

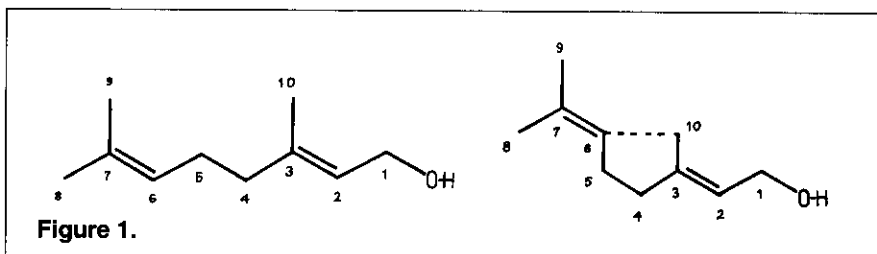
Synthesis and Odor Characteristics of Some Cyclopentane Derivatives

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Continuing our studies on the relationship between structure and odor properties of the isoprenoid compounds, we took into consideration the influence of conformation of the isoprenoid chain on the odor. In our opinion, it seems that some information concerning this influence can be obtained by comparison of odors of acyclic compounds and their cyclic analogues. The additional C-C bond present in the cyclic analogues forces only some conformations of the isoprenoid chain. This type of the comparative study can be carried out only for pairs of acyclic and cyclic compounds which have the same number of the carbon atoms as well as functional groups.

In our previous paper we described the synthesis and odor characteristics of some gem-dimethylcyclohexane derivatives which were considered as cyclic analogues of dihydrocitronellol, dihydrogeraniol, menthocytronellol and their derivatives.¹

In this work we present the synthesis and odor characteristics of some cyclopentane derivatives. Compounds described in this paper can be considered as cyclic analogues of geraniol, citronellol, dihydrocitronellol and their derivatives. As it is shown in Figure 1, the isoprenoid chain in these com-



pounds is folded in the cyclopentane ring by junction of two carbon atoms—C₆ and C₁₀.

Materials and Methods

Racemic α -terpineol [1] was used as a starting material for the synthesis (Figures 2 and 3).

One of the key intermediates, hydroxy ketone 4, was prepared by the method described by Kuczynski and Marks.² Thus, 1 was oxidized with KMnO_4 in aqueous solution to give p-methane-1,2,8-triol [2], which was converted into tosylate 3. Detosylation of 3 with methanolic KOH gave a mixture of the cis- and trans-isomers of hydroxy ketone 4. In the next step of the synthesis, the Baeyer-Villiger reaction provided the hydroxy acetate 5 which was then reduced with LiAlH_4 .

A mixture of isomeric diols 6 (cis-60%, trans-40%) was obtained.³ This mixture was oxidized with pyridinium dichromate⁴ to hydroxy ketone 7 which

in the reaction with triethyl phosphonoacetate in diethyl ether gave the mixture (Z-59%, E-41%) of isomeric hydroxy esters 8a and 8b. Attempts to separate this mixture by column chromatography failed. Pure isomers were isolated in low efficiency by preparative gas chromatography. Dehydration of hydroxy ester 8a with POCl_3 afforded the mixture of esters 9 (10% gc) and 10 (90% gc) in good overall yield (87%). More details concerning this synthesis and spectral data of esters 8a, 8b, 9 and 10 were presented elsewhere.⁵

Cyclic analogue of geraniol, alcohol 11a, was obtained in 83% yield by reduction of ester 10 with diisobutylaluminium hydride (i-BAH).

Cyclic analogue of citronellol, alcohol 11b, was synthesized in the racemic form by the following reaction sequence. Mixture of hydroxy esters 8a and 8b was catalytically (5% Pd on C) hydrogenated to hydroxy ester 12 which was dehydrated with POCl_3 to

