

GAS-CHROMATOGRAPHIC ANALYSIS OF ALKYLATED DERIVATIVES OF CARANE
AND OF CYCLOHEPTANE IN CAPILLARY COLUMNS

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The retention indices of synthesized alkyl derivatives of carane and of cycloheptane in capillary columns with tricresyl phosphate and squalane at 70°C have been determined. The influence of the structure of the hydrocarbons studied on the values of their retention parameters is considered. An estimate is given of the nature of the interrelationship between the physical properties of these hydrocarbons and their retention indices on a nonpolar stationary phase.

In natural mixtures of terpenoids, compounds of the 1,1,4-trimethylcycloheptane series are encountered rarely and in small amounts, which for a long time interfered with their isolation and investigation. In recent years, the study of such compounds has intensified thanks to the fact that their synthesis is being carried out from 3-carene - the main component of natural turpentes [1]. A study of the mechanism of the mutual transformations of cycloheptane and carene derivatives required the use of GLC analysis, since the reactions under investigation form multicomponent mixtures containing compounds of both series. However, the identification of the components of the mixtures being analyzed is made difficult by the closeness of the physicochemical properties of these compounds and by the absence from the literature of information on the retention properties of many of them.

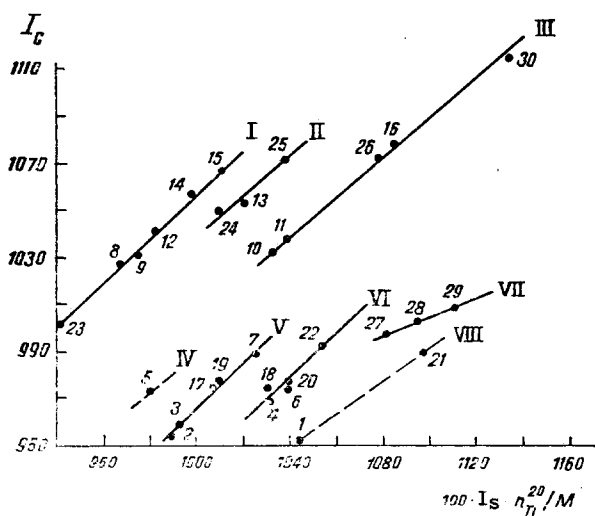


Fig. 1. Relationship between the retention indices of hydrocarbons 1-30 [(I-XXX) in Table 1] on squalane at 70°C (I_S) on the magnitude $100 \cdot I_S \cdot n_D^{20} / M$, n_D^{20} and M being the refractive indices and molecular weights of the hydrocarbons, respectively. Curve I) is for hydrocarbons with $M = 152$; II) $M = 150$; III) $M = 148$; IV) $M = 140$; V) $M = 138$; VI) $M = 136$; VII and VIII) $M = 134$.

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TABLE 1. Logarithmic Retention Indices on Squalane (I_s) and on Tricresyl Phosphate (I_t), Refractive Indices (n_D^{20}) and Molecular Refractions (MR_D) on the Hydrocarbons

