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Note

The chemistry of carbazoles

IX. Substituent effect in the gas–liquid chromatography of methylcarbazoles

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Although the presence of methylcarbazoles in natural products has often been reported[1–9], all of them have not fully been identified. In a previous paper[10] dealing with the electronic absorption spectra of a large number of methylcarbazoles, we reported that the additivity of the spectral shifts provides a useful method for determination of unknown methylated carbazoles. In combination with such spectroscopic methods, gas–liquid chromatography (GLC) should serve as the technique for identification of the carbazoles, if some relationship between the retention values and the number or positions of methyl groups can be derived. The chromatographic data on 36 methylcarbazoles presented here provide useful clues for future research on the naturally occurring carbazoles.

EXPERIMENTAL

Methylcarbazoles were prepared by the method described previously[11,12]. Gas–liquid chromatography was performed on a Shimadzu 4PBTF chromatograph with a flame ionization detector (FID). Conditions: stainless-steel column (3 m × 3 mm) packed with 5% silicone SE-30 on Chromosorb W (60–80 mesh); carrier gas (nitrogen) flow-rate, 40 ml/min; column temperature, 200°C; detector temperature, 230°C; injection port temperature, 250°C; sample size, 1 μl (*ca.* 2% acetone solutions).

The nuclear magnetic resonance (NMR) spectra were recorded on a Jeol JNM-PS-100 spectrometer using tetramethylsilane as an internal standard. The infrared (IR) spectra of KBr discs were obtained on a Jasco IRA-2 spectrophotometer. Absorptions in the N–H vibration region were measured by scanning three times for each on an expanded scale.

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TABLE I

RETENTION TIMES (t_R) OF CARBAZOLE AND METHYLCARBAZOLES

No.	*Compound*	t_R *(min)*	*No.*	*Compound*	t_R *(min)*	*No.*	*Compound*	t_R *(min)*
1	Carbazole	4.2	14	2,4-Dimethyl-	7.8	27	2,4,5-Trimethyl-	12.6
2	1-Methyl-	5.2	15	2,5-Dimethyl-	8.1	28	2,4,6-Trimethyl-	10.9
3	2-Methyl-	5.7	16	2,6-Dimethyl-	7.5	29	2,4,7-Trimethyl-	11.0
4	3-Methyl-	5.6	17	2,7-Dimethyl-	7.6	30	3,4,6-Trimethyl-	12.4
5	4-Methyl-	5.8	18	3,4-Dimethyl-	8.7	31	1,2,5,7-Tetramethyl-	15.9
6	1,2-Dimethyl-	7.7	19	3,5-Dimethyl-	7.8	32	1,2,6,7-Tetramethyl-	16.9
7	1,3-Dimethyl-	6.7	20	3,6-Dimethyl-	7.4	33	1,3,4,6-Tetramethyl-	15.1
8	1,4-Dimethyl-	7.4	21	4,5-Dimethyl-	9.9	34	1,4,5,8-Tetramethyl-	14.4
9	1,5-Dimethyl-	7.6	22	1,3,4-Trimethyl-	10.9	35	2,3,5,7-Tetramethyl-	16.3
10	1,6-Dimethyl-	6.9	23	1,4,8-Trimethyl-	9.6	36	2,3,6,7-Tetramethyl-	18.3
11	1,7-Dimethyl-	6.9	24	1,5,7-Trimethyl-	11.0	37	2,4,5,6-Tetramethyl-	18.4
12	1,8-Dimethyl-	6.2	25	2,3,5-Trimethyl-	12.3			
13	2,3-Dimethyl-	8.4	26	2,3,6-Trimethyl-	12.3			

RESULTS AND DISCUSSION

Relation between retention time and the number of methyl groups

Table I lists the retention times determined for carbazole and 36 methylcarbazoles. As shown in Table II, the range of the retention values are separated sufficiently to permit estimation of the number of methyl groups, if the retention time of 4,5-dimethylcarbazole is overlooked. Strictly speaking, however, this relation is effective only up to dimethylcarbazoles, since the boundary between dimethyl- and trimethylcarbazoles remains equivocal on account of the value for 4,5-dimethylcarbazole, and the data are incomplete for the series of trimethyl- and tetramethylcarbazoles.

Relation between retention time and the positions of methyl groups

For the monomethylcarbazoles, the order of retention times is 4-methyl (5) > 2-methyl (3) > 3-methyl (4) > 1-methyl (2), where the numerals in parentheses denote the compounds in Table I. This order is found to hold in certain sets of polymethylcarbazoles.

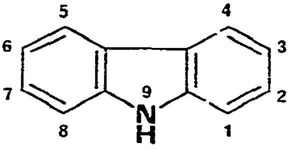
TABLE II

RETENTION TIME RANGES ACCORDING TO THE NUMBER OF METHYL GROUPS

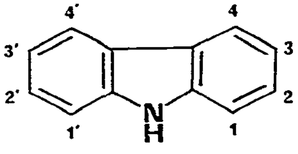
Compounds	t_R *(min)*	*No. of samples*	*No. of isomers*
Carbazole	4.2	1	1
Monomethylcarbazoles	5.2– 5.8	4	4
Dimethylcarbazoles	6.2– 8.7 (9,9*)	16	16
Trimethylcarbazoles	9.6–12.6	9	28
Tetramethylcarbazoles	14.4–18.4	7	35

* Value for 4,5-dimethylcarbazole.

For the symmetrically substituted dimethylcarbazoles, the retention times increase in the order 4,4′ (21) > 2,2′ (17) > 3,3′ (20) > 1,1′ (12), where the positions of the methyl groups are indicated according to the numbering system B:



A



B

This indicates that the order for monomethylcarbazoles is not altered by the second methyl substitution at the symmetrical positions of the carbazole ring.

The order 4 > 2 > 3 > 1 is applicable to the unsymmetrically methylated carbazoles, with a few exceptions. This trend will be more obvious when the data on the symmetrical dimethylcarbazoles are included, as is shown in Table III. All the carbazoles bearing two adjacent methyl groups exhibit exceptional deviations which are indicated by an asterisk in this table.

TABLE III

ORDERS OF RETENTION TIMES FOR DIMETHYLCARBAZOLES

Carbazoles	*Positions of another methyl group, x, according to the numbering system B*
1,*x*-Dimethylcarbazole	2* (6) > 4′ (9) > 4 (8) > 2′ (11) = 3′ (10) > 3 (7) > 1′ (12)
2,*x*-Dimethylcarbazole	3* (13) > 4′ (15) > 4 (14) > 1* (6) > 2′ (17) > 3′ (16) > 1′ (11)
3,*x*-Dimethylcarbazole	4 (18) > 2 (13) > 4′* (19) > 2′ (16) > 3′ (20) > 1′ (10) > 1 (7)
4,*x*-Dimethylcarbazole	4′ (21) > 3* (18) > 2′ (15) > 2 (14) = 3′ (19) > 1′ (9) > 1 (8)

It is difficult to find a close relation between the chromatographic data and methyl substitution for trimethyl- and tetramethylcarbazoles. Thus, in the case of four 2,4,*x*-trimethylcarbazoles, the elution order is *x* = 4′ (27) > 2′ (29) = 1′ (24) > 3′ (28). However, the order 4 > 2 > 3 > 1 still partially holds in some cases. For several tetramethylcarbazoles, the order 2,4,3′,4 (37) > 2,4,2′,3′ (35) > 2,4,1′,2′ (31) corresponds consistently to the orders 4′ > 2′ and 3′ > 1′, and a tendency 2′,4′ > 1,3′ is obvious from the result 3,4,2′,4′ (37) > 3,4,1,3′ (33).

Relation between retention time and physical properties of methylcarbazoles

The physical properties, which should be related to interactions between monomethylcarbazoles and the stationary phase, are given in Table IV.

Although the boiling point is expected to be a primary factor determining the retention time, the carbazoles are not eluted in the order of their boiling points. Even if the boiling points of 1- and 4-methylcarbazoles are excluded because of the uncertainty in their values, the longer retention time of 2-methylcarbazole compared with that of 3-methylcarbazole is unexpected.

The imino-hydrogen is capable of interacting with the stationary phase through hydrogen-bonding, which influences the elution parameters[15]. But the

TABLE IV

PHYSICAL PROPERTIES OF CARBAZOLES

Compound	*Boiling point ($^\circ C$)*	*Equilibrium constant of hydrogen-bonding*[13] *(l/mole)*		*NMR in* $[^2H_6]$*acetone: δ (N–H) (ppm)*	*IR in KBr:*	
		In diethyl ether	*In THF*		*ν (N–H) (cm^{-1})*	*Δν (cm^{-1})*
Carbazole	354.76*				3420	
1-Methylcarbazole	360**	2.80	4.01	10.15	3410	10
2-Methylcarbazole	363/765 mmHg*	5.00	7.50	10.16	3400	20
3-Methylcarbazole	365/765 mmHg*	3.37	4.30	10.21	3403	17
4-Methylcarbazole	360**	4.00	6.80	10.27	3385	35

* Ref. 14.

** Ref. 1.

proton donating powers of monomethylcarbazoles were reported to be in the order 2 > 4 > 3 > 1 (ref. 13). The NMR chemical shifts of the imino-proton are also independent of the elution order. Only the vibrational frequencies of the N–H bond seem to be correlated to the elution order, but the meaning of this is still obscure. Consequently, there is no information available to justify any conclusion as to the relation of the retention times to the physical properties. However, the interaction between the imino-hydrogen and stationary phase is a dominant factor, because 1-methyl-, 1,8-dimethyl-, 1,4,8-trimethyl- and 1,4,5,8-tetramethylcarbazoles showed the shortest retention times among their respective isomers. Methyl substituents at the 1- and 8-positions of carbazole should sterically hinder the interactions with the stationary phase, which decrease the retention times, as is known for the chromatographic behaviours of 2- and 2,5-alkylated pyrroles[16].

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