

13. K. Gollnik, *Tetrahedron Lett.*, 327 (1966).
14. É. N. Manukov, V. A. Chuiko, and O. G. Vyglazov, *Zh. Org. Khim.*, 19, 662 (1983).
15. I. I. Bardyshev and V. I. Efimenko, *Dokl. Akad. Nauk BSSR*, 3, 150 (1959).
16. G. Ohloff, H. Farnow, and W. Phillipp, *Ann. Chem.*, 613, 43 (1958).
17. Ho. Tse-Lok, *Synth. Commun.*, 13, 761 (1983).
18. L. K. Novikova, O. B. Skripnik, G. N. Bikbulatova, S. G. Vul'fson, Z. G. Isaeva, and A. N. Vereshchagin, *Izv. Akad. Nauk Ser. Khim.*, No. 3, 605 (1978).
19. V. V. Bazyl'chik, I. I. Bardyshev, N. I. Ryabushkina, N. P. Polyakova, and P. I. Fedorov, *Izv. Akad. Nauk BSSR, Ser. Khim. Nauk*, No. 6, 104 (1973).
20. G. Bourgeois and R. Lalande, *Bull. Soc. Chim. Fr.*, 4324 (1972).

## 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  $\text{POCl}_3/\text{Py}$  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  $\text{POCl}_3/\text{Py}$  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  $\text{CH}_3$  groups.

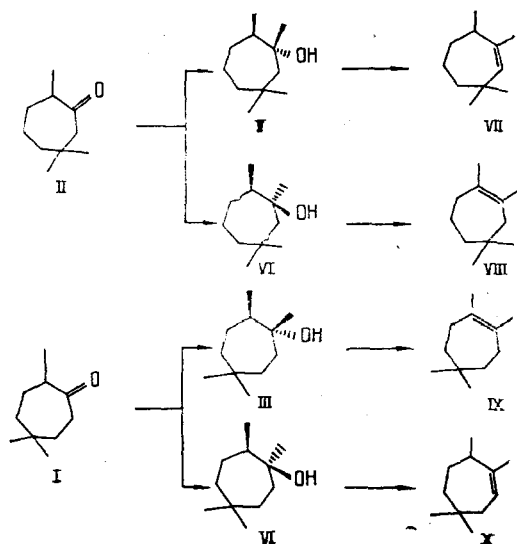
Oxygen-containing monoterpenoids with seven-membered rings are present in the essential oils and balsams of a number of plants [1, 2]. Individual representatives of this class exhibit a high biological activity, form part of complex catalysts, and are effective stabilizers of unstable compounds [3, 4]. 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  $\text{CH}_3\text{MgI}$ , 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 ( $\text{POCl}_3/\text{Py}$ ). Since the use of the  $\text{POCl}_3/\text{Py}$  system excludes isomerization with the migration of the double bond, then, taking the stereochemistry of the

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dehydration of alcohols into account, it is possible from the ratio of the cycloalkenes formed to judge the ratio of stereoisomers in the initial alcohols.

It may be assumed by analogy with the conformations of cycloheptane [6] that the initial ketone (II) has the skew-boat conformation. In accordance with this, and in view of the directivity of the attack of a  $sp^2$ -carbon atom by  $CH_3MgI$ , it was to be expected that 1,2,6,6-tetramethylcycloheptan-trans-ol (V) would predominate in the product of the Grignard reaction. The main stereoelectronic requirement for bimolecular elimination with the aid of  $POCl_3/Py$  is the anticoplanarity of the four centers participating in the reaction [8]. In the light of this, the dehydration of alcohol (V) should lead to 1,3,3,7-tetramethylcycloheptene (VII) and that of 1,2,6,6-tetramethylcycloheptan-cis-ol (VI) correspondingly to 1,2,4,4-tetramethylcycloheptene (VIII). When a mixture of the stereoisomers (V) and (VI) was dehydrated, a mixture of the cycloalkenes (VII) and (VIII) in a ratio of 3:1 was obtained, which may serve as a confirmation of the predominant formation of the alcohol (V).

An analogous series of transformations was also carried out for 2,5,5-trimethylcycloheptanone (I). The reaction of this compound with  $CH_3MgI$  gave a mixture of stereoisomeric 1,2,5,5-tetramethylcycloheptanols. When the mixture of stereoisomeric alcohols (III) and (IV) was dehydrated, a mixture of 1,2,5,5- and 1,4,4,7-tetramethylcycloheptenes (IX and X) in a ratio of 4:3 was obtained.

