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2-CARENE IN THE PRINS REACTION

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UDC 547.597

The Prins reaction of 2-carene with formaldehyde has been studied. The main reaction product is 2-hydroxymethyl-3-carene. The dehydration of 2-hydroxymethyl-3-carene is accompanied by a skeletal rearrangement of the carane structure with the formation of products having a seven-membered ring.

The monoterpene hydrocarbon 2-carene is a component of pine turpentines [1]. In contrast to those of its isomer – 3-carene – its chemical transformations taking place with the retention of the bicyclic structure have been little studied. In the patent literature the possibility has been shown of its use in the direct synthesis of derivatives of practical value. Thus, amino ethers of 2-hydroxymethyl-3-carene obtained from 2-carene by the Prins condensation with formaldehyde possess spasmolitic activity [2]. However, the condensation reaction itself has not been described in the scientific literature. Nevertheless, this reaction is of definite interest both from the theoretical and from the practical points of view: Its main product, 2-hydroxymethyl-3-carene can, by analogy with the isomeric 4-hydroxymethyl-2-carene, be used as a perfume substance. Furthermore, the dehydration of this primary alcohol should lead to 2-methylene-3-carene – a compound with a crossed system of conjugation one of the elements of which is a cyclopropane ring.

When 2-carene (I) was condensed with paraformaldehyde in the absence of a solvent or in pyridine (180°C, 6 h), trans-2-hydroxymethyl-3-carene (II) was formed in 30-38% yield. When the reaction was performed in acetic acid (120°C, 48 h), in addition to unchanged (I)

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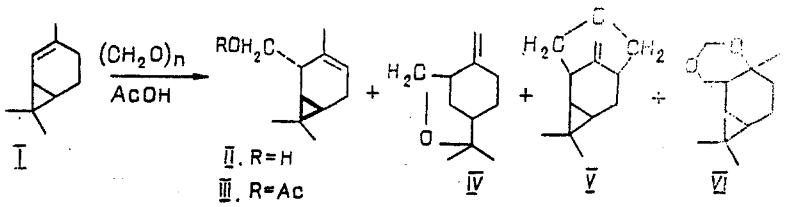
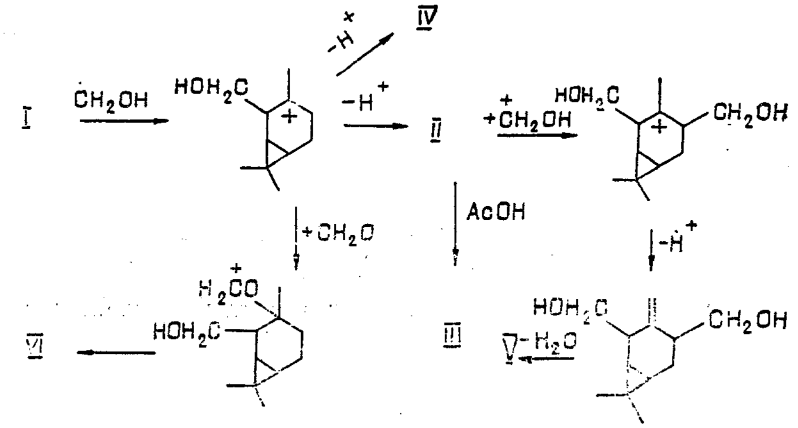
(40%), the following compounds were isolated and identified: trans-2-acetoxymethyl-3-carene (III) (28%), the alcohol (II) (7%), 2,2-dimethyl-6-methylene-3-oxabicyclo[3.3.1]nonane (IV) (3%), 3,3-dimethyl-10-methylene-8-oxatricyclo[4.3.1.$0^{2,4}$]decane (V) (5%), and 3,7,7-trimethyl-8,10-dioxatricyclo[5.4.0.$0^{2,4}$]undecane (VI) (2%), together with 10% of a fraction (bp 135-155°C/7 mm) the composition of which has not been studied.



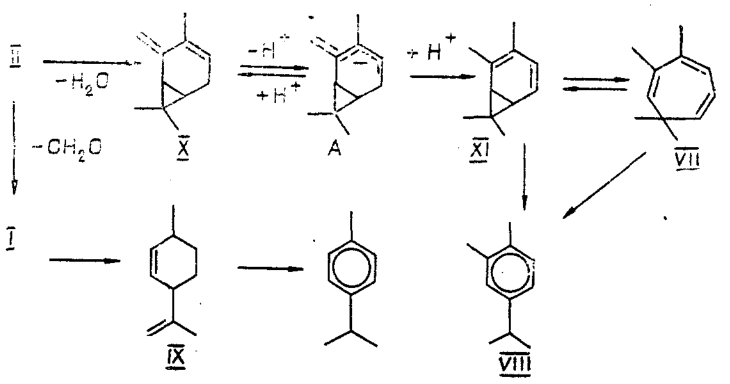
The properties of the ethers (IV) and (V) correspond to those of the same compounds isolated previously from the products of the Prins reaction of 3-carene [3, 4]. The bicyclic structures of the dioxane (VI), obtained for the first time, and of the alcohol (II) and the ester (III) were established on the basis of spectral characteristics. In the PMR spectra of these compounds, characteristic multiplets in the δ 0.48-0.96 ppm region corresponded to the two protons of the cyclopropane ring. For compounds (II) and (III), singlets in the 5.37-5.42 ppm region corresponded to a vinyl proton. The formation both of the main products (II) and (III) and of the minor products (IV)-(VI) when the reaction was performed in acetic acid is explained by the following scheme:



