INDOLES

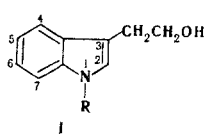
XLVIII.* STRUCTURE AND GAS CHROMATOGRAPHIC CHARACTERISTICS OF COMPOUNDS OF THE TRYPTOPHOL AND HOMOTRYPTOPHOL SERIES

L. B. Dmitriev and I. I. Grandberg

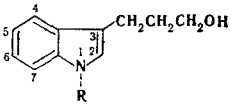
UDC 543.544.45;547.755

The Kovacs indexes in two steady-state phases of differing polarities and at two temperatures were determined for a series of tryptophols and homotryptophols. The results indicate that the indexes of retention of the individual structural elements of the molecules of these series are extremely characteristic functions that reflect the steric environment of the nitrogen center of the indole ring and the specific character of their interaction with the stationary phase.

A definite relationship between the degree of shielding of the ring nitrogen atom and the relative retention volume is observed for nitrogen heterocycles [2-4]. In a preceding paper [5] we gave a semiquantitative evaluation of this relationship by means of Kovacs indexes for tryptamine and homotryptamine systems. In the present paper we have made an attempt to trace this relationship in the case of tryptophol (I) and homotryptophol (II) derivatives.



I



II

The corrected retention times and Kovacs indexes of the indicated group of compounds are presented in Tables 1 and 2 for two columns with differing polarities and for two temperatures [t_r^I and I^I for column I (a weakly polar column) and t_r^{II} and I^{II} for column II (a polar column)] [5].

The observed changes in the retention factors of methyl derivatives of tryptophol and homotryptophol can probably be considered to be primarily due to interaction of the NH group of the indole ring with the stationary phase, inasmuch as it is difficult to assume any substantial effect of the ring alkyl groups on the properties of the hydroxyl group in the compounds under consideration. Consequently, its contribution to the interaction with the stationary phase can, to a first approximation, be considered to be constant for the compounds presented in the tables. Thus a comparison of the corrected retention times and Kovacs indexes makes it possible to follow the change in the contribution of the "nitrogen function" of the indole ring to the overall retention of the compound as a function of the position of the substituent in the ring.

The interaction of a substance with the stationary phase is determined primarily by the sum of the dipole-dipole, dispersion, and specific interactions. The hydrogen bonds and the donor-acceptor interaction of the π-electron aromatic systems play the greatest role in the specific interaction of indole derivatives [6-8]. By comparing the retention parameters in two phases of differing polarities one can to some

*See [1] for communication XLVII.

K. A. Timiryazev Agricultural Academy, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 946-949, July, 1975. Original article submitted November 25, 1974.

TABLE 1. Gas-Chromatographic Characteristics of N-Unsubstituted and N-Alkyltryptophols

No.	Compound	200° C					220° C							
		t_r I	I	t_r II	II	$\Delta I^{200°}$	t_r I	I	t_r II	II	$\Delta I^{220°}$	$\Delta I^{220°} - \Delta I^{200°}$	ΔI	ΔII
1	Tryptophol	3,87	1784	17,62	3224	1440	2,08	1806	13,44	3232	1426	−14	22	8
2	5-Methyltryptophol	5,19	1869	20,25	3274	1405	2,65	1887	15,42	3280	1393	−12	18	6
3	2-Methyltryptophol	4,60	1834	14,36	3155	1321	2,38	1851	11,33	3172	1321	0	17	17
4	Homotryptophol	5,10	1864	21,06	3284	1420	2,59	1879	15,64	3285	1406	−14	15	1
5	5-Methylhomo-tryptophol	6,61	1939	23,79	3325	1386	3,28	1959	17,99	3334	1375	−11	20	9
6	7-Methylhomo-tryptophol	6,30	1925	19,38	3256	1331	3,16	1946	14,56	3260	1314	−17	21	4
7	1-Methyltrytophol	3,24	1732	3,92	2718	986	1,80	1757	3,44	2755	998	+12	25	37
8	1,2-Dimethyl-tryptophol	5,00	1858	5,57	2836	978	2,62	1883	4,76	2868	985	+7	25	32
9	1-Methylhomo-tryptophol	4,46	1825	5,62	2839	1014	2,39	1852	4,93	2881	1029	+15	27	42
10	1-Isopropyl-tryptophol	4,28	1813	5,45	2829	1016	2,23	1829	4,32	2834	1005	−11	16	5
11	2-Methyl-1-iso-propyltryptophol	6,00	1911	4,88	2792	881	2,97	1926	3,88	2797	871	−10	15	5

TABLE 2. Gas-Chromatographic Characteristics of 1-Phenyl- and 1-Benzyltryptophols

No.	Compound	220° C					240° C							
		t_r I	I	t_r II	II	$\Delta I^{200°}$	t_r I	I	t_r II	II	$\Delta I^{220°}$	$\Delta I^{240°} - \Delta I^{200°}$	ΔI	ΔII
1	1-Phenyltryptophol	8,76	2268	19,35	3310	1042	4,73	2272	14,36	3342	1070	+28	4	32
2	1-Phenyl-2-methyl-tryptophol	8,91	2274	18,38	3292	1018	4,94	2288	13,54	3319	1031	+13	14	27
3	1-Phenylhomo-tryptophol	11,45	2358	32,68	3492	1134	6,06	2362	21,95	3506	1144	+10	4	14
4	1-Benzyltryptophol	10,21	2320	28,95	3450	1130	5,60	2333	20,68	3483	1150	+20	13	33
5	1-Benzyl-2-methyl-tryptophol	12,50	2388	31,30	3477	1089	6,76	2401	21,55	3499	1098	+9	13	33
6	1-Benzyl-2-propyl-tryptophol	17,56	2502	45,36	3606	1104	9,11	2509	29,77	3624	1115	+11	7	18
7	1-Benzyl-2-iso-propyltryptophol	17,41	2499	42,94	3587	1088	9,08	2508	28,27	3604	1096	+8	9	17
8	1-Benzylhomo-tryptophol	13,43	2412	46,01	3611	1199	7,14	2421	31,61	3647	1226	+27	9	36
9	1-Benzyl-2-methyl-homotryptophol	18,24	2511	47,73	3623	1112	8,80	2505	30,00	3627	1122	+10	−6	4
10	1-Benzyl-2-(γ-hydroxypropyl)-3-ethylindole	16,45	2477	34,50	3511	1034	8,66	2491	23,11	3526	1035	+1	14	15
11	1-Benzyl-2-(δ-hydroxybutyl)indole	16,88	2485	23,60	3379	894	8,62	2489	16,35	3392	903	+9	4	13

degree evaluate the contribution of the dipole–dipole and specific interactions to the total dissolving energy. In this case, it is assumed that the manifestation of these forces increases as the polarity of the stationary phase increases, whereas the forces of the dispersion interaction change only slightly. Thus the total contribution of the dipole–dipole and specific interactions is reflected in the difference in the retention indexes (ΔI) for stationary phases of different polarities ($\Delta I = I^{II} - I^{I}$, see Tables 1 and 2). In the case of N-unsubstituted tryptophols and homotryptophols (Table 1), tryptophol, homotryptophol, and 5-methyltryptophol have the highest ΔI values. Just as in the case of the corresponding tryptamines [5], the introduction of a methyl group in the 2 or 7 position leads to a considerable decrease in this value. The difference in the dipole moments between the 5- and 7(2)-methyltryptophols evidently does not exceed 0.4 D [9, 10]. Thus the observed changes in the retention indexes on passing from 5- to 7- or 2-substituted compounds, as in the case of tryptamines, cannot be completely explained by changes in the dipole–dipole interaction. It is most probable to assume that the methyl groups in the 2 and 7 positions create steric hindrance to interaction of the NH group with the stationary phase, lowering the contribution of the specific interaction of the "nitrogen function" of the indole ring to the total dissolving energy, which leads to a decrease in the retention indexes of the indicated isomers as compared with the 5-methyl derivatives. These results are in agreement with the results obtained for the corresponding alkyl derivatives of pyrrole, indole, and tryptamine [5-8].

TABLE 3. Retention Increments of the Methyl Groups of Trpytophol Derivatives

Compound	$\delta I_{1\text{-}CH_2(H)}$		$\delta I_{2\text{-}CH_2(H)}$		$\delta I_{5\text{-}CH_2(H)}$		$\delta I_{7\text{-}CH_2(H)}$		$\delta I_{3\text{-}CH_2(R)}$	
	columns									
	I	II	I	II	I	II	I	II	I	II
2-Methyltryptophol	—	—	+47,5	−64,5	—	—	—	—	—	—
5-Methyltryptophol	—	—	—	—	+83	+49	—	—	—	—
5-Methylhomo-tryptophol	—	—	—	—	+77,5	+45	—	—	+71	+52,5
7-Methylhomo-tryptophol	—	—	—	—	—	—	+64	−26,5	—	—
1-Methyltryptophol	−50,5	−491,5	—	—	—	—	—	—	—	—
1-Methylhomo-tryptophol	−33	−424,5	—	—	—	—	—	—	+94	+123,5
1,2-Dimethyl-tryptophol	−28	−311,5	+126	+115,5	—	—	—	—	—	—

On the basis of the Kovacs additivity indexes we calculated the increments of retention of the methyl group for various positions of the indole ring, $\delta I_{-CH_2(H)} = I_A - I_B$, where I_A is the average retention index of the compound for which the increment is determined at two temperatures, and I_B is the average value of the index of the corresponding derivative that does not contain this methyl group. The increments obtained undoubtedly cannot be absolute in character, inasmuch as their values depend markedly on the various structural factors of the molecule (see Table 3). Nevertheless, these values make it possible to graphically trace the relationship between the position of the methyl group and its effect on the overall character of the interaction of the molecule with the stationary phase.

