CONCLUSIONS

1. We have proposed a method of reaction chromatography-mass spectrometry based on use of a gas chromatograph-hydrogenation microreactor-mass spectrometer system (chromatography in a stream of hydrogen) in order to establish the structure of the carbon skeleton of olefins.

2. When using this system, carrying out the chromatography in a stream of deuterium allows us to determine the position of the double bond in some branched olefins.

LITERATURE CITED

- 1. P. Issenberg, A. Kobayashi, and T. J. Mysliwy, Agr. and Food Chem., 17, 1377 (1969).
- 2. V. G. Berezkin, Chemical Methods in Gas Chromatography [in Russian], Khimiya, Moscow (1980), p. 119.
- 3. H. Budzikiewicz, C. Djerassi, and D. H. Williams, Mass Spectrometry of Organic Compounds, Holden-Day, San Francisco (1967), p. 55.
- 4. G. Spiteller, Mass Spectrometric Structure Analysis of Organic Compounds [in German], Verlag Chemie, Weinheim (1966), p. 98.
- 5. D. G. Earnshaw, F. G. Doolittle, and A. W. Decora, Org. Mass Spectrom., 5, 801 (1971).
- 6. G. C. Bond and P. B. Wells, in: Catalysis. Physical Chemistry of Heterogeneous Catalysis [Russian translation], Mir, Moscow (1967), p. 351.

GAS CHROMATOGRAPHIC SEPARATION OF SOME STEREOISOMERIC DIOXOLANES AND THEIR IDENTIFICATION USING PMR SPECTROSCOPY

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Five-membered cyclic acetals are of considerable interest to researchers as model systems for the study of the stereochemistry of certain natural physiologically active substances. To this class of compounds belong the isomeric 1,3-dioxolanes, which have been studied earlier using PMR spectroscopy and for which the equilibrium isomeric composition has been established [1-8]. In these papers, the separation of pure isomers was carried out by the GLC method on long preparative columns.

It was shown [8] that the thermodynamically more stable cis isomer in the series of 2,4-disubstituted 1,3-dioxolanes has the lowest index of refraction and retention volume, and also has an upfield chemical shift for the C^2 proton compared with the trans isomer. This conclusion is confirmed by data obtained in [9]. Exceptions are the isomers of 2,4-di-tert-butyl-1,3-dioxolane, for which the reverse pattern is observed.

In [9], the behavior of di- and trisubstituted 1,3-dioxolanes was also studied. For the cis, trans isomers of 4,5-dimethyl-1,3-dioxolane, the order of elution is inverted compared with the corresponding 2,4-substituted compounds. The signal for C^2 protons for trans-4,5-dimethyl-1,3-dioxolane has a chemical shift which is intermediate between the values of the chemical shifts for protons of the corresponding cis isomer. For 2,4,5-trimethyl-1,3-dioxolane, the order of elution of the isomers is as follows: trans > cis-syn > cis-anti. Due to the shielding effect of methyl groups in the 4 and 5 positions, the chemical shifts of the C^2 protons are displaced upfield in the sequence: cis-syn > trans > cis-anti.

In this paper, we separated isomers of 2-substituted 4,5-diisopropyl-1,3-dioxolanes by the method of preparative circulatory GLC [10] and identified the isomers by PMR spectroscopy. Using high-efficiency capillary chromatography, we determined the thermodynamic characteristics of solution for cis-syn and cis-anti isomers.

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Fig. 1. Chromatogram of preparative circulatory chromatographic separation of a mixture of stereoisomers of 2-methyl-2-phenyl-4,5-diisopropyl-1,3-dioxolane. The sample volume is

EXPERIMENTAL

τ, h

Mixtures of the diastereomers of 2,4,5-triisopropyl-(I), 2-phenyl-4,5-diisopropyl-(II), and 2-methyl-2-phenyl-4,5-diisopropyl-1,3-dioxolanes (III) were synthesized by acid-catalyzed condensation of meso- and dl-2, 5-dimethylhexane-3, 4-diols with the corresponding carbonyl compounds according to standard techniques [5]. Meso- and dl-dimethylhexane-3,4-diols were synthesized by reduction of 2,5-dimethyl-3-hexanol-4-one by LiAlH₄ in ether; the ratio of meso- and dl-isomers was 23:2. The isomers were separated by fractional crystallization from cold CCl₄ and purified by vacuum sublimation analogously to [11].

The isomeric derivatives of 1,3-dioxolane obtained were separated on a circulating apparatus constructed on the basis of the LKhP-5I chromatograph (Special Design Bureau, Institute of Organic Chemistry, Academy of Sciences of the USSR). Taking into account the requirements for operational reliability of the switching device at elevated temperatures, we used circulation schemes with a gas-flow switching valve [10] and a valve switching system [12]. Two stainless steel columns of dimensions 4 m \times 23 mm were filled with the solid support Chromaton N-AW-DMCS with particle sizes 0.20-0.25 mm. The stationary phases were Carbowax-20M and DC-550. The volume of injected samples was 0.4-0.8 ml. Preparative separations were carried out at a temperature of 145°C for (I) and 210°C for (II) and (III). The quality of the preparative separation of isomers was monitored by analysis of the separated fractions in a capillary column of length 40 m with the stationary phase Ucon LB-550-X at 130 and 170°C, having an efficiency of 55,000 theoretical plates (with respect to benzene). On the same column we determined the thermodynamic parameters of solution for the separated isomers at several temperatures.

The NMR spectra were taken on the Tesla BS-497 instrument (Czechoslovak SSR) with an operating frequency of 100 MHz for 20-30% solutions in CCl_4 with an internal standard HMDS on the δ scale.

DISCUSSION OF RESULTS

The establishment of the precise configuration of the cis-syn and cis-anti isomers of 2,4,5-trisubstituted 1,3-dioxolanes is based on the chemical shifts of the signals for the C^2 protons in the cis-syn isomers upfield compared with the cis-anti isomers, and the reverse displacement of the signals from the C^2 substituents [5]. Protons at the 4,5 positions of the ring and the methine protons of the isopropyl groups form an AA'XX' system in the cis-syn and cis-anti isomers, and an ABXY system in the trans isomer [5], which allows us to assign the cis and trans arrangement to substituents at C^4 and C^5 .

TABLE 2. Enthalpy of Solution ΔH_S for Stereoisomers of 4,5-Diisopropyl-1,3-dioxolanes

R1	R ²	Isomer	∆Ħs, kJ/mole	
$egin{array}{c} \mathbf{H} \\ \mathbf{H} \\ \mathbf{H} \\ \mathbf{H} \\ \mathbf{CH}_3 \\ \mathbf{CH}_3 \end{array}$	(CH ₃) ₂ CH	cis-syn	37,8	
	(CH ₃) ₂ CH	cis-anti	38,1	
	C ₆ H ₅	cis-syn	54,5	
	C ₆ H ₅	cis-anti	54,1	
	C ₆ H ₅	cis-syn	52,0	
	C ₆ H ₅	cis-anti	51,6	

TABLE 3. Separation Coefficients and Differences in Thermodynamic Parameters of Solution for Stereoisomeric Pairs of 2-Substituted 4,5-Diisopropyl-1,3-dioxolanes

R'	\mathbf{R}^2	Isomeric pair	T of sep- aration, ℃	Separation coefficient α	∆∆F _s J/m	ΔΔH _s nole	مم≲ _e , J/K•mole
$_{ m H}^{ m H}$ CH $_3$	$({ m CH}_3) _2 { m CH} \ { m C}_6 { m H}_5 \ { m C}_6 { m H}_5$	cis-syn/anti cis-syn/anti cis-syn/anti	126 190 190	1,015 1,054 1,081	46,4 203,8 299,0	284,5 397,5 418,4	0,84 1,30 1,54

Preparative separation of the stereoisomers (I) required highly efficient separation, which was achieved by use of circulatory chromatography. In the separation of these isomers, we carried out up to 24 half-cycles; and a total separation efficiency of about 50 thousand theoretical plates was achieved, which is close to the values for the efficiency usually achieved only with the aid of capillary chromatography. The first separated fraction was the cis-syn isomer with a purity of 98-99%. In the PMR spectrum, there were signals from the methyl groups, the isopropyl substituents, the methine proton of the isopropyl group at C² (multiplet at 1.82 ppm), and the proton at C² (doublet at 4.30 ppm). The spectrum of the AA'XX' type was due to the presence of protons in the 4,5 positions and the methine protons of the isopropyl substituents at C⁴ and C⁵ (AA' - 3.52 ppm, XX' - 1.83 ppm). Such chemical shifts are characteristic for cis and syn conformations [5].

The second and third fractions of the second peak were a mixture of cis-(syn, anti) isomers in the ratio 2:1 and 1:1 respectively. The cis-anti isomer is identified from the chemical shift of the C^2 proton (4.70 ppm) and the AA'XX' spectrum of the methine protons of the isopropyl groups in the 4,5 positions and the $C^{4,5}$ protons (AA' = 3.59 ppm, XX' = 1.72 ppm).

Traces of trans isomer in (I) were not observed. Nevertheless, we would expect that the chemical shifts of the C^2 protons in the trans and cis-syn isomers (I) will apparently be close to the chemical shifts of the same protons in the trans and cis isomers of 2,4-diisopropyl-1,3-dioxolane respectively. Furthermore, the difference in the chemical shifts of the C^2 protons in the cis-syn and cis-anti isomers (I), in all probability, should correspond to the difference in the chemical shifts of the C^2 protons in cis-4,5-diisopropyl-1,3-dioxolane.

Using the PMR spectra, we established the following order of elution for the isomers of (II): trans > cissyn > cis-anti. In Table 1 we give the values for the chemical shifts of the C² protons and the C^{4,5} methine protons. As in the first case, for the cis-syn isomer the C² proton signal is observed upfield relative to the cis-anti isomer. The chemical shift of the C² proton in the cis-anti isomer of (II) downfield is due to the shielding effect of the isopropyl groups in the 4 and 5 positions.