The ratio of the cycloalkenes (IX) and (X) formed indicated a sterically unhindered attack of a  $sp^2$ -carbon atom by the Grignard reagent from both sides of the seven-membered ring. In 2,6,6-trimethylcycloheptanone (II), the methyl groups at the  $C^6$  atom and the pseudo-axial hydrogen atoms at the  $C^3$  and  $C^5$  atoms create steric hindrance for the formation of the intermediate organometallic complex [9].

Thus, the presence in a 7-membered ring of a trigonal carbon atom changes its spatial structure to only an insignificant degree. As was assumed, its conformation in monoterpenoids with seven-membered rings corresponds to the conformation of cycloheptane - skew-boat.

#### EXPERIMENTAL

IR spectra were taken on a UR-20 instrument in a thin layer. PMR spectra were recorded on WM-360 and Jeol PS-100 spectrometers in deuteriochloroform with TMS as internal standard. The analysis of mixtures and the preparative isolation of the individual components by the GLC method were performed under the conditions described in previous papers [10, 11].

The initial 1,4,4- and 1,5,5-trimethylcycloheptenes were obtained as in [12].

2,5,5-Trimethylcycloheptanone (I) was obtained by the oxidative hydroboration of 1,5,5-trimethylcycloheptene [13]. From 20 g of hydrocarbon was obtained 15.1 g of product (8% of the initial compound and 92% of the ketone (I)) from which by the PGLC method the ketone (I) was isolated (purity 96.8%),  $n_D^{20}$  1.4599,  $d_4^{20}$  0.9022. IR spectrum ( $cm^{-1}$ ): 1347, 1366 (gem.  $2CH_3$ ); 1705 ( $C=O$ ). PMR spectrum ( $\delta$ , ppm): 0.89 s and 0.96 s (6H,  $2CH_3$ ); 1.05 d (3 H,

$J = 7.1$  Hz,  $\text{CH}_3$ ); 1.36-1.55 m and 1.62-1.72 m (6H,  $3\text{CH}_2$ ); 2.31-2.38 m (1H, CH in the  $\alpha$  position to a carbonyl group). Found %: C 77.85; H 11.63.  $\text{C}_{10}\text{H}_{18}\text{O}$ . Calculated %: C 77.92; H 11.668.

2,6,6-Trimethylcycloheptanone (II) was obtained by the oxidative hydroboration of 1,4,4-trimethylcycloheptene [13]. From 20 g of hydrocarbon was obtained 16.4 g of product (6% of the initial substance and 94% of the ketone (II)) from which the ketone (II) (with a purity of 97.8%) was isolated by the GLC method. Its physicochemical properties and spectral characteristics corresponded to those given in the literature [14].

The 1,2,5,5-Tetramethylcyclopentanol (III) and (IV) were obtained by the reaction of ketone (I) with  $\text{CH}_3\text{MgI}$  [15]. From 15 g of (I) was obtained 15.3 g of a mixture of products (11% of the initial ketone (I) and 89% of the alcohols (III) and (IV)) from which the alcohols (III) and (IV) were isolated by the PGLC method with a purity of 98.1%;  $n_D^{20}$  1.4661,  $d_4^{20}$  0.9708. IR spectrum ( $\text{cm}^{-1}$ ): 1364, 1385 (gem.  $2\text{CH}_3$ ); 3625 ( $-\text{OH}$ ). PMR spectrum ( $\delta$ , ppm): 0.87 s and 0.88 s (6H,  $2\text{CH}_3$ ); 0.95 (3H,  $J = 6.7$  Hz,  $\text{CH}_3$ ); 1.20 s (3H,  $\text{CH}_3$  geminal to an OH group); 1.12-1.22 m (2H,  $\text{CH}_2$ ); 1.32-1.38 m (1H, CH); 1.41-1.65 m (6H,  $3\text{CH}_2$ ). Found %: C 77.63, H 12.90.  $\text{C}_{11}\text{H}_{22}\text{O}$ . Calculated %: C 77.68; H 12.94.

The 1,2,6,6-Tetramethylcycloheptanol (V and VI) were obtained by the reaction of ketone (II) with  $\text{CH}_3\text{MgI}$  [15]. From 15 g of ketone (II) was obtained 16.7 g of a mixture of products (7% of the initial ketone (II) and 93% of the alcohols (V) and (VI)), from which the alcohols (V) and (VI) were isolated by the PGLC method in a purity of 98.4%;  $n_D^{20}$  1.4687,  $d_4^{20}$  0.9320. IR spectrum ( $\text{cm}^{-1}$ ): 1378, 1382 (gem.  $2\text{CH}_3$ ); 3625 ( $-\text{OH}$ ). PMR spectrum ( $\delta$ , ppm): 0.94 s and 0.99 s (6H,  $2\text{CH}_3$ ); 0.93 d (3H,  $J = 5.8$  Hz,  $\text{CH}_3$ ); 1.24 s (3H,  $\text{CH}_3$  geminal to OH); 1.13-1.21 m (1H, CH); 1.36-1.63 m (6H,  $3\text{CH}_2$ ); 1.55 d and 1.68 d (2H,  $J = 14.3$  Hz,  $\text{CH}_2$ ). Found %: C 77.65; H 12.89.  $\text{C}_{11}\text{H}_{22}\text{O}$ . Calculated %: C 77.68; H 12.94.

