OXYGEN-CONTAINING TERPENOIDS OF THE
1,1,4-TRIMETHYLCYCLOHEPTANE SERIES

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This review, which covers the literature up to 1992, gives information on the occurrence in nature, the practical use, the synthesis, and the chemical transformations of oxygen-containing terpenoids of the 1,1,4-trimethylcycloheptane series.

In terpenoid chemistry, compounds with a 1,1,4-trimethylcycloheptane skeleton are perhaps the least studied of all monoterpenoids. Only eucarvone and its derivatives have been investigated in very great detail. Nevertheless, compounds of this series are present in the essential oils and balsams of various plants. There are reports of biological activity shown by them and of their use in perfumery compositions. The study of terpenoids with a seven-membered carbon ring is therefore of interest from both the theoretical and the practical points of view.

Occurrence in Nature of Terpenoids with a Seven-Membered
Ring and Their Practical Utilization

At the present time the existence of a genetic link beween terpenoids of the bicyclo[4.1.0]heptane and cycloheptane series has been established theoretically. But, as compared with the compounds possessing a bicyclic structure (carane series), their monocyclic isomers are considerably less common in nature. Thus, 3-carene − 3,7,7-trimethylbicyclo[4.1.0]hept-4-ene (1) is one of the main components of natural turpentines [1], while the level of 3,7,7-trimethylcyclohepta-1,3,5-triene (2) does not exceed 0.2% [2].

The only oxygen-containing terpenoids of the 1,1,4-trimethylcycloheptane series that have been detected in plant essential oils are eucarvone − 2,6,6-trimethylcyclohepta-2,4-dienone (3), 3,6,6-trimethylcyclohepta-2,4-dienone (4), karahanoenone − 2,2,5-trimethylcyclohept-4-enone (5), and karahanoenol (6).

$\underline{3}$ $\underline{4}$ $\underline{5}$ $\underline{6}$ $\underline{7}$
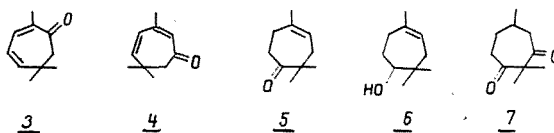
Of these compounds, that most widely distributed in natural essential oils is eucarvone. Japanese and Chinese researchers have detected eucarvone as a component of the essential oils of various species of the genera *Asarum* [3-6], *Asiasarum* [7-9], and *Heterotropa* [10-13]. Depending on the species, the content of the ketone (5) ranged from 0.1 to 3.0%, except for the essential oils of some plants of the *Asarum* genus growing in China, in which its level reached 6.0%. The presence of eucarvone has also been established in the essential oils of Moroccan wild chamomile [14], in an oil obtained from the leaves and flowers of a wormwood growing in Egypt and Italy [15, 16] and in the oils of sweet grass [17] and germander [18]. Eucarvone is present in the essential oils of citruses − orange [19, 20] and lemon [21, 22] and also in those of mango

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[23] and olive [24]. In addition, eucarvone has been detected in the essential oil of juniper [25] and in pine oleoresin turpentine [26]. As well as in the plants mentioned above, eucarvone is present in the essential oils of a number of herbs growing mainly in countries of South-East Asia, in southern Europe, and in Africa, Australia, and South America.

The ketone (4), isomeric with eucarvone, has been detected in black pepper oil [27, 28] and in Scots pine oleoresin turpentine [26].

Karahanoenone (5) was first isolated by Japanese workers from hop oil [29]. This ketone (5) and the alcohol corresponding to it (6) have been isolated from the essential oil of cypress branches [30-32].

In addition to natural monoterpenoids with a seven-membered ring, a large number of diverse compounds of this series have been obtained synthetically. However, in view of the difficulties in their preparation and isolation, these compounds have not found wide use.

Since many substances with a trimethylcycloheptane skeleton possess a pleasant odor, they are most frequently used as ingredients in perfumery compositions [33]. Thus, 2,2,5-trimethylcyclohepta-1,3-dione (7) is used in cosmetics, perfumery compositions, and toothpastes as an aroma-retaining agent [34]. Karahanoenol (6) and its esters (formate, acetate, propionate) are also used in perfumery [35].

It has been shown that eucarvone is a biologically active compound. It exhibits bacteriostatic and fungistatic activities [36] and is a termite repellant [37]; however there are no reports on its practical use.