In Fig. 1 we present the chromatogram for preparative separation of the stereoisomers of (III) by the method of circulatory GLC. After 4 half-cycles (m), the separation criterion of 1.58 for the second and third components of the sample was reached with an efficiency (for the second component) of 8000 theoretical plates. The separation coefficient for the given pair of stereoisomers, from the data of the analytic chromatogram, is 1.07; the yield of separated products is 84%.

The PMR spectra of the separated fractions of (III) indicate the following order of elution of the isomers: cis-syn > cis-anti > trans. In Table 1 we give the values of the chemical shifts for protons of the CH₃ group at C² and the methine protons at C^{4,5}.

For the stereoisomeric pairs (cis-syn:cis-anti) of 2,4,5-trisubstituted 1,3-dioxolanes, existing in acid media in thermodynamic equilibrium, we determined the differences in the heats and entropies of solution.

These stereoisomers in the reaction mixtures upon synthesis of 1,3-dioxolanes from meso-diol are also found in equilibrium, which determines their ratio in the final production of the reaction [5, 7].

The thermodynamic parameters, calculated according to [13], are given in Tables 2 and 3. From the data presented it is obvious that the thermodynamic characteristics of the stereoisomeric dioxolanes are very close to one another. Differences in the free energies of solution for 1,3-dioxolanes having one substituent in the 2 position are not more than 203-219 J/mole, which corresponds to values of the separation coefficients less than 1.06 (for 2,4,5-triisopropyl-1,3-dioxolane, less than 1.02). Such small separation coefficients determine the necessity for using high-efficiency capillary and circulatory chromatography for analysis of these substances and separation of the pure isomers. The separation coefficients and differences in the free energies were determined at three temperatures, including a 30° range. In Table 3 we present the data for only one temperature, corresponding to the middle of the interval used. The values for the enthalpy of solution for the studied stereoisomers in the stationary phase used are 37-55 kJ/mole, and for the cis-syn and cis-anti isomers they differ by 0.28-0.42 kJ/mole. The entropies of solution for the cis-syn and cis-anti isomers are also very close. The difference in the entropies for 2,4,5-substituted 1,3-dioxolanes is not more than $1.54 \text{ J/}^{\circ}\text{K}$. mole, which indicates the closeness of the molar volumes of these compounds. In the studied series of 2phenylsubstituted compounds, the cis-anti isomers were eluted earlier than the cis-syn isomers. However, in the case of isomers of 2,4,5-triisopropyl-1,3-dioxolane, we observe the reverse order for elution of these isomers. This fact suggests a complex effect of steric and electronic factors on the process of solution of substituted 1,3-dioxolanes in oxygen-containing solvents.

CONCLUSIONS

1. We accomplished the preparative separation of a number of stereoisomeric 1,3-dioxolanes by the circulatory GLC method with an efficiency greater than 30 thousand theoretical plates.

2. Using the PMR spectra of 2-substituted 4,5-diisopropyl-1,3-dioxolanes, we identified the isomers on the basis of differences in the chemical shifts of the signals from the proton and substituent in the 2 position in cis-syn and cis-anti isomers.

3. We determined the thermodynamic parameters of solution for the indicated stereoisomers. The given compounds have very small differences in the thermodynamic characteristics.

LITERATURE CITED

- 1. M. Anteunis and F. Alderweireldt, Bull. Soc. Chim. Belg., 73, 889 (1964).
- 2. M. Anteunis and F. Alderweireldt, Bull. Soc. Chim. Belg., 73, 903 (1964).
- 3. M. Anteunis and F. Alderweireldt, Bull. Soc. Chim. Belg., 74, 488 (1965).
- 4. R. U. Lemieux, J. D. Stevens, and R. R. Fraser, Can. J. Chem., <u>40</u>, 1955 (1962).
- 5. W. E. Willy, G. Binsch, and E. L. Eliel, J. Am. Chem. Soc., 92, 5394 (1970).
- 6. R. Böhm and E. Hannig, Pharmazie, 26, 600 (1971).
- 7. Sa Le Thi Shuan and J. Wiemann, Bull. Soc. Chim. France, 4550 (1968).
- 8. Y. Rommelaere and M. Anteunis, Bull. Soc. Chim. Belg., 79, 11 (1970).
- 9. F. Kametani and Y. Sumi, Chem. and Pharm. Bull., 20, 1479 (1972).
- 10. M. P. Zabokritskii, B. A. Rudenko, and V. P. Chizhkov, Izv. Akad. Nauk SSSR, Ser. Khim., 1627 (1977).
- 11. L. P. Kuhn, J. Am. Chem. Soc., 80, 5950 (1958).
- 12. M. P. Zabokritskii, B. A. Rudenko, and V. P. Chizhkov, in: Analytical and Preparative Application of Chromatography [in Russian], VNIITÉKhim., Moscow (1980), p. 62.
- 13. M. S. Vigdergauz and R. I. Izmailov, Application of Gas Chromatography for Determination of the Physicochemical Properties of Substances [in Russian], Nauka, Moscow (1970).