Dehydration with the  $\text{POCl}_3/\text{Py}$  System was carried out as described in [15]. From 15.0 g of 1,2,6,6-tetramethylcycloheptanol (V and VI) was obtained 8.1 g (61.1%) of a mixture of hydrocarbons isolated by the PGLC method had the following characteristics.

1,3,3,7-Tetramethylcycloheptene (VII), purity 98.8% (GLC results);  $n_D^{20}$  1.4609,  $d_4^{20}$  0.8122. IR spectrum ( $\text{cm}^{-1}$ ): 1365, 1375 (gem.  $2\text{CH}_3$ ); 1665 ( $\text{C}=\text{CH}$ ). PMR spectrum ( $\delta$ , ppm): 0.87 s and 0.96 s (6H,  $2\text{CH}_3$ ); 1.02 d (3H,  $J = 7$  Hz,  $\text{CH}_3$ ); 1.09-1.22 m and 1.34-1.42 m (4H,  $2\text{CH}_2$ ); 1.66 s (3H, vicinal  $\text{CH}_3$ ); 1.91-2.06 m (2H,  $\text{CH}_2$ ); 2.44-2.53 m (1H, CH); 5.45-5.52 m (1H,  $=\text{CH}$ ). Found %: C 86.83; H 12.82.  $\text{C}_{11}\text{H}_{20}$ . Calculated %: C 87.01; H 12.99.

1,2,4,4-Tetramethylcycloheptene (VIII), purity 97.3% (GLC results),  $n_D^{20}$  1.4606,  $d_4^{20}$  0.8021. IR spectrum ( $\text{cm}^{-1}$ ): 1370, 1390 (gem.  $2\text{CH}_3$ ); 1670 ( $\text{CH}_3\text{C}=\text{CCH}_3$ ). PMR spectrum ( $\delta$ , ppm): 0.87 s (6H, gem.  $2\text{CH}_3$ ); 1.42-1.44 m (4H,  $2\text{CH}_2$ ); 1.62 s (3H, vinyl  $\text{CH}_3$ ); 1.67 s (3H, vinyl  $\text{CH}_3$ ); 1.99 s (2H,  $\text{CH}_2$  in the  $\alpha$  position to a double bond); 2.02-2.06 m (2H,  $\text{CH}_2$  in the  $\alpha$  position to a double bond). Found %: C 86.90; H 12.86.  $\text{C}_{11}\text{H}_{20}$ . Calculated %: C 87.01; H 12.99.

From 15.0 g of the 1,2,5,5-tetramethylcycloheptanol (III and IV) was obtained 7.44 g (55.6%) of a mixture of hydrocarbons. The individual hydrocarbons (IX) and (X) isolated by the PGLC method had the following characteristics.

1,2,5,5-Tetramethylcycloheptene (IX), purity 98.4% (GLC results),  $n_D^{20}$  1.4667,  $d_4^{20}$  0.8102. IR spectrum ( $\text{cm}^{-1}$ ): 1371, 1388 (gem.  $2\text{CH}_3$ ); 1674 ( $\text{CH}_3\text{C}=\text{CCH}_3$ ). PMR spectrum ( $\delta$ , ppm): 1.09 s (6H, gem.  $2\text{CH}_3$ ); 1.46-1.51 m (4H,  $2\text{CH}_2$ ); 1.84 s (6H,  $\text{CH}_3\text{C}=\text{CCH}_3$ ); 2.19-2.24 m (4H,  $2\text{CH}_2$  in the  $\alpha$  position to a double bond). Found %: C 86.98; H 13.01.  $\text{C}_{11}\text{H}_{20}$ . Calculated %: C 87.01; H 12.99.

1,4,4,7-Tetramethylcycloheptene (X), purity 97.9% (GLC results),  $n_D^{20}$  1.4584,  $d_4^{20}$  0.8010. IR spectrum ( $\text{cm}^{-1}$ ): 1365, 1375 (gem.  $2\text{CH}_3$ ); 1630 ( $\text{C}=\text{CH}$ ). PMR spectrum ( $\delta$ , ppm): 0.87 s and 0.90 s (6H, gem.  $2\text{CH}_3$ ); 1.05 d (3H,  $J = 6.8$  Hz,  $\text{CH}_3$ ); 1.35-1.40 m and 1.51-1.56 m (4H,  $2\text{CH}_2$ ); 1.68 s (3H, vinyl  $\text{CH}_3$ ); 1.72-1.80 m and 1.95-2.04 m (2H,  $\text{CH}_2$  in the  $\alpha$  position to a double bond); 2.22-2.29 m (1H, CH); 5.23-5.29 m (1H,  $=\text{CH}$ ). Found %: C 86.91; H 13.00.  $\text{C}_{11}\text{H}_{20}$ . Calculated %: C 87.01; H 12.99.

#### SUMMARY

On the basis of the results of the dehydration of the alcohols with the  $\text{POCl}_3/\text{Py}$  system it has been shown that the Grignard reaction with 2,5,5- and 2,6,6-trimethylcycloheptanones

forms predominantly tertiary alcohols with the trans orientation of the vicinal OH and CH<sub>3</sub> groups.

#### LITERATURE CITED

1. K. Görler, W. Molls, U. U. Siehl, J. Strähle, and C. Westphal, *Ann. Chem.*, No. 5, 1006 (1982).
2. T. Soced, P. J. Sondra, and M. J. E. Verzele, *Phytochemistry*, 17, 1433 (1978).
3. T. L. Macdonald, *J. Org. Chem.*, 43, 3621 (1978).
4. P. Dauchev, A. Gorgiev, E. Chalina, V. Spasov, and P. Staneva, *Farmatsiya*, 29, 1 (1979).
5. F. H. Cano and C. Foces-Foces, *Theochem.*, 11, 209 (1983).
6. V. Elser and H. L. Straus, *Chem. Phys. Lett.*, 93, 2768 (1983).
7. J. Hendrickson, R. K. Boeckman, J. D. Glickson, and E. Grundwald, *J. Am. Chem. Soc.*, 95, 494 (1973).
8. E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, *Conformational Analysis*, Interscience, New York (1965).
9. F. A. Carey and R. J. Sundberg, *Advanced Organic Chemistry*, Plenum Press, New York, Part B, 1st ed. (1977).
10. É. N. Manukov, V. A. Chuiko, and P. P. Kuz'michkin, *Khim. Prir. Soedin.*, 783 (1979).
11. É. N. Manukov and T. R. Urbanovich, *Izv. Akad. Nauk BSSR, Ser. Khim. Nauk*, 3, 70 (1985).
12. I. I. Bardyshev, G. V. Deschits, and A. A. Vakhrameeva, *Izv. Akad. Nauk BSSR, Ser. Khim. Nauk*, 2, 65 (1980).
13. H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, 83, 295 (1961).
14. F. Rulko and J. Mielczarek, *Pol. J. Chem.*, 55, 1709 (1984).
15. L. K. Novikova, O. B. Skripnik, G. N. Bikbulatova, S. N. Vul'fson, Z. G. Isaeva, and A. N. Vereshchagin, *Izv. Akad. Nauk SSSR, Ser. Khim. Nauk*, No. 3, 603 (1978).

#### X-RAY STRUCTURAL INVESTIGATION OF SESQUITERPENE ESTERS FROM PLANTS

OF THE GENUS *Ferula*.

#### III. CRYSTAL AND MOLECULAR STRUCTURE OF THE GERMAGRANE

#### ESTER CHIMGANIDIN

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An x-ray structural investigation of the germacrane ester chimganidin (diffractometer Cu K $\alpha$  radiation, 1028 reflections, direct method, R factor 0.114) has been carried out. The stereochemistry of chimganidin has been established; it is 6 $\alpha$ -hydroxy-8 $\beta$ -vanilloyloxygermacra-1(10),4(5)-diene. The double bonds in the macrocycle have the trans configuration.

Chimganidin - a germacrane ester with the composition C<sub>23</sub>H<sub>32</sub>O<sub>5</sub>, was isolated from the plants *Ferula pallida* Korov. and *Ferula tschimganica* Lypsky [1, 2]. Structure (Ia) with a germacrane macrocycle was proposed for chimganidin on the basis of IR, mass, and PMR spectroscopy and some chemical transformations [3]. However, an unambiguous determination of the structure and stereochemistry of chimganidin by spectroscopic methods especially PMR, proved to be difficult because of the presence of a labile ten-membered macrocyclic unit; moreover, the Cope chemical transformation performed did not permit the positions of the double bonds in the germacrane ring to be fixed definitively as 1(10),4(5) or 1(10),5(6) [3].

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