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PREDICTION OF RETENTION INDICES OF N^1,N^1-DIALKYLFORMAMIDINES ON A NON-POLAR COLUMN*

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SUMMARY

The retention indices of 80 compounds comprising four series of N^2-substituted N^1,N^1-dialkylformamidines, each containing the same set of 20 variable substituents R_x at the imino nitrogen atom N^2, have been measured on a non-polar silicon gum rubber GE SE-30 column. The values obtained for each series were correlated with those of corresponding model compounds such as primary amines R_xNH_2 and substituted hydrocarbons R_xH. Further support is provided for an earlier conclusion that in the prediction of retention indices the correlation method should be used instead of additivity rules. A two-parameter regression of the retention indices of N^1,N^1-dialkylformamidines *vs.* corresponding primary amines and secondary amines $(R_y)_2NH$ is of excellent quality and can be used for prediction of the retention indices of trisubstituted formamidines.

INTRODUCTION

In the course of our study on the gas chromatography (GC) of amidines and the prediction of their retention indices[1–3], we have shown that a linear correlation of the form

$$I_{\text{amidine}} = aI_{\text{Std}} + b \tag{1}$$

should be applied, where I are Kováts retention indices[4,5], and that the additivity rule, which can be treated as a very specific case of eqn. 1, where $a = 1$, may yield erroneous results.

It was also shown[3] that for compounds (Cpd) such as N^1,N^1-dimethylbenzamidines or benzylideneamines containing two different substituents, their retention indices can be successfully predicted by a two-parameter linear regression

$$I_{\text{Cpd}} = a_1 I_{\text{Std}_1} + a_2 I_{\text{Std}_2} + b \tag{2}$$

* Amidines, Part XXIII; for Part XXII see J. Oszczapowicz, W. Krawczyk, J. Osek and E. Raczyńska, *Pol. J. Chem.*, submitted for publication.

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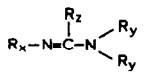
where Std_1 and Std_2 are suitable simple model compounds.

It was then observed that a change in the substituent at a certain site of the molecule, in that instance at the carbon atom of the C=N double bond, may result in considerable differences in the parameter *a* describing substitution at the other site, in that instance the imino nitrogen atom. Thus the question arose as to whether substitution at one of the nitrogen atoms in the amidine group $-N=C-N\leq$ has any effect on the parameter *a* describing substitution at the second nitrogen atom. In other words, whether a two parameter equation of the type 2 can be applied to prediction of the retention indices of trisubstituted amidines or a more complex equation should be used.

In this work, the retention indices of four series of dialkylformamidines (R_z = H), each containing the same set of 20 variable substituents R_x (Table I) at the imino nitrogen atom, were determined on a non-polar GE SE-30 column.



R_z = H

$-N(R_y)_2$	Series	
	N^1,N^1–Tetramethyleneformamidines	(FTM)
	N^1,N^1–Pentamethyleneformamidines	(FPM)
	N^1,N^1–Hexamethyleneformamidines	(FHM)
	N^1,N^1–3–Oxapentamethyleneformamidines	(FOPM)

Using the same column, the retention indices of the corresponding secondary amines $(R_y)_2NH$ were determined for comparison.

EXPERIMENTAL

Materials

Formamidines were synthesized according to Scoggins[6], by reaction of a dialkylformamide dimethyl acetal $(R_y)_2N$–$CH(OCH_3)_2$ also synthesized[7] in our laboratory with a primary amine R_xNH_2. The secondary amines were commercial samples. C_{12}–C_{20} *n*-alkanes were purchased from Applied Science Labs.

Gas chromatography

A Chromatron Model GCHF 18.3.4 gas chromatograph (VEB Chromatron, Berlin, G.D.R.) equipped with a flame ionization detector and a 3 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 for amidines and at 180°C for secondary amines. The carrier gas (nitrogen) flow-rate was 25 ml/min. Samples of 1.0 μl of 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[8], as improved by Haken *et al.*[9], using the series of nine C_{12}–C_{20} *n*-alkanes, under the same conditions as for the studied sample. The retention times were recorded by means of a Cobrabid KB 5503 electronic integrator with an accuracy of 0.5 s.

RESULTS AND DISCUSSION

The retention indices of the formamidines, with confidence intervals at a significance level of 0.05, calculated from at least five measurements, are given in Table I, and those of the secondary amines in Table II.