The alcohol (II) was dehydrated by Ohloff's method [5] over anhydrous KOH, since the use of acid catalysts leads to deformylation of primary homoallyl alcohols [6]. The reaction product consisted of mixture containing 2,3,7,7-tetramethylcyclohepta-1,3,5-triene (VII) (55.1%), 4-isopropyl-1,2-dimethylbenzene (VIII) (15.7%), isolimonene (IX) (0.5%), p-cymene (1.3%), and the unchanged alcohol (II) (27.4%). The reaction mixture did not contain the product of the 1,2-elimination of water – 2-methylene-3-carene (X) – the formation of which might have been expected by analogy with the formation of 4-methylene-2-carene on the dehydration of 4-hydroxymethyl-2-carene [7].

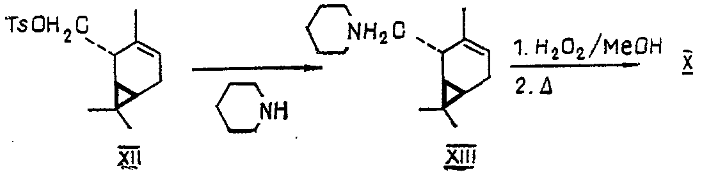
It was obvious that the hydrocarbons (VII) and (VIII) cannot be primary dehydration products and are formed as the result of secondary transformations. A scheme of these transformations can be represented in the following way (see scheme on top of following page).

The splitting out of water from the molecule of (II) should lead to the expected bicyclic hydrocarbon. Ionization under the action of a base gives the pentadienyl anion A, which is stabilized by the addition of a proton either to the C-11 or to the C-5 atom. The first route makes the ionization stage reversible, while the second leads to 2-methyl-2,4-caradiene (XI). Since methyl substituents at the C-7 atom cannot stabilize the cis-divinylcyclopropane fragment of compound (XI) [8], the bicyclic hydrocarbon (XI) tautomerizes into the triene (VII). Thus, the hydrocarbon (X) formed initially is "pumped over" via ion A into the stable monocyclic triene (VIII). The thermal deformylation of (II) taking place in parallel (to a very small degree) gives 2-carene, which undergoes thermal isomerization into (IX) [9].



To confirm the mechanism of skeletal rearrangement suggested above, we synthesized the intermediate hydrocarbon (X) and studied its basic isomerization.

Compound (X) was synthesized by the following scheme. The alcohol (II) was converted into its tosylate (XII). The nucleophilic replacement of the tosyl group in the tosylate (XII) by an amino group gave 2-piperidinomethyl-3-carene (XIII). The oxidation of the latter with H_2O_2 in MeOH led to the N-oxide, which, on Cope decomposition gave a 34% yield of 2-methylene-3-carene (X).



Boiling the diene (X) over KOH for 30 min gave a mixture of hydrocarbons containing 2,3,7,7-tetramethylcyclohepta-1,3,5-triene (78%) and 4-isopropyl-1,2-dimethylbenzene (22%). A similar mixture was obtained when the diene (X) was treated with potassium tert-amylate in benzene.

EXPERIMENTAL

IR spectra were taken on a UR-20 instrument in a thin layer, and ^1H and ^{13}C NMR spectra on a WM-360 spectrometer in deuterochloroform with HMDS as internal standard. Mass spectra were taken on a Varian MAT-311 instrument with cathode emission current of 1000 mA and an energy of the ionizing electrons of 10 eV, the temperature of the ion source being 200°C. The analysis of mixtures and the preparative isolation of the components by the GLC method were performed under the conditions described in [10, 11].

The initial 2-carene was obtained by isomerizing 3-carene with N-lithoethylenediamine [12]. Its condensation with paraformaldehyde was performed by the method of Ohloff et al. [13]. The acetate (III), the alcohol (II), and a concentrate of the ethers (IV)-(VI) was isolated from the redistilled condensation product by the PGLC method.

trans-2-Acetoxymethyl-3-carene (III), purity 97.3%, d_4^{20} 0.9870, n_D^{20} 1.4990. IR spectrum, cm^{-1}: 1365, 1375 (gem. $-2CH_3$); 1654 (C=CH); 1240 (C—O—C); 1740 (C=O). PMR (360 MHz, $CDCl_3$): 0.72-0.84 (2 H, m, CPR); 0.87 and 1.05 (6 H, s, gem. $-2CH_3$); 1.65 (3 H, s, vinyl CH_3); 1.84-2.00 (2H, m, methylene protons at C-5); 1.95 (3 H, s, CH_3 in the α-position to a carbonyl group); 2.11-2.22 (1 H, m, methine proton at C-2); 3.80-4.15 (2 H, m, methylene protons at C-11); 5.42 (1 H, s, vinyl proton at C-4). Mass spectrum, m/z (%): 208 (M^+, 100).

trans-2-Hydroxymethyl-3-carene (II), purity 98.9%, d_4^{20} 0.9606, n_D^{20} 1.4948. IR spectrum, cm^{-1}: 1374, 1394 (gem. $-2CH_3$); 1647 (C=CH); 1225 (C—O—C); 3350 (—OH). PMR (360 MHz, $CDCl_3$): 0.63-0.96 (2 H, m, CPR), 0.81 and 0.99 (6 H, s, gem. $-2CH_3$); 170 (3 H, s, vinyl CH_3); 1.95-2.10 (2 H, m, methylene protons at C-5); 2.12-2.25 (1 H, m, methine proton at C-2); 3.46-3.68 (2 H, m, methylene protons at C-11); 5.37 (1 H, s, vinyl proton at C-4); ^{13}C NMR (22.63 MHz, $CDCl_3$): 18.0 (d, C-1), 38.7 (d, C-2), 131.3 (s, C-3), 125.4 (d, C-4), 21.7 (t, C-5), 24.5 (d, C-6), 21.3 (s, C-7), 29.3 (q, C-8), 13.8 (q, C-9), 22.1 (q, C-10), 65.7 (t, C-11). Mass spectrum, m/z (%): 166 (M^+, 100).

The individual ethers (IV), (V), and (VI) were isolated from a concentrate of a mixture of them by column chromatography [alumina of Brockmann's second activity grade; eluent: pentane–diethyl ether (20:1)]. The physicochemical and spectral properties of the ethers (IV) and (V) corresponded to those given in the literature [3, 4].

3,7,7-Trimethyl-8,10-dioxatricyclo[5.4.0.$0^{2,4}$]undecane (VI), purity 98.8%, mp 62°C. IR spectrum, cm^{-1}: 1380, 1395 (gem. $=CH_3$); 1035, 1082, 1110, 1170 ($-C-O-CH_2-O-C$), PMR (360 MHz, $CDCl_3$): 0.48-0.52 (2 H, m, CPR), 0.68-0.79 (2 H, m, CPR); 1.00 and 1.06 (6 H, s, gem. $-2CH_3$); 1.20-1.28 and 1.42-1.70 (4 H, m, methylene protons at C-4 and C-5); 1.82-1.91 (1 H, m, methine proton at C-2); 3.38-3.42 and 3.60-3.68 (2 H, m, methylene protons at C-12). Mass spectrum, m/z (%): 196 (M^+, 100).

The dehydration of the alcohol (II) was carried out by Ohloff's procedure [5]. The physicochemical and spectral properties of the 2,3,7,7-tetramethylcyclohepta-1,3,5-triene (VII), and of the 4-isopropyl-1,2-dimethylbenzene (VIII) corresponded to those given in the literature [12, 13].

trans-2-Tosyloxymethyl-3-carene (XII), mp 40-41°C (hexane). IR spectrum, cm^{-1}: 1184, 1190, 1355 ($O-SO_2-Ar$); 1605 ($CH=C$). PMR spectrum (360 MHz, $CDCl_3$): 0.50-0.58 and 0.74-0.84 (2 H, m, CPR); 0.85 and 1.02 (6 H, s, gem. $-2CH_3$); 1.65 (s, vinyl CH_3); 1.95-2.09 (2 H, m, methylene protons at C-5); 2.15-2.21 (1 H, m, methine proton at C-2); 5.46 (1 H, s, vinyl proton); 7.40 and 7.82 (4H, d, J = 7.9 Hz, aromatic protons).

trans-2-Piperidinomethyl-3-carene (XIII) was obtained from the tosylate (XII) by the procedure of [14] with a purity of 98.6%, d_4^{20} 0.9310, n_D^{20} 1.4978. IR spectrum, cm^{-1}: 1125, 1166 ($N-C$); 1368, 1382 (gem. $-2CH_3$); 1660 ($C=CH$). PMR (360 MHz, $CDCl_3$): 0.60-0.66 and 0.96-1.00 (2 H, m, CPR); 0.85 and 1.02 (6 H, s, gem. $-2CH_3$); 1.40-1.45, 1.52-1.60, and 2.20-2.38 (10 H, m, methylene protons of a heterocycle); 2.03-2.09 (1 H, m, methine proton at C-2); 2.45-2.52 (2 H, m, methylene protons at C-5); and 5.23 (1 H, s, vinyl proton at C-4). Mass spectrum, m/z (%): 233 (M^+, 100).

The oxidation of trans-2-piperidinomethyl-3-carene was performed by a standard procedure [15]. The thermal decomposition of the N-oxide was achieved without its isolation from the reaction mixture by heating the latter to 120°C (10 mm) with the simultaneous removal by distillation of the 2-methylene-3-carene (X) formed.

2-Methylene-3-carene (X), purity 96.1%, d_4^{20} 0.8901, n_D^{20} 1.5046. IR spectrum, cm^{-1}: 868 ($CH_2=C$); 1010 and 3050 (CPR); 1370 and 1387 (gem. $-2CH_3$); 1610 and 1645 (two conjugated double bonds). PMR (360 MHz, $CDCl_3$): 0.83-0.89 (2 H, m, CPR); 0.81 and 1.09 (6 H, s, gem. $-2CH_3$); 1.79 (3 H, s, vinyl CH_3); 2.15 and 2.48 (2 H, d, J = 12 Hz, methylene protons at C-5); 4.94 and 5.07 (2 H, s, methylene protons at C-11); 5.41 (1 H, s, vinyl proton at C-4). Mass spectrum, m/z (%): 148 (M^+, 100).

The results of the analysis of all the compounds given above corresponded to the calculated figures.

Hydrocarbon (X) was isomerized by boiling it over anhydrous KOH for 30 min in the presence of hydroquinone. After being washed with water, the organic fraction was dried over $MgSO_4$ and was distilled under reduced pressure.

The isomerization of the diene (X) under the conditions of phase-transfer catalysis was carried out by mixing 0.1 mole of the diene with 0.01 mole of t-AmONa and 0.001 mole of dibenzo-18-crown-6 in 10 ml of benzene for 4 h. After being washed with water, the organic fraction was dried with $MgSO_4$. The solvent was driven off and the product was distilled under reduced pressure.

SUMMARY

1. It has been shown that under the conditions of the Prins reaction of 2-carene the main reaction product is 2-hydroxymethyl-3-carene. When the reaction is performed in acetic acid, the formation of an ester and of ethers was observed.

2. The dehydration of 2-hydroxymethyl-3-carene is accompanied by a skeletal rearrangement of the carane structure.

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SPATIAL STRUCTURES OF THE SESQUITERPENE GERMACRANE LACTONES TANACHIN AND TAMIRIN

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An x-ray investigation has been made of the sesquiterpene lactones tanachin and tamarin: diffractometer, $CuK\alpha$-radiation, 845 and 981 reflections, respectively, direct method, R factors 0.064 and 0.065. The conformations of both molecules are boat-boat with configurations of the $^{1}D_{14}$ and $^{15}D_{5}$ types.

The structures of the sesquiterpine germacrane lactone tanachin and tamirin were established on the basis of spectral characteristics and chemical transformations [1-6]. However, stereochemical aspects of the structures of these compounds (the linkage of the rings and the conformation of ten-membered ring) on the basis of their PMR spectra caused difficulties because of the lability of the germacrane ring.

In order to establish reliably the spatial structures of tanachin and tamarin, we have carried out an x-ray structural investigation of them, results of which are shown in Fig. 1. It can be seen from Fig. 1 that the lactone ring in the 7,8 positions of these molecules is linked with the germacrane ring in the trans manner, as suggested previously [2]. The hydroxy groups in positions 1 and 6 in tanachin and in position 6 in tamirin are α-oriented. The conformation of the germacrane ring is characterized by the torsion angles given in Table 1. The values of −157.6° for the C9C10C1C2 torsion angle and 165.9° for the C3C4C5C6 torsion angle around the double bond in tanachin and corresponding values of −153.7° and 166.4° in tamirin permit these compounds to be assigned to the trans-trans germacranolides, i.e., to the germacrolides [7].

By projecting the molecule onto the plane perpendicular to the mean square plane of the germacrane ring it can be seen that the C1=C10 and C4=C5 double bonds are practically parallel while the methyl and methylene groups at C10 and C4 have the anti orientation similar to that found in mucrin [8]. Consequently, the germacrane rings in tanachin and tamirin have the boat-boat conformation with configurations of the $^{1}D_{14}$ and $^{15}D_{5}$ types.

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