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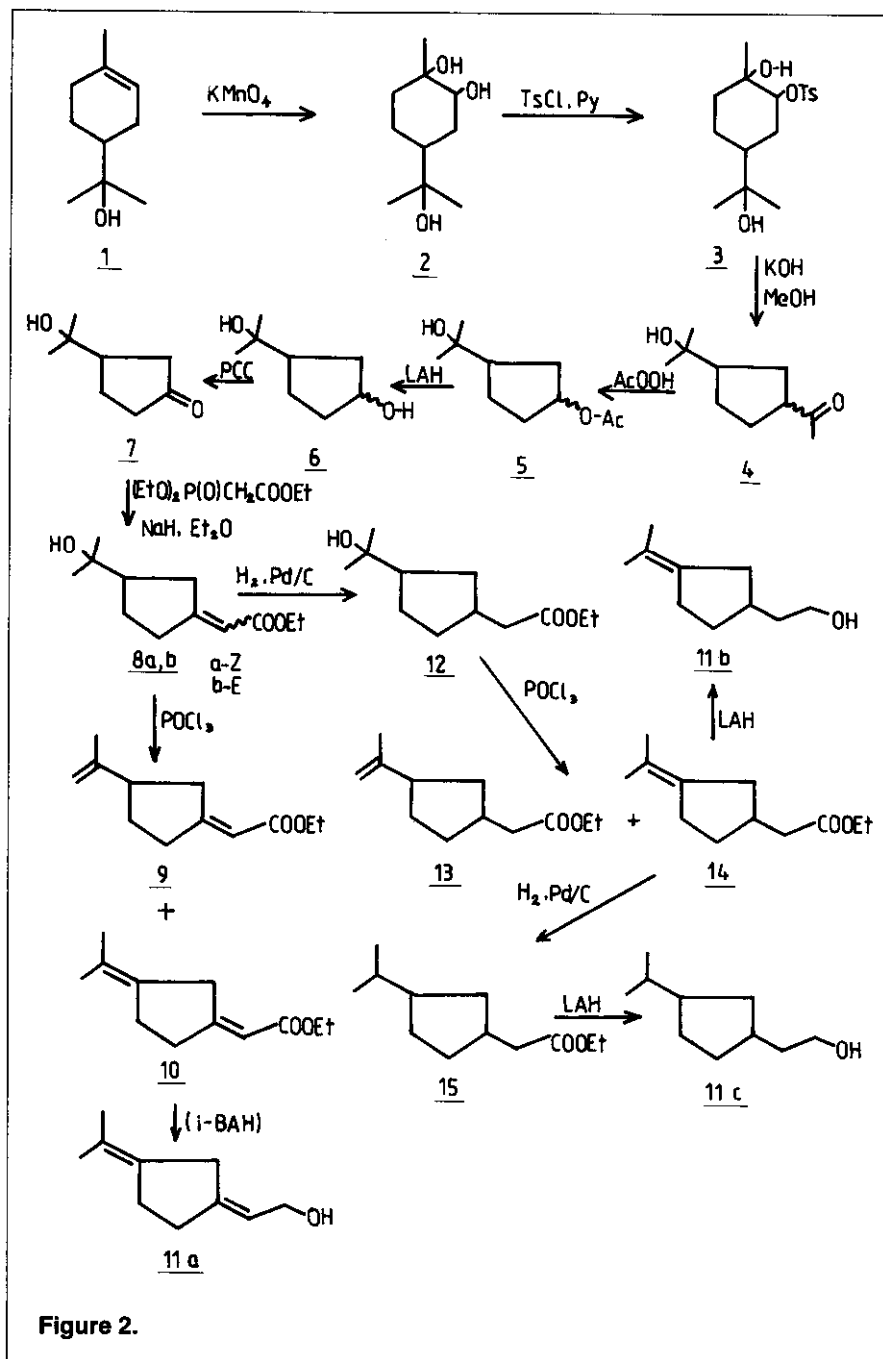


Figure 2.

the mixture of esters **13** (7%) and **14** (93%).⁶

Pure ester **14** was isolated by column chromatography and then was reduced with LiAlH_4 to the desired alcohol **11b**.

The saturated alcohol **11c**, cyclic analogue of dihydrocitronellol, was obtained by reduction (LiAlH_4) of ester **15** which was a product of catalytic hydrogenation (5% Pd on C) of a mixture of esters **13** and **14** as well as a mixture of esters **9** and **10**.

The first group of derivatives of alcohols **11a**, **11b** and **11c** acetates **16a**, **16b**, **16c** were obtained in good yield (80-95%) by esterification of corresponding alcohols with acetyl chloride or acetic acid anhydride in the presence of anhydrous pyridine.⁷

Aldehydes **17a**, **17b**, **17c** were obtained as products of direct oxidation of corresponding alcohols with manganese dioxide (aldehyde **17a**) or with pyridinium dichromate (aldehydes **17b**, **17c**).

Ketones **20a**, **20b**, **20c** were synthesized from corresponding alcohols (**11a**, **11b**, **11c**) which were converted into bromides **19a**, **19b**, **19c**. Bromide **19a** was obtained by direct exchange of the hydroxy group on bromine⁸ whereas bromides **19b**, **19c** were obtained via tosylates **18b**, **18c**. These bromides were used as alkylating agents in the reactions with ethyl acetoacetate. Alkaline hydrolysis and subsequent decarboxylation of intermediate keto esters afforded desired ketones.

The course of all reactions and purities of compounds were monitored by means of gas and thin-layer chromatography. All compounds, for which the odor was evaluated, were above 97% purity (GC). Their odor characteristics are given in Table I.

Results and Discussion

Most of the known and odoriferously described compounds with cyclopentane system are characterized by sandalwood odor.^{9,10}

They are mainly tri- or tetra-substituted cyclopentane derivatives. Cyclic monoterpenoids obtained by us are, therefore, one of the first di-substituted cyclopentane derivatives in the odoriferous compounds family. Moreover, they are "true" cyclic analogues of known acyclic terpenic derivatives.

Having at our disposal 15 new compounds, differing both in number of the double bonds and in the kind of functional groups, and their odor characteristics (Table I), we could draw some conclusions concerning the structure-odor relationship.

Comparing odors of our compounds with odors of corresponding acyclic analogues we could state that stiffening the structure of the isoprenoid chain by introduction of the cyclopentane ring causes significant changes in the odoriferous properties. All cyclopentane monoterpenoids obtained by us exhibit different odors than that of their known acyclic analogue, though the general odor profile, e.g., floral for alcohols and their acetates, and fruity for ketones and ethyl esters, was maintained.

The regularity, that the kind of the

Synthesis and Odor Characteristics of Some Cyclopentane Derivatives

functional groups has a decisive influence on odor, and that the double bonds play a minor role, was confirmed. Alcohols **11a,b,c** irrespective of the saturation degree, are characterized by a pleasant floral odor, the floral note being distinctly "sweeter" in the case of unsaturated alcohols. More distinct differences in odor are observed in the group of aldehydes. Saturated aