact that the boiling points of sulphur-containing pyrazines are higher than those of corresponding oxygen-containing pyrazines. Table I lists the observed and calculated retention indices ($I_{obsd.}$ and $I_{calcd.}$) for monosub-

stituted pyrazines on OV-101 and CW-20M columns. The difference between the observed and the calculated values (D) is decreased when a non-polar stationary phase (OV-101) is used.

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