## Synthesis of Oxygen-Containing Terpenoids of the 1,1,4-Trimethylcycloheptane Series

The best-studied oxygen-containing terpenoid of the 1,1,4-trimethylcycloheptane series is eucarvone — 2,6,6-trimethylcyclohepta-2,4-dienone (3). Eucarvone was first synthesized by Bayer in 1894 from carvone — p-mentha-2,8-dienone [38].
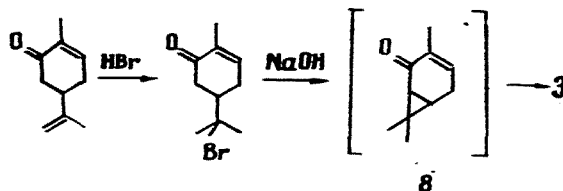
Bayer believed that he had obtained a bicyclic ketone — 3-caren-2-one (8). Later, Wallach showed that the product synthesized was a monocyclic seven-membered ketone, and it was named eucarvone [39]. With the determination of the true structure of eucarvone, the question of the mechanism of its formation arose. Wallach suggested that the formation of the ketone (3) from carvone hydrobromide took place through the intermediate 3-caren-2-one, but he did not succeed in detecting this ketone in the reaction mixture. In 1957, on the basis of UV-spectroscopic results, Van Tamelen et al. [40] deduced that the carenone (8) was present in the reaction mixture. Individual 3-caren-2-one was isolated only in 1984 by treating carvone hydrochloride with a solution of NaOH in DMSO [41].

For a long time, the method of synthesizing eucarvone from carvone hydrobromide remained the main way of obtaining this ketone (3), thanks to the ready availability of the starting material and the considerable yield (65-70%).

In 1961, Barnes proposed a method of synthesizing eucarvone from 2,2-dimethylcyclohexanone [42] by the following scheme:
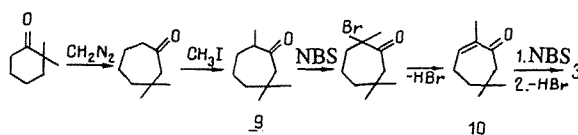
Successive bromination and dehydrobromination of the tetrahydroeucarvone (9) obtained and then of the dihydroeucarvone (10) led to the desired product (3). Deficiencies of this method are its multistage nature and the low yields of the intermediate ketone (9) (10-15%) and, consequently, of eucarvone (3).

At about the same time communications appeared by B. A. Arbuzov et al. on the formation of ketones (3) and (4) on the oxidation of 3-carene in the presence of lead tetraacetate [43], chromic anhydride [44, 45], and other catalysts [46-48]. Somewhat later, similar investigations on the oxidation of 3-carene by potassium permanganate [49] and chromic anhydride [50] were pursued by Cocker et al. They studied the composition of the reaction products and suggested that the ketones (3) and (4) with a seven-membered ring were formed from ketones of the carane series (3-caren-2-one and 3-caren-4-one), which were also detected in the reaction products. However, this route cannot be regarded as a method for the preparative formation of compounds (3) and (4), since the result of oxidation is the formation of multicomponent mixtures and the level of ketones (3) and (4) is low.

Eucarvone is formed in the oxidation 3-carene by thallium compounds [51]. The results of a study of the autooxidation of 3-carene in the presence of 13 different catalytic systems including compounds of cobalt and manganese have been given in the literature [52]. In all the experiments ketones (3) and (4) were detected in the oxidates but their amounts did not exceed 8.0 and 10.0%, respectively. Only with the use as catalyst of an aqueous solution of NaOH with the addition of cobalt stearate and o-phenanthroline did the level of ketones (3) and (4) reach 20.0-28.0%. The same ketones are formed in small amounts in the autooxidation of 1,4,4- and 1,5,5-trimethylcycloheptenes (11 and 12, respectively) [53].

At the beginning of the 1970's reports appeared that referred to the formation of eucarvone in the rearrangement of (+)-2-hydroxypinocamphone (13) in the presence of anhydrous oxalic acid [54-56] and p-toluenesulfonic acid [57]. According to different authors, the yields of eucarvone ranged from 9.8% [55] to 20.0% [56]. The initial ketoalcohol (13) was obtained by the oxidation of α-pinene with potassium permanganate.