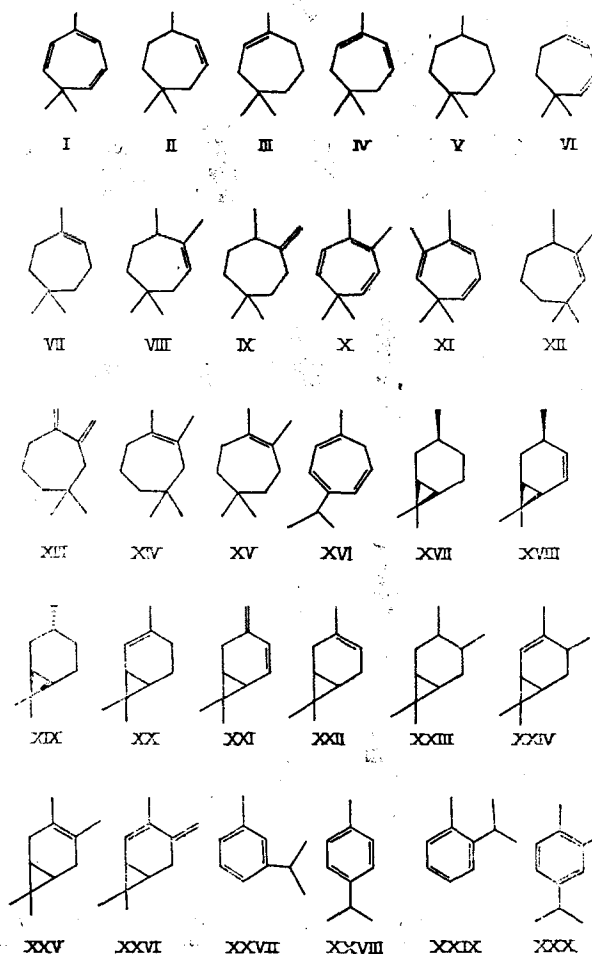
Compound	I_s	I_t	ΔI	n_D^{20}	MR_D		Purity according to GLC, %	Method of production
					calc.	found		
I	953	1121	168	1,4960	44,99	45,83	99,7	1
II	953	1041	88	1,4631	45,69	45,92	98,7	1
III	959	1003	44	1,4586	45,76	49,41	97,6	7
IV	969,5	1102	132,5	1,4764	45,38	45,64	98,5	1
V	974	984	10	1,4418	46,08	46,63	99,8	8
VI	976,5	1091	114,5	1,4758	45,38	46,06	98,8	1
VII	989	1046	57	1,4592	45,76	49,12	98,2	7
VIII	1029,5	1078	48,5	1,4584	50,38	51,82	97,9	*
IX	1031	1088	57	1,4687	50,23	52,35	98,6	*
X	1034,5	1182	147	1,5072	49,73	51,33	98,9	9
XI	1040	1194	154	1,5058	49,68	51,17	96,8	10
XII	1042,5	1119	76,5	1,4609	50,38	51,35	98,8	*
XIII	1054,5	1165,5	111	1,4809	46,76	50,33	99,1	*
XIV	1058,5	1124	65,5	1,4606	50,50	51,96	97,3	*
XV	1069	1135	66	1,4667	50,50	50,66	98,4	*
XVI	1082,5	1257,5	175	1,5134	49,68	49,79	97,6	11
XVII	975	1020	45	1,4558	44,69	44,65	98,3	12
XVIII	975	1040	65	1,4660	44,30	44,17	96,6	13
XIX	977,5	1026,5	49	1,4575	44,69	44,69	96,7	14
XX	978,5	1073	94,5	1,4738	44,37	44,31	100	8
XXI	991	1139,5	148,5	1,5107	43,84	47,36	99,6	14
XXII	993	1089	96	1,4730	44,37	44,17	100	15
XXIII	1004	1075	71	1,4560	49,31	49,42	96,9	16
XXIV	1051,5	1141	89,5	1,4684	48,99	49,03	97,5	17
XXV	1074	1174	100	1,4782	49,11	48,79	98,3	18
XXVI	1076	1223	147	1,5121	48,52	50,44	98,7	9
XXVII	999	1178,5	179,5	1,4920	45,16	45,16	100	1
XXVIII	1004	1183	179	1,4904	45,16	45,22	100	1
XXIX	1011	1209,5	198,5	1,4996	45,16	44,80	99,5	19
XXX	1117,5	1314	196,5	1,5303	49,90	50,57	98,9	20

*Synthesized by ourselves.

I) 3,7,7-Trimethylcyclohepta-1,3,5-triene; II) 3,6,6-trimethylcycloheptene; III) 1,4,4-trimethylcycloheptene; IV) 2,6,6-trimethylcyclohepta-1,3-diene; v) 1,1,4-trimethylcycloheptane; VI) 1,5,5-trimethylcyclohepta-1,3-diene; VII) 1,5,5-trimethylcycloheptene; VIII) 1,4,4,7-tetramethylcycloheptene; IX) 2,5,5-trimethyl-1-methylenecycloheptane; X) 3,4,7,7-tetramethylcyclohepta-1,3,5-triene; XI) 2,3,7,7-tetramethylcyclohepta-1,3,5-triene; XII) 1,3,3,7-tetramethylcycloheptene; XIII) 4,4-dimethyl-1,2-dimethylencycloheptane; XIV) 1,2,4,4-tetramethylcycloheptene; XV) 1,2,5,5-tetramethylcycloheptene; XVI) 4-isopropyl-1-methylcyclohepta-1,3,5-triene; XVII) cis-carane; XVIII) cis-4-carene; XIX) trans-carane; XX) 2-carene; XXI) cara-3(10),4-diene; XXII) 3-carene; XXIII) cis-4-methylcarene; XXIV) 4-methyl-2-carene; XXV) 4-methyl-3-carene; XXVI) 4-methylcara-3(10),4-diene; XXVII) m-cymene; XXVIII) p-cymene; XXIX) o-cymene; XXX) 4-isopropyl-1,2-dimethylbenzene.

The aim of the present work was to determine the logarithmic retention indices in capillary columns with polar and nonpolar stationary phases of alkyl-substituted hydrocarbons of the cycloheptane and carane series that had been synthesized; to estimate the applicability of the physical constants of the hydrocarbons - refractive indices and molecular refractions - as additional parameters for the gas-chromatographic identification of these substances; and to consider the influence of the structure of the molecules of the hydrocarbons being analyzed on their retention parameters.

The investigations showed that the more selective stationary phase was the polar one - tricresyl phosphate. In a column with this phase, compounds (II) and (XVIII) (Table 1) were poorly separated. In a column with the nonpolar phase, squalane, three pairs of hydro-



carbons had the same retention values: (I) and (II), (XVII) and (XVIII), and (XXVIII) and (XXIX). The use of the two columns ensured the separation of mixtures of any combination of the compounds studied.

It is considered that the refractive index (n_D^{20}) and the molecular refraction (MR_D) may be measures of the sorbate-sorbent dispersion interaction. Since the value of the retention index of a hydrocarbon on squalane (I_S) is also determined by this type of interaction, it appeared of interest to find the relationship between the n_D^{20} and MR_D values of the hydrocarbons and their I_S values.

As follows from the figures in Table 1, there is no linear correlation between the I_S values of the hydrocarbons and their n_D^{20} and MR_D values or the exaltations of their refraction. However, in chromatographic identification it is possible to use a graph of the dependence of I_S on $100 \cdot I_S \cdot n_D^{20} / M$, where M is the molecular weight of the hydrocarbon. On such a graph hydrocarbons with the same molecular weight are located close to a straight line. Deviations of the points from straight lines are probably the result of steric hindrance to the intermolecular interaction of the hydrocarbons with the squalane. In the graph, the line for compounds with $M = 152$ is the highest, and that for $M = 134$ the lowest.

The cymenes with $M = 134$ form a second line located above the line of carane and cyclopentane derivatives with the same values of M . This relationship permits the n_D^{20} values of the hydrocarbons to be determined approximately from their I_S and M values. It must be mentioned that for the majority of alkyl derivatives of cycloheptane the values of MR_D found are higher than those calculated. This is apparently connected with the existence of intramolecular interactions in the molecules of the hydrocarbons the influence of which is not taken into account in the calculations of MR_D from the formulas of the compounds [5].

As is well known, for given conditions of GLC analysis the difference between the retention indices of compounds on polar and nonpolar stationary phases (ΔI) is a constant, the numerical value of which depends on the structure of the molecule of the substance being analyzed. Thus, a double bond in the molecule of a hydrocarbon being studied makes a small

contribution to its I_s value. The magnitude of the contribution of this bond to the retention index on a polar stationary phase (I_t) ranges from 20 to 80 units, depending on its position in the molecule. The introduction of a double bond into the ring of 1,1,4-trimethylcycloheptane (V) in various positions with respect to the methyl substituent leads to compounds (III), (VII), and (II), the ΔI values of which are, respectively, 44, 57, and 88 units. This difference in the values of ΔI for these compounds can be explained by the dissimilar degrees of polarization of the double bond. In actual fact, in the PMR spectra the centers of the signals of the vinyl protons at the double bonds of (III), (VII), and (II) are, respectively, 5.31, 5.43, and 5.80 ppm, which shows different degrees of action of π -electrons of the double bond on these hydrogen atoms. A substantial influence on ΔI is also exerted by the position of geminal methyl substituents with respect to its double bond. The value of ΔI for compound (VIII) is more than 1.5 times lower than for (XII), which is probably due to a weak intramolecular interaction between the π -electrons of the double bond and one of the geminal methyl groups of compound (VIII), lowering the energy of its interaction with a polar stationary phase [3]. In favor of such an explanation is the difference in the values of the chemical shifts of the geminal methyl groups and the PMR spectra of these hydrocarbons. In compound (VIII) they are 0.87 and 0.96 ppm, while in (XII) these magnitudes are close to one another, being 0.87 and 0.89 ppm, respectively, which shows the absence of such intramolecular interaction. The lower value of I_s for compound (VIII) than for (XII) also confirms the assumption of the existence of an intramolecular interaction leading to a more hindered configuration of the molecule, the energy of the dispersion interaction of which with a nonpolar stationary phase is lower than for its structural isomer (XII).

It is known that the existence of conjugation between double bonds in a hydrocarbon molecule lowers the value of ΔI [4]. Among the compounds with a seven-membered ring that were investigated there were three hydrocarbons possessing a dienic system. In compounds (IV) and (VI) the double bonds are included in the seven-membered ring, which leads to a distortion of the valence angles and to an appreciable disturbance of the interaction of the double bonds with one another. Because of this, compounds (IV) and (VI) have higher ΔI values than compound (XIII), in which a more complete conjugation of the exocyclic double bonds is achieved.

An influence of the position of a double bond in the molecule on retention indices has also been found for the bicyclic compound that we investigated. When a double bond is introduced into the molecule of carane (XVII), the greatest increase in ΔI is observed in the case of the polarization of the double bond by a methyl substituent. Thus, ΔI for compound (XVIII), where the double bond is not polarized, is higher by 20 units than that of compound (XVII), while ΔI for (XX) and for (XXII) is 50 units greater.

The replacement of hydrogen by a methyl group in the carenes (XX) and (XXII) and the caradiene (XXI) leads basically to an increase in I_s for the compounds formed (XXIV-XXVI). An analogous substitution in carane (XVII), leading to compound (XXIII), causes an increase not only in I_s but also in ΔI by 26 units. The tetramethylcycloheptenes (XIV) and (XV) are characterized by values of ΔI that are 22 and 18 units, respectively, greater than those of the trimethylcycloheptenes (III) and (VIII). Conversely, the tetramethylcycloheptatrienes (X) and (XI) have values of ΔI that are 21 and 14 units lower than that of the trimethylcycloheptatriene (I), which is apparently connected with an increase in steric hindrance for the interaction of the double bonds with a polar stationary phase. In actual fact, it can be seen from a comparison of the ΔI values of compounds (XXX) and (XXVIII) that an arrangement of methyl substituents in the plane of the ring, which does not prevent such interaction, led to a rise in ΔI by 18 units.

The 1,2-dialkyl-substituted benzenes (XXIX and XXX), in the molecules of which there are nonbond interactions of the alkyl substituents are characterized by ΔI values almost 20 units greater than their analogues in which there are no such interactions (XXVII and XXVIII).

Thus, the magnitude of the contribution of double bonds and alkyl substituents to the values of I_s , I_t , and ΔI of the hydrocarbons studied depends to a substantial extent on their positions in the molecule, the nature of any interaction between them, and the presence of steric hindrance to sorbate-sorbent interaction. Nevertheless, the value of ΔI permits us to judge the presence of multiple bonds in the molecules of the compounds being analyzed. Thus, if ΔI of a hydrocarbon is in the range of 30-70 units, it may be assumed that its molecule contains a double bond or a cyclopropane ring, for ΔI values between 90 and 135

units it contains two double bonds or a double bond and a cyclopropane ring, and for ΔI values between 145 and 200 units it contains three double bonds or two double bonds and a cyclopropane ring.

EXPERIMENTAL

The work was carried out on a Chrom-4 gas chromatograph with a flame-ionization detector. Stainless-steel capillary columns (0.25 × 50 mm) were used at a column temperature of 70°C, the temperature of the evaporator being 170°C. Column I was prepared by the deposition of a 5% solution of squalane in chloroform by the dynamic method, and column II by the deposition of a 10% solution of tricresyl phosphate. The efficiencies of columns I and II for 3-carene, expressed as the number of effective theoretical plates, amounted to 48,000 and 37,400, respectively [6]. The velocity of flow of carrier gas (nitrogen) was 15-20 cm/sec, the flow being split in a ratio of 1:100. The volume of the sample of hydrocarbons diluted with ethyl ether that was injected did not exceed 1-2 μ l. The logarithmic retention indices of the hydrocarbons (I) were calculated by means of a well-known relation [2], using normal paraffins with from 8 to 12 C atoms. The absolute error in the calculation of I for the hydrocarbons at a confidence level of 0.95 was not greater than ± 0.05 unit. The hydrocarbons were obtained by known methods (see Table 1) and were isolated by fractional distillation in a column with an efficiency of 100 theoretical plates or by preparative GLC on a PAKhV-0.5 chromatograph with a 4 × 8000 mm column filled with Chromaton N-AW-DMCS (grain size 0.25-0.316 mm) impregnated with diethyleneglycol adipate (20% on the weight of the Chromaton). Isolation was carried out in the temperature interval of from 80 to 120°C at a rate of flow of carrier gas (helium) of 50-60 ml/min. Molecular refractions were calculated by a known method [5]. The PMR spectra of individual hydrocarbons were taken on Jeol PS-100 and WM-310 spectrometers in CDCl_3 solution with TMS as internal standard.

SUMMARY

1. The contributions of double bonds and alkyl substituents to the retention indices of alkyl-substituted hydrocarbons of the carane and cycloheptane series on polar and nonpolar stationary phases depend to a considerable extent on the positions of these bonds and of substituents in the molecule, on the existence of an intramolecular interaction between them, and on steric hindrance to sorbate-sorbent interaction.

2. The difference in the retention indices of hydrocarbons on polar and nonpolar stationary phases gives an idea of the number of multiple bonds in the hydrocarbon molecule.

3. No linear relationship has been observed between the magnitude of the sorbate-sorbent dispersion interaction determined by the retention index on a nonpolar phase and the electronic polarizability of hydrocarbon molecules, which is proportional to their molecular refraction.

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STEREOCHEMISTRY OF THE ADDITION OF A GRIGNARD REAGENT TO TERPENE
KETONES WITH SEVEN-MEMBERED RINGS

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The dehydration of 1,2,5,5- and 1,2,6,6-tetramethylcycloheptanols by the POCl_3/Py system has been studied. It has been established that the products of the dehydration of 1,2,5,5-tetramethylcycloheptanols are 1,2,5,5- and 1,4,4,7-tetramethylcycloheptenes, and those of the dehydration of 1,2,6,6-tetramethylcycloheptanols are 1,3,3,7- and 1,2,4,4-tetramethylcycloheptenes. On the basis of the results of dehydration by the POCl_3/Py system it has been shown that the Grignard reactions of 2,5,5- and 2,6,6-trimethylcycloheptanols form mainly tertiary alcohols with the trans orientation of the vicinal OH and CH_3 groups.

Oxygen-containing monoterpenoids with seven-membered rings are present in the essential oils and balsams of a number of plants [1, 2]. Individual representatives of this class exhibit a high biological activity, form part of complex catalysts, and are effective stabilizers of unstable compounds [3, 4]. Definite interest is presented by a study of this class of terpenoids in the stereochemical aspect. Recently, theoretical papers devoted to the conformations of cycloheptane have appeared [5, 6]. However, the practical study of the stereochemistry of cycloheptane and its derivatives is made difficult by the low energy barrier of the conformational transitions and by the existence of pseudorotation [7]. The presence of methyl substituents in monoterpenoids with seven-membered rings makes them convenient models for investigations in the field of cycloheptane as a whole. However, no systematic study of these compounds has so far been carried out. Work with such compounds is complicated by the smallness of their amounts in natural mixtures and with difficulties in their isolation.

We have used a simple method of obtaining oxygen-containing terpenoids with 7-membered rings from one of the commonest natural hydrocarbons - 3-carene. Disproportionation reactions of 3-carene have given 1,4,4- and 1,5,5-trimethylcycloheptenes, from which by hydroboration and oxidation 2,5,5- and 2,6,6-trimethylcycloheptanones (I) and (II) have been synthesized. When the Grignard reaction was performed with the latter, it was found that in each case a mixture of stereoisomeric alcohols was obtained the ratio of which could not be determined by spectral methods.

In order to determine the ratio of the stereoisomeric tertiary alcohols that we obtained and, consequently, to elucidate the stereochemical features of the spatial attack of ketones (I) and (II) by CH_3MgI , we studied the dehydration of the stereoisomeric 1,2,5,5-tetramethylcycloheptanols (III and IV) and 1,2,6,6-tetramethylcycloheptanols (V and VI) by phosphorus oxychloride in pyridine (POCl_3/Py). Since the use of the POCl_3/Py system excludes isomerization with the migration of the double bond, then, taking the stereochemistry of the

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