As the retention index depends to a small extent on temperature, for higher accuracy of the correlations, we have determined the retention indices at the same temperature as for previously studied N¹,N¹-dimethylformamidines[2] (FDM), *i.e.*, at 240°C.

TABLE I

RETENTION INDICES OF N¹,N¹-DIALKYLFORMAMIDINES ON A GE SE-30 NON-POLAR COLUMN AT 240°C

No.	R_x	*FDM**	*FTM*	*FPM*	*FHM*	*FOPM*
1	*n*-C_3H_7–	864 ± 0	1202 ± 4	1273 ± 4	1378 ± 0	1255 ± 4
2	*n*-C_4H_9–	985 ± 10	1320 ± 3	1378 ± 4	1478 ± 2	1356 ± 3
3	*n*-C_5H_{11}–	1042 ± 3	1403 ± 2	1473 ± 5	1569 ± 2	1451 ± 4
4	*n*-C_6H_{13}–	1166 ± 6	1501 ± 4	1577 ± 3	1668 ± 0	1551 ± 2
5	*iso*-C_4H_9–	938 ± 7	1249 ± 4	1324 ± 4	1423 ± 4	1305 ± 4
6	cyclo-C_6H_{11}–	1229 ± 0	1556 ± 4	1622 ± 4	1729 ± 1	1612 ± 0
7	$C_6H_5CH_2$–	1408 ± 5	1751 ± 7	1821 ± 4	1918 ± 2	1792 ± 3
8	C_6H_5–	1385 ± 7	1733 ± 6	1798 ± 4	1898 ± 5	1792 ± 6
9	3-CH_3-C_6H_5–	1491 ± 7	1831 ± 3	1900 ± 9	1991 ± 1	1876 ± 4
10	4-CH_3-C_6H_5–	1493 ± 6	1828 ± 4	1902 ± 4	1988 ± 6	1881 ± 9
11	3-OCH_3-C_6H_5–	1641 ± 4	1985 ± 2	2059 ± 7	2144 ± 1	2048 ± 5
12	4-OCH_3-C_6H_5–	1636 ± 4	1978 ± 1	2052 ± 3	2130 ± 6	2046 ± 9
13	3-OC_2H_5-C_6H_5–	1682 ± 3	2034 ± 0	2110 ± 6	2199 ± 2	2095 ± 4
14	4-OC_2H_5-C_6H_5–	1705 ± 3	2042 ± 6	2113 ± 3	2192 ± 7	2101 ± 9
15	3-Cl-C_6H_5–	1612 ± 3	1948 ± 1	2006 ± 7	2118 ± 1	2011 ± 5
16	4-Cl-C_6H_5–	1611 ± 4	1956 ± 0	2019 ± 4	2133 ± 1	2015 ± 7
17	3-Br-C_6H_5–	1709 ± 3	2048 ± 3	2102 ± 6	2217 ± 1	2119 ± 2
18	4-Br-C_6H_5–	1732 ± 1	2060 ± 5	2126 ± 3	2239 ± 1	2122 ± 4
19	3-NO_2-C_6H_5–	1877 ± 1	2188 ± 6	2255 ± 5	2366 ± 1	2419 ± 0
20	4-NO_2-C_6H_5–	1968 ± 4	2295 ± 2	2365 ± 9	2475 ± 1	2487 ± 0

* According to ref. 2.

TABLE II

RETENTION INDICES OF SECONDARY AMINES ON A GE SE-30 NON-POLAR COLUMN AT 180°C

$(CH_3)_2NH$				
421 ± 10	701 ± 5	788 ± 8	885 ± 3	800 ± 7

We have correlated the retention indices of the formamidines with those of corresponding primary amines R_xNH_2 and substituted hydrocarbons R_xH, used previously for correlations with the retention indices of other amidines[2,3]. For comparison, we have correlated also the retention indices of corresponding series of dimethylformamidines (FDM).

Calculations were made by means of a least squares method. The regression coefficients, *a* and *b* in, eqn. 1, with confidence intervals calculated at a significance level of 0.05, and the correlation coefficient, *r*, and Exner's ψ function[10] are given in Table III. The regressions indicate that, as in our previous studies[2,3], the retention indices of amidines correlate with those of the primary amines R_xNH_2 as well as those of the substituted hydrocarbons R_xH, the former correlations being of much higher quality. It should be mentioned that the differences in quality are better indicated by the ψ function than by the commonly used correlation coefficient, *r*.

TABLE III

REGRESSION PARAMETERS FOR CORRELATION OF RETENTION INDICES OF N^1,N^1-DIALKYLFORMAMIDINES *VS.* RETENTION INDICES OF STANDARDS

Standard	*Series*	*a*	*b*	*r*	ψ	*n*
R_xNH_2	FDM	1.107 ± 0.033	275	0.9982	0.063	20
	FTM	1.104 ± 0.038	615	0.9976	0.072	20
	FPM	1.103 ± 0.037	685	0.9977	0.071	20
	FHM	1.106 ± 0.032	780	0.9983	0.062	20
	FOPM	1.202 ± 0.059	581	0.9953	0.102	20
R_xH	FDM	1.329 ± 0.099	421	0.9895	0.153	19
	FTM	1.314 ± 0.097	771	0.9897	0.151	19
	FPM	1.316 ± 0.094	838	0.9904	0.147	19
	FHM	1.317 ± 0.103	935	0.9885	0.160	19
	FOPM	1.437 ± 0.146	744	0.9809	0.206	19

The slopes of the correlations with the amines are different from unity, and with the hydrocarbons the difference is much greater. This provides further support for the conclusion[2] that the use of the additivity rule for prediction of retention indices of some compounds may cause discernible errors and that the correlation method should be used instead.

The slopes of the correlations are different from those of various benzamidines[3] ($R_z = C_6H_4Z$). This provides further support for an observation[2] that the regression coefficient, *a* in eqn. 1, for substitution at the imino nitrogen atom depends on the substituent at the amidino carbon atom.

The regression coefficients, *a*, for the correlation of retention indices of amidines containing purely alkyl substituents at the amino nitrogen atom (FDM, FTM, FPM and FHM) *vs.* retention indices of both standards are identical (the differences being much lower than the confidence intervals), but for amidines containing the oxo group (FOPM series) the coefficient *a* is considerably higher. This leads to the con-

clusion that the substituent at one of the nitrogen atoms may affect the parameter a for substitution at the second nitrogen atom. However, in some cases, a two-parameter linear regression of the type 2 may be used for prediction of retention indices of N^2-substituted N^1,N^1-dialkylformamidines (at least those containing purely aliphatic substituents at N^1) and the two standard series are necessary.

We have found primary amines R_xNH_2 to be the most suitable standards, for substitution at the imino nitrogen atom, and secondary amines $(R_y)_2NH$ for substitution at the amino one. A substantial advantage of this choice is the fact that both types of amines are the substrates for synthesis of the trisubstituted amidine.

Thus we have used the two-parameter regression (eqn. 2) with these standards for all five series, and for only those concerning purely aliphatic substituents at the amino nitrogen atom, *i.e.*, without FOPM. The parameters with confidence intervals at a significance level of 0.05 are given in Table IV. Parameters a_1 and a_2 are different from unity. Both correlations are of high quality, but without the FOPM series the correlation is better, as shown by the ψ function.

TABLE IV

MULTIPLE REGRESSION PARAMETERS FOR CORRELATION OF RETENTION INDICES OF N^1,N^1-DIALKYLFORMAMIDINES *vs.* RETENTION INDICES OF STANDARDS (EQN. 2)

Standards		a_1	a_2	b	r	ψ	n
1	*2*						
R_xNH_2	$(R_y)_2NH$	1.123 ± 0.020	1.083 ± 0.036	−190	0.9969	0.080	100*
		1.104 ± 0.019	1.091 ± 0.031	−174	0.9979	0.067	80**

* All five series.
** Without FOPM.

This means that, as it was mentioned above, the two-parameter regression can be used for prediction of the retention indices of trisubstituted amidines, however the parameters a_1 and a_2 found here may be limited to formamidines containing two alkyl substituents at the amino nitrogen atom. The question remains as to how far the structure of the substituents at these sites may be changed without discernible change in the regression parameters, so that the error in the prediction of retention indices is within acceptable limits.

CONCLUSIONS

The results presented indicate that the retention indices of trisubstituted amidines can be predicted with satisfactory accuracy using a two-parameter linear regression. Retention indices of formamidines are calculated as follows: $I_{\text{amidine}} = 1.123I_{R_xNH_2} + 1.083I_{(R_y)_2NH} - 190$. Further support is provided for the conclusion that the slope of the correlation for substiutuents at the imino nitrogen atom depends on the substituent at the amidino carbon atom. The regression parameters indicate that it may depend also on the substituent at the amino nitrogen atom.

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