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Note

Gas chromatographic analysis of tautomerizing amidines

Retention indices of N,N'-diphenylformamidines on a non-polar column*

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In the course of our studies on the applicability of gas chromatography to the analysis of amidines[1–6], the relationships between the structure and retention indices of trisubstituted amidines, $R_xN=CR_zN(R_y)_2$, have been investigated. We have found that in the series of amidines containing variable substituent R_x at the imino nitrogen atom the retention indices correlate well with those of corresponding simple model compounds such as substituted hydrocarbons, R_xH, or primary amines, R_xNH_2, taken as standards (Std), and that the correlations with primary amines are of much higher quality[2–4,6]:

$$I(\text{amidine}) = a \cdot I(\text{Std}) + b \tag{1}$$

where I are the Kováts[7,8] retention indices.

In the series of amidines containing variable substituents R_y at the amino nitrogen atom, their retention indices can be correlated with those of corresponding secondary amines, $R_yR'_yNH$. The conclusion was drawn that for the prediction of the retention indices of trisubstituted amidines a diparameter linear regresssion (eqn. 2) can be used[4].

$$I(\text{amidine}) = a_1 \cdot I(R_xNH_2) + a_2 \cdot I(R_yR'_yNH) + b \tag{2}$$

It was also found that, in most instances, the regression coefficients a are different from unity[2–4,6] and that they depend to some extent on the substituent R_z at the amidino carbon atom.[3] Therefore, the use of additivity rules may lead to erroneous results in many instances.

The above results concerned trisubstituted amidines, but N,N'-disubstituted amidines display tautomerism[9,10]:

$$R_xN=CR_zNHR_y \rightleftharpoons R_xNHCR_z=NR_y \tag{3}$$

* Amidines, Part XXVII; for Part XXVI, see ref. 6.

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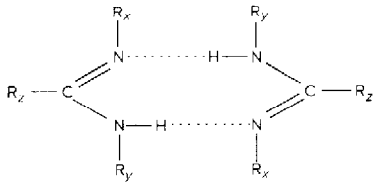
If the substituents R_x and R_y are not identical, the tautomers have different physical and chemical characteristics[9,11,12], so it would be expected that their retentions would also be different. On the other hand, it is known[9,10,13,14] that such amidines may form hydrogen-bonded cyclic dimers (I). It might be expected that the formation of the dimers would cause an increase in boiling points and a consequent increase in retention indices.



I

Thus the question arose of whether a diparameter regression of the type in eqn. 2 can be applied for the prediction of the retention indices of N,N'-disubstituted amidines, and how far the regression parameters differ from those for trisubstituted amidines. The value of a and b in eqn. 2 may serve as an indication of whether amidines in the gas phase exist as monomeric species or as hydrogen-bonded dimers, analogous to those of carboxylic acids.

In this work the retention indices of 38 disubstituted N,N'-diphenylformamidines were determined on a non-polar GE SE-30 column. The compounds investigated have the general formula II.

$$[XC_6H_4N{=}CHNHC_6H_4Y \underset{II}{\rightleftharpoons} XC_6H_4NHCH{=}NC_6H_4Y]$$

The substituent X and Y are listed in Table I.

EXPERIMENTAL

Materials

N,N'-Diphenylformamidines were synthesized in our laboratory according to known procedures[15–17]. C_{12}–C_{24} *n*-alkanes were purchased from Applied Science Labs. (State College, PA, U.S.A.).

Gas chromatography

A Chromatron Model GCHF 18.3.4 gas chromatograph (VEB Chromatron, Berlin, G.D.R.) equipped with a flame ionization detector and 1 m × 3 mm I.D. column filled with 15% GE SE-30 silicone gum rubber on Chromosorb W AW (60–80 mesh) was used. The column temperature was maintained at 240°C. The carrier gas (nitrogen) flow-rate was 25 ml/min. Samples of approximately 0.1 *M* solutions in methanol (or pentane for hydrocarbons) were injected by means of a 10-μl Hamilton syringe.

Retention indices and dead times were determined by regression analysis by the method of Grobler and Bálizs[18], as improved by Haken *et al.*[19], and modified

by us to permit the use as standards of a series containing only *n*-alkanes with an even number of carbon atoms. The retention times were recorded by means of a Cobrabid (Poland) KB 5503 electronic integrator with an accuracy of 0.5 s.

RESULTS AND DISCUSSION

The retention indices of the N,N′-diphenylformamidines with confidence intervals at a significance level of 0.05, calculated from at least five measurements, are given in Table I. As the retention index depends to a small extent on temperature, we determined the retention indices at the same temperature as for previously studied trisubstituted formamidines[4], *i.e.*, 240°C. Under these conditions only one peak was observed for each unsymmetrically substituted ($X \neq Y$) N,N′-diphenylformamidine, with no evidence that the two tautomers have different retentions.

We correlated the retention indices of the N,N′-diphenylformamidines with those of corresponding anilines[2]. Calculations were made by means of the least-squares method. The regression coefficients *a* and *b* with confidence intervals calculated at a significance level of 0.05 and the estimators of correlation, *i.e.*, the correlation coefficient (*r*) and Exner's ψ function[20], are given in Table II.

The regression parameters are very close to those calculated for the series of trisubstituted N^1,N^1-dialkyl-N^2-phenylformamidines[4], limited to compounds containing the same set of substitutents X on the phenyl ring:

$$I(\text{amidine}) = (1.078 \pm 0.059) \cdot I(R_xNH_2) + (1.080 \pm 0.035) \cdot I(R_yR'_yNH) - 127.7 \quad (2a)$$

TABLE I

RETENTION INDICES OF N,N′-DIPHENYLFORMAMIDINES ON A GE SE-30 NON-POLAR COLUMN AT 240°C

X	*Y*	*I*	*X*	*Y*	*I*
H	H	1933 ± 1	*p*-OCH_3	*p*-Br	2543 ± 1
H	*p*-CH_3	2122 ± 3	*p*-OC_2H_5	*p*-OC_2H_5	2619 ± 5
H	*p*-OCH_3	2266 ± 3	*p*-OC_2H_5	*p*-Cl	2509 ± 5
H	*p*-OC_2H_5	2319 ± 3	*p*-Cl	*p*-Cl	2419 ± 2
H	*p*-Cl	2215 ± 2	*p*-Cl	*p*-Br	2535 ± 1
H	*p*-Br	2321 ± 4	*p*-Br	*p*-Br	2633 ± 2
H	*m*-CH_3	2095 ± 2	*m*-CH_3	*m*-CH_3	2180 ± 2
H	*m*-OCH_3	2230 ± 1	*m*-CH_3	*m*-OCH_3	2315 ± 1
H	*m*-OC_2H_5	2291 ± 3	*m*-CH_3	*m*-OC_2H_5	2384 ± 4
H	*m*-Cl	2200 ± 3	*m*-CH_3	*m*-Cl	2296 ± 2
H	*m*-Br	2294 ± 2	*m*-CH_3	*m*-Br	2404 ± 8
p-CH_3	*p*-CH_3	2199 ± 4	*m*-OCH_3	*m*-OCH_3	2477 ± 3
p-CH_3	*p*-OCH_3	2326 ± 1	*m*-OCH_3	*m*-OC_2H_5	2550 ± 3
p-CH_3	*p*-OC_2H_5	2409 ± 3	*m*-OCH_3	*m*-Cl	2458 ± 0
p-CH_3	*p*-Cl	2304 ± 1	*m*-OC_2H_5	*m*-OC_2H_5	2586 ± 6
p-CH_3	*p*-Br	2406 ± 1	*m*-OC_2H_5	*m*-Cl	2509 ± 1
p-OCH_3	*p*-OCH_3	2485 ± 3	*m*-Cl	*m*-Cl	2399 ± 2
p-OCH_3	*p*-OC_2H_5	2539 ± 3	*m*-Cl	*m*-Br	2518 ± 1
p-OCH_3	*p*-Cl	2443 ± 1	*m*-Br	*m*-Br	2604 ± 6

TABLE II

MULTIPLE REGRESSION PARAMETERS FOR CORRELATION OF RETENTION INDICES OF N,N'-DIPHENYLFORMAMIDINES *VS.* RETENTION INDICES OF CORRESPONDING ANILINES

Standard	$a_1 = a_2$	b	r	ψ	*Eqn.*
$XC_6H_4NH_2$ and $YC_6H_4NH_2$	1.028 ± 0.025	−42.7	0.9902	0.1132	4
$XC_6H_4NH_2$	1.039 ± 0.106	−72.6	0.9910	0.1480	5

indicating that the N,N'-diphenylformamidines are not dimerized in the gas phase.

The regression coefficients a_1 and a_2 obtained for N,N'-diphenylformamidines are identical because the retentions of both tautomers are indistinguishable. Hence the equation for the prediction of retention indices of N,N'-diphenylformamidines (FDPh) takes the form

$$I(\text{FDPh}) = a[I(XC_6H_4NH_2) + I(YC_6H_4NH_2)] + b \quad (4)$$

This equation implies that the retention index of an unsymmetrically disubstituted formamidine is the mean of the retention indices of the two symmetrically disubstituted compounds.

The preparation of symmetrically N,N'-disubstituted amidines (X = Y in eqn. 4 or $R_x = R_y$ in eqn. 3) is less complicated than the preparation of unsymmetrically disubstituted compounds, as in the latter instance considerable amounts of side products are formed. Therefore, it seems reasonable to find the parameters of the equations for the prediction of the retention indices of various types of amidines (various

TABLE III

DISTRIBUTION OF ERRORS OF PREDICTIONS OF RETENTION INDICES BASED ON EQNS. 2a, 4 AND 5

I(calc) − I(exp)	*Equation*		
	2a	*4*	*5*
0–10	4	12	15
10–20	2	16	13
20–30	8	3	4
30–40	3	4	3
40–50	12	0	0
50–60	5	1	1
60–70	1	1	2
70–80	2	1	0
80–90	1	0	0
Mean accuracy of prediction	39.6 ± 6.4	18.0 ± 5.4	17.4 ± 5.5

R_z) on the basis of correlations of retention indices of symmetrically disubstituted compounds:

$$I(R_xN{=}CR_zNHR_x) = 2a \cdot I(R_xNH_2) \quad (5)$$

The parameters of such an equation for the N,N'-diphenylformamidines (Table II), although they were obtained from smaller amount of compounds, were within the confidence intervals the same as based on all the compounds studied.

We compared the retention indices calculated with the use of the three sets of parameters (eqns. 2a, 4 and 5) with the experimental values and the distributions of errors are summarized in Table III. As can be seen, in most instances the error does not exceed 20 retention index units (i.u.) and, if parameters obtained for trisubstituted amidines are used, it does not exceed 50 i.u.

CONCLUSIONS

The results presented show that tautomerizing amidines can be analysed by gas chromatography. Their retention indices can be predicted with satisfactory accuracy using a linear regression in the form of eqn. 4.

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