The retention increments of the 5-methyl group (δI_{5-CH_3}), calculated as the difference in the retention indexes of 5-methyltryptophol (5-methylhomotryptophol) and tryptophol (homotryptophol), have positive values and correspond approximately to the increase in the retention index on passing from the tryptophol derivatives to the corresponding homotryptophol derivatives [$\delta I_{3-CH_2(R)}$]. Thus the 5-methyl group has practically no effect on the interaction of the "nitrogen function" of the indole ring with the stationary phase.

As in the case of tryptamine [5], one observes a pronounced decrease in the increments for 2- and 7-methyl groups [$\delta I_{2-CH_2(H)}$ and $\delta I_{7-CH_2(H)}$], calculated from the retention indexes of the 2-methyl- and 7-methyltryptophols and tryptophols, particularly for the polar phase (the δI values are negative, which indicates their considerable shielding effect).

As one should have expected, the retention indexes and the ΔI values for 1-substituted tryptophols (Tables 1 and 2) fall sharply as compared with the values of N-unsubstituted compounds. Of particular interest is the fact that the retention index increases both in the polar phase and in the weakly polar phase for 1-isopropyl-substituted compounds as compared with 1-methyl-substituted compounds. In this case the large volume of the substituent evidently leads to a decrease in the donor–acceptor interaction of the indole ring with the stationary phase.

The negative value of the change in the difference in the retention indexes for phases of differing polarities as a function of the temperature ($\Delta I^{20} = \Delta I^{220} - \Delta I^{200}$) for N-unsubstituted tryptophols indicates that the role of the dipole–dipole and donor–acceptor interactions in the total interaction with the stationary phase is high for these compounds as compared with the corresponding tryptamines, in which this value is positive [5].

The decrease in the ΔI value and the positive ΔI^{20} value for 1-phenyl and 1-benzyl derivatives can probably be explained by the considerable increase in the molecular weight and, consequently, by the increase in the specific weight of the dispersion interaction with the stationary phase.

EXPERIMENTAL

The gas-chromatographic parameters of the compounds indicated above were determined with a Yanaco G-800T chromatograph [5] with a 2-m long column with a diameter of 4 mm.

The stationary phase of column I (weakly polar) was 5% SE-30 silicone on Chezasorb (Czechoslovakian SSR) washed with acid and silanized with hexamethyldisiloxane; the stationary phase of column II (polar) was 5% polyethylene glycol (mol. wt. 6000) on Porolit (Czechoslovakian SSR) containing 5% KOH. The relative polarities of the columns were 14 and 41%, respectively (the polarity of β,β-hydroxydipropionitrile was taken as 100%).

The determinations were made at two temperatures: 200 and 220° for the N-unsubstituted and N-methylated compounds and 220 and 240° for the N-phenyl- and N-benzyl-substituted compounds. The carrier-gas (H_2) flow rate was 40 ml/min under all conditions. The detector was a catharometer. The accuracy in the determination of the retention times was ± 2 units.

The syntheses of the investigated systems are presented in our earlier papers [1, 11].

LITERATURE CITED

1. E. I. Grandberg and G. P. Tokmakov, Khim. Geterotsikl. Soedin., 207 (1975).
2. B. A. Rudenko, É. A. Il'kova, V. F. Kucherov, and N. A. Kerimov, Zh. Analiticheskoi Khim., 25, 1405 (1970).
3. B. Holmstedt, W. I. A. Van den Heuvel, W. L. Gardiner, E. L. Gardiner, and E. C. Horning, Anal. Biochem., 8, 151 (1964).
4. E. C. Horning, M. G. Horning, W. I. A. Van den Heuvel, K. L. Knox, B. Holmstedt, and C. I. W. Brooks, Anal. Chem., 36(8), 1546 (1964).
5. L. B. Dmitriev and I. I. Grandberg, Izv. Timiryazev. Sel'skokhoz. Akad., 5, 206 (1973).
6. A. I. Shatenshtein, Usp. Khim., 25, 377 (1955).
7. Y. L. Gol'dfarb (Goldfarb), V. I. Yakerson, V. A. Ferapontov, S. Z. Taits, and F. M. Stoganovich, Physical Methods in Heterocyclic Chemistry, 3, 297 (1971).
8. I. Janak and M. Hrivnac, Coll. Czech. Chem. Commun., 25, 1557 (1960).
9. H. Z. Lütgert, Z. phys. Chem., B14, 31 (1931).
10. E. F. Janetzky and M. C. Lebret, Rec. Trav. Chim., 63, 123 (1944).
11. I. I. Grandberg and T. A. Moskvina, Khim. Geterotsikl. Soedin., 66 (1972).