In 1981, Blanco et al. [58] proposed a method for the synthesis of eucarvone from 3,3-dimethylcyclohex-5-en-1-one by the reaction of chloromethylcarbene with the trimethylsilyl enol ester obtained from the above-mentioned ketone. The yield of eucarvone was 30%, calculated on the initial ketone.

Thus, common defects of all the methods proposed for the synthesis of eucarvone are the comparatively low yield of the desired product and the multistage nature of the synthesis or the formation of multicomponent systems from which the isolation of eucarvone is difficult. As before, Wallach's method remains the most convenient (yield 65-70%).

In addition to the large number of studies on the synthesis of eucarvone there are reports on the production of its saturated analogs. A mixture of the two stereoisomers trans- and cis-3,3,7-trimethylcycloheptanols (14 and 15, respectively) in a ratio of 4:1 has been obtained by the cyclization of dihydromyrcene (2,6-dimethylocta-2,7-diene) in acetic acid in the presence of a strong inorganic acid. The combined yield of alcohols (14) and (15) was 20%.
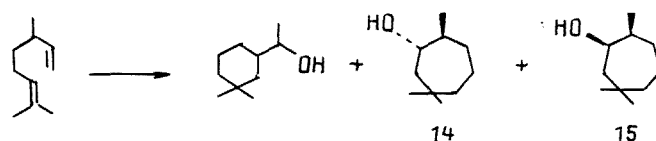
Analogous products are formed when dihydromyrcene is treated with chloroacetic acid [60] and also on its cyclization in formic acid in the presence of boron trifluoride etherate [61]. Oxidation of the products obtained leads to the formation of tetrahydroeucarvone (9) [61].

The second most common natural terpenoid with a seven-membered ring is karahanoenone − 2,2,5-trimethylcyclohept-4-ene (5). The majority of published papers on the chemistry of ketone (5) are devoted to its synthesis.

Demole [62, 63] has synthesized karahanoenone by the cyclization of linalool with the aid of N-bromosuccinimide, followed by dehydrobromination and a 3,3-sigmatropic rearrangement of the products formed. The yield of the desired ketone (5) was 62%.
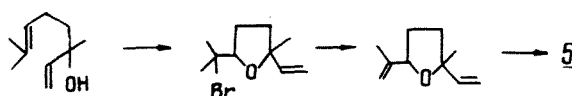
Karahanoenone is also formed in the acid-catalyzed rearrangements of linalool oxide [64] and its esters [65] and of terpinolene oxide [66].

Klein [67], performing the isomerization of terpinolene 4,8-oxide with boron trifluoride etherate, obtained karahanoenone (5) and isokarahanoenone (16) with yields of 26.1 and 20.5%, respectively. Besides the ketones (5) and (16), the reaction mixture contained hydrocarbons and alcohols of the *p*-menthane series.
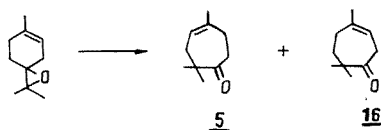
In 1977-1980, investigations of Japanese authors on the synthesis of karahanoenone using organosiloxanes were published [68-72]. The yield of ketone (5) reached 95%, but these syntheses are extemely laborious. Karahanoenol (6) has been obtained from geraniol in five stages via an allylsilane [73].

Bhushan has proposed a two-stage method of synthesizing karahanoenone by the acid-catalyzed rearrangement of a pinacol [74]. The ratio of the ketones (5) and (16) formed was 7:3, and their total yield amounted to 80%.

Several other methods of synthesizing karahanoenone have been proposed: by the addition of thiophenols to alkenylidenecyclopropanes [75], and electrochemically from 2-acetoxy-2,6-dimethylhept-5-en-1-yne [76]. The yield of desired product by the latter method was 51%.

Thus, the proposed methods of synthesizing karahanoenone are characterized by higher yields than in the case of eucarvone but they are all associated with certain technological difficulties.

In addition to the synthesis of natural terpenoids of the 1,1,4-trimethylcycloheptane series, compounds of the same series not found in nature have been obtained. As early as 1940, 1,1,4-trimethylcycloheptene (11) was oxidized with selenium dioxide [77] to give 2,5,5-trimethylcyclohept-2-enone and 4,4-dimethylcycloheptenecarbaldehyde.

2,2,6-Trimethylcyclohept-4-enone was synthesized by the cyclization of 2,5,5-trimethylhepta-1,6-dien-4-one, and its hydrogenation over Raney nickel led to 2,2,6-trimethylcycloheptanone [78].
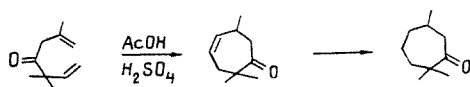

A. L. Liberman and T. V. Vasina [79] obtained 3,6,6-trimethylcycloheptanone with a yield of 80% by decomposing the cadmium salt of 3,3,6-trimethylsuberic acid. The same ketone has been detected in the product of the rearrangement of 3-carene oxide on a rhenium-containing catalyst, but in very small amounts [80]. The treatment of 2,2,6-trimethylcyclohexanone with cyanogen azide forms 2,2,6- and 3,3,7-trimethylcycloheptanones [81]. During hydrogenation of cis-caran-4-trans-one on a carbon copper catalyst, 2,5,5-trimethylcyclopentanone was obtained in a yield of 39% [82, 83].

Unsaturated ketones of the 1,1,4-trimethylcycloheptane series are present in the products of the autooxidation of 1,4,4- and 1,5,5-trimethylcycloheptenes [53]. Among them − in addition to the above-mentioned ketones (3) and (4) − 3,7,7-trimethylcyclohepta-2,4-dienone and 3,6,6- and 2,6,6-trimethylcyclohept-2-enones were identified.

Besides the synthesis of ketones of the 1,1,4-trimethylcycloheptane series, there have been a number of reports of the production of 2,2,5-trimethylcyclohepta-1,3-dione (7). Reusch et al. obtained the diketone (7) by the pyrolysis of pulegone oxide at 200°C [84]. The same compound, (7), is formed on the rearrangement of pulegone oxide in boiling benzene with various catalysts [85, 86]. The yield of desired product reached 99%. The diketone (7) has been obtained with a yield of 90% from pulegone by the use of organoaluminum reagents [87].

As well as ketones, acids of the 1,1,4-trimethylcycloheptane series have been synthesized. A characteristic representative of them is thujic acid (17), which was obtained by Campbell from eucarvone [88]. Pasto reduced the acid (17) with sodium amalgam in the presence of boric acid [89] to 4,4-dimethylcyclohepta-2,6-dien-1-carboxylic acid (18). Isomerization of the acid obtained in a basic medium led to migration of the double bonds in the seven-membered ring. The acids obtained as a result of isomerization proved to be identical with acids isolated from the essential oils of the plant *Libocedrus formosana*.
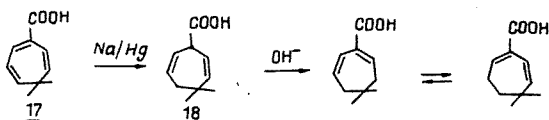
The reaction of 3,7-dimethylocta-1,6-diene with formic and sulfuric acids in CCl_4 gives a 42% yield of 1,4,4-trimethylcycloheptanecarboxylic [90]. The reaction of this acid with diazomethane gave its methyl ester, the reduction of which with lithium tetrahydroaluminate led to 1-hydroxymethyl-1,4,4-trimethylcycloheptane.

The carbonylation of 2,6-dimethyloctadiene in the presence of a catalyst containing a BF_3 derivative forms not only alklycyclohexane acids but also, with a yield of 10-12%, 1,4,4- and 3,3,7-trimethylcycloheptanecarboxylic acids [91].

There are a number of publications on the synthesis of oxygen-containing monoterpenoids with a seven-membered ring from 1,4,4- and 1,5,5-trimethylcycloheptenes (11 and 12, respectively). The epoxidation of cycloolefins (11) and (12) with iminoperbenzoic acid gave the corresponding epoxides, the acid hydrolysis of which led to the formation of 1,2-diols with both the *trans*- and the *cis*- positions of the hydroxy groups [92]. The hydroboration and subsequent oxidation of the trimethylcycloheptenes (11) and (12) led to the formation of 3,3,7- and 2,5,5-trimethylcycloheptanols, from which tri- and tetramethylcycloheptanones were subsequently obtained [93]. The condensation of the alkylcycloheptenes (11) and (12) with formaldehyde in acetic acid yielded acetates with an exocyclic double bond [94]. After hydrolysis of the condensation product, the corresponding alcohols and diols were isolated from the reaction mixture as shown in the scheme:

$$ \mathbf{11} \xrightarrow[\text{2.KOH/EtOH}]{\text{1.CH}_2\text{O/AcOH}} $$
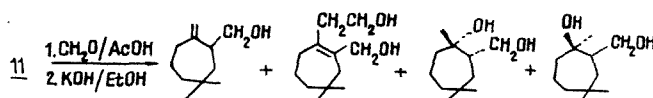
The composition of the hydrolysis product from the cycloolefin (12) was analogous.

Friedel—Crafts acylation of the alkylcycloheptenes (11) and (12) gave alkylacetylcycloheptenes with both endo- and exocyclic double bonds [95]. Reduction of the ketones obtained with lithium tetrahydroaluminate led to the corresponding secondary alcohol.

$$ \mathbf{11} \xrightarrow[\text{ZnCl}_2]{(\text{CH}_3\text{CO})_2\text{O}} $$
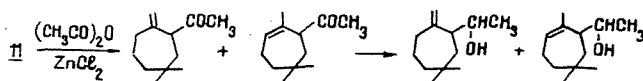
Chemical Transformations of Terpenoids with a Seven-Membered Ring

Among oxygen-containing terpenoids of the 1,1,4-trimethylcycloheptane series the chemical transformations of eucarvone have been the most studied. There have been literally few papers on the chemical transformations of karahanoenone derivatives: the isomerization of karahanoenone epoxide in a basic medium [96] and the solvolysis of karahanoenol tosylate and mesylate [97] have been studied.

After the development of a method for synthesizing eucarvone by Wallach, various derivatives of it (dihydro- and tetrahydroeucarvones, their semicarbazones, and an oxime) were obtained [98], and their physicochemical properties were studied. In 1940, for the first time, West obtained an adduct of eucarvone with maleic anhydride [99]. Later, the behavior of eucarvone in the Diels—Alder reaction was studied in detail [100, 101]. An adduct of eucarvone with nitrobenzene has also been obtained [102].

With the development of spectral methods of investigation, papers appeared describing the spectral characteristics of eucarvone and its derivatives [103-105]. The structure of eucarvone has been studied in very great detail with the aid of NMR spectroscopy [106-109].

A paper by Campbell [88], in which reduction, hydrogenation, and oxidation reactions of ketone (3) are considered, may be regarded as the first example of a more detailed and systematic study of the chemical transformations of eucarvone. From eucarvone Campbell obtained a large number of new, previously undescribed, compounds. The reduction of eucarvone with lithium tetrahydroaluminate gives 2,6,6-trimethylcyclohepta-2,4-dienol (19), the acid-catalyzed isomerization which led to α- and β-dihydroeucarvones (20 and 10, respectively). The hydrogenation of eucarvone over Pd/C gave 3,3,7-trimethylcycloheptanone (9), while the dehydrogenation of the alcohol (19) with boric acid led to hydrocarbon (2), the subsequent bromination and oxidation of which provided the possibility of obtaining thujic acid (17). In addition, ketone (20) was oxidized with selenium dioxide, and the resulting ketoenol was oxidized further with periodic acid to 2,6,6-trimethylcyclohept-2-ene-1,4-dione.

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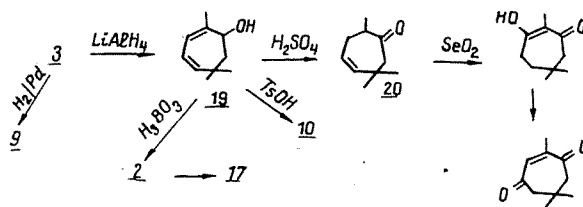
The oxidation of eucarvone took place differently, leading to the formation of compounds of the carane series.
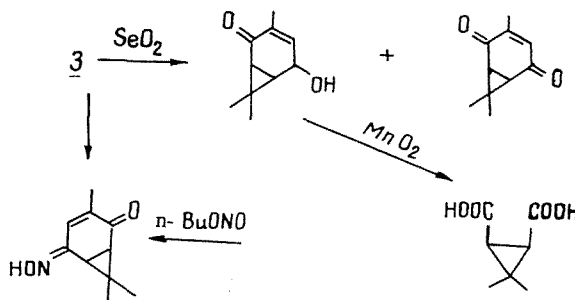
The formation of compounds of the carane series has been studied in detail by Corey and Burke [110, 111]. They also performed the oxidation of ketone (3) with selenium dioxide, established the structure of the hydroxyketone formed with the aid of IR and UV spectra, and confirmed it by a series of chemical transformations. The formation of a bicyclic structure has also been observed on the treatment of eucarvone with n-butyllithium in the presence of sodium ethanolate.

The authors showed that ammonia is liberated when eucarvone is treated with sodium amide in dioxane, and a sodium derivative of eucarvone is formed, which they subsequently called sodioeucarvone without giving any information about its structure. When the compound obtained was treated with various acid chlorides, enol esters were formed. They considered that the enol esters obtained exist in the form of mono- and bicyclic structures that are valence tautomers and undergo interconversion through an electron shift and changes in angles and bond lengths.
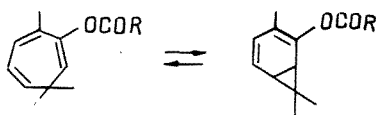
Attempts to obtain a bicyclic isomer of eucarvone − 3-caren-2-one − did not lead to the desired result: in all cases the only reaction product was eucarvone. However, it was shown that derivatives of the carane series are formed in practically all reactions proceeding through enols or enolate ions.

Corey and Burke attempted to establish the mechanism of the formation of carane derivatives from eucarvone [111]. They suggested two possible mechanisms, but it did not appear possible to determine the real reaction pathway because of an inadequate number of experimental results, which is connected with the short lifetime of the enolate ions and the pronounced shift of the valence equilibrium in the direction of the monocyclic tautomer.

Later, a reaction of eucarvone with tetracyanoethylene also taking place with contraction of the seven-membered ring was found [112].
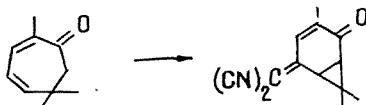
A series of publications by Polish authors on the synthesis of various compounds with a seven-membered ring from eucarvone appeared in the 1970's. Hendrich and Kuczinski [113] studied the selective reduction of eucarvone with the aim of

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obtaining all the isomeric dihydroeucarvones. The reduction of ketone (3) with the Li−EtNH$_2$ system produced a mixture of tetrahydroeucarvone (9) and the previously unknown γ-dihydrocarvone − 2,6,6-trimethylcyclohept-3-enone (21). The reduction of ketone (21) with sodium tetrahydroborate led to 2,6,6-trimethylcyclohept-3-enol (22). The alcohol (22) obtained
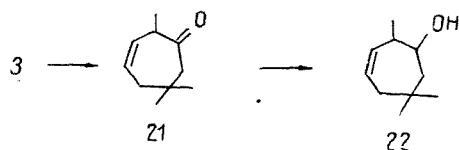

was isolated in the individual form and was ascribed the *trans*- configuration. However, later (1981) Rulko and Mielczarek [114] showed that the alcohol (22) obtained by Kuczinski had the *cis*- configuration. This investigation was performed with the wide use of PMR spectral results and conformational analysis. To obtain possible isomeric alcohols, these authors [114] performed the reduction of ketone (21) under various conditions. On the use of the LiAlH$_4$−Et$_2$O system, alcohol (22) in the *cis*- configuration was obtained, while the reduction of ketone (21) with lithium isopropanolate led to the formation of the epimeric γ-dihydroeucarveol in the *trans*- configuration (23). Hydrogenation of the alcohols obtained led to their saturated analogs − *cis*- and *trans*-tetrahydroeucarveols, (15 and 14), respectively.
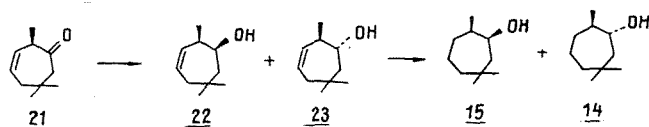

Chabudzinski and Skwarek studied the epoxidation of eucarvone with the subsequent reduction of the products obtained [115]. They synthesized a series of derivatives of 1,1,4-trimethylcycloheptane: epoxides, a diol, alcohols. They showed that while the reduction of 1,4,4-trimethyl-8-oxabicyclo[5.1.0]oct-5-en-2-one (24) takes place readily, in the case of 1,5,5-trimethyl-8-oxabicyclo[5.1.0]oct-3-ene (25) the reaction proceeds with difficulty. Furthermore there was practically no hydration of epoxide (25) by a dilute solution of sulfuric acid. On the basis of the spatial structure of this epoxide, the authors suggested that the low reactivity of the oxide ring was due to its shielding by the geminal methyl groups.
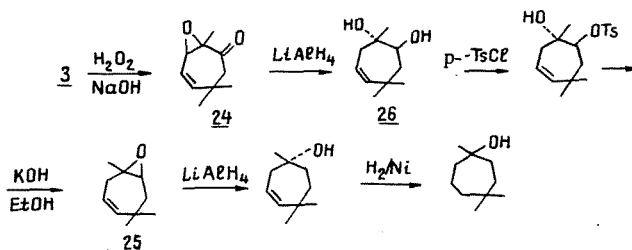
The same authors [116] obtained the saturated *cis*- and *trans*-1,4,4,-trimethylcycloheptane-1,2-diols [(27) and (28), respectively], from the epoxyketone (24) and the unsaturated diol (26). In addition to the diols (27) and (28,) they synthesized the previously undescribed 1,5,5-trimethyl-8-oxabicyclo[5.1.0]octane (29), the reduction of which with lithium tetrahydroaluminate gave 3,3,7-trimethylcycloheptanol (30) and 1,4,4-trimethylcycloheptanol (14). The structures of the compounds synthesized were established by chemical transformations into known substances and were confirmed by the results of elementary analysis and IR spectra.
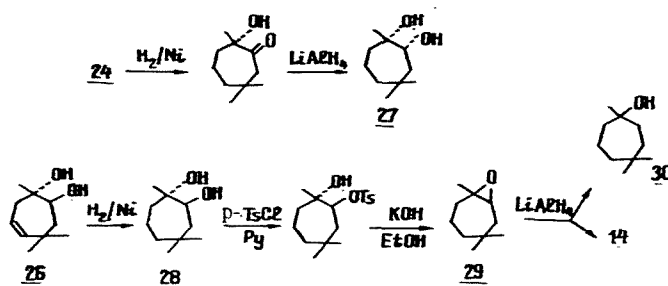
The development of methods of NMR spectroscopy and conformational analysis has made it possible to undertake a study of the stereochemistry of isomeric compounds of the 1,1,4-trimethylcycloheptane series. In 1980, Mielczarek and Rulko published papers on the stereochemistry of the nucleophilic opening of an epoxide ring in the 1,1,4-trimethylcycloheptane series [117, 118]. The stereoselective epoxidation of compounds (21) and (22) gave 2,6,6-trimethyl-3,4-epoxycycloheptanone (31) and 2,6,6-trimethyl-*cis*-3,4-epoxy-*cis*-cycloheptanol (32). The epoxide rings were opened with the aid of NaN_3 in DMSO. The reactions take place by a S_N2 mechanism but the final products of the two reactions differ greatly. In the case of the epoxide (32) the authors explain the high stereo- and regioselectivity of azidolysis with the formation of 4-azido-2,6,6-trimethylcycloheptane-1,3-diol (33) by the anchimeric effect of the axial hydroxy group.
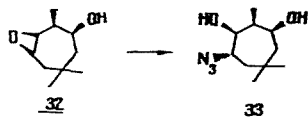
The azidolysis of the epoxyketone (31) gave not an azido compound but the hydroxyketone (34). The authors explain the unusual occurrence of the reaction by the formation of the intermediate 3-azido-4-hydroxy-2,6,6-trimethylcycloheptanone (35) in the first stage. In this case, nucleophilic attack takes place at the C-3 atom. The authors connect this with the presence of the electron-accepting carbonyl group, which lowers the electron density on the C-3 atom.
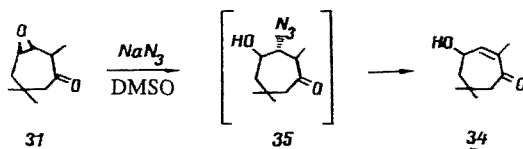
The azidolysis of 2,6,6-trimethyl-2,3-epoxycyclohept-4-en-1-one (24) is described in [118]. In this case, as was to be expected, nucleophilic attack again proceeds at the C-3 atom. In both these papers [117 and 118] the authors consider in detail the conformations of the initial and final compounds, the configurations of the substances obtained, having been established with the aid of PMR spectroscopy.

Isaeva et al. have investigated the transformations of eucarvone oxide (24) under the action of bases and acids [119, 120]. They showed that under the action of alcoholates and caustic soda the epoxide (24) rearranges into cyclohexane derivatives. An analogous contraction of the seven-membered ring has been observed by other authors, as well [116, 121].
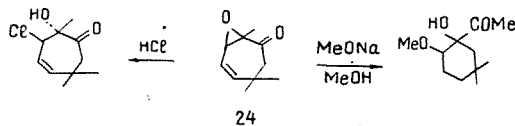
In the presence of acids, however, the reaction proceeds with retention of the carbon skeleton, i.e., *trans*-opening of the epoxide ring at the C^3-O bond takes place. A similar directivity of the opening of the epoxide ring is preserved for eucarveol oxide.

In the 1960's and 1970's the attention of researchers was attracted by photochemical reactions. A large number of publications appeared on the photoisomerization of eucarvone and its oxides. The irradiation of eucarvone (3) led to a large set of bicyclic compounds [122-127]. As a rule, the main component of the mixtures obtained in the photoisomerization of ketone (3) was 1,4,4-trimethylbicyclo[3.2.0]hept-6-en-2-one (36).
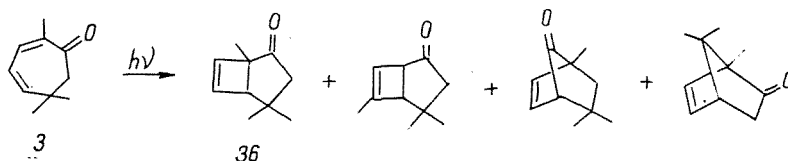
Wolf studied the photochemical reactions of eucarvone epoxides [128-130]. From the different epoxides he obtained sets of mono- and bicyclic compounds with different properties having various functional groups.

The study of the photochemical reactions of eucarvone and its derivatives is of interest from the point of view of possible transformations of the seven-membered ring and the synthesis of new compounds from it.

As already mentioned, in addition to eucarvone derivatives, a number of new compounds based on 1,4,4- and 1,5,5-trimethylcycloheptenes have been synthesized and their chemical transformations have been studied. Manukov et al. [131] have described the products of the thermal decomposition of boric esters of 2-hydroxymethyl-4,4- and -5,5-dimethyl-1-methylenecycloheptenes obtained by the Prins reaction from the cycloolefins (11) and (12). Contrary to expectations, the main pyrolysis products were not 1,3-dienes with two terminal double bonds but 1,4,4- and 1,5,5-trimethylcycloheptenes.

In [132] the results are given of a study of the transformations of 1,4,4- and 1,5,5-trimethylcycloheptene epoxides on alumina and aluminum−rhenium catalysts. The isomerizates contained compounds with seven- and with six-membered rings. The carbonium-ion rearrangement of the initial epoxides leads to the formation of 1,3,3- and 1,4,4-trimethyl-cyclohexanecarbaldehydes, which are partially reduced to alcohols under the reaction conditions. During the reaction the epoxides also undergo isomerization into 2,5,5- and 2,6,6-trimethylcycloheptanones and conversion into allyl alcohols with endo- and with exocyclic double bonds.

The stereochemistry of the addition of a Grignard reagent to 2,5,5- and 2,6,6-trimethylcycloheptanones with the formation of stereoisomeric 1,2,5,5- and 1,2,6,6-tetramethylcycloheptanones has also been studied [133].

Thus, it follows from an analysis of the literature on oxygen-containing terpenoids with a seven-membered ring that only the synthesis of eucarvone and its derivatives has been studied in adequate detail. In addition, there is a number of papers on the synthesis and chemical transformations of monoterpenoids obtained from 1,4,4- and 1,5,5-trimethylcycloheptenes. However, only isolated papers have been devoted to the study of other terpenoids with a seven-membered ring. At the same time, an all-sided study of terpenoids with the cycloheptane skeleton is of interest from both the theoretical and the practical points of view. These compounds can serve as convenient models for the study of the stereochemistry of cycloheptane derivatives. An all-sided investigation of terpenoids with a seven-membered ring would permit the supplementation of general schemes for the genesis of terpenes in which pathways for the appearance of such compounds are not reflected. Since individual representatives of this class of monoterpenoids exhibit high biological activity and are components of perfumery compositions, the development of methods for synthesizing new compounds of this series is a matter of urgency.

Thus, the further study of oxygen-containing terpenoids of the 1,4,4-trimethylcyclopentane series is extremely interesting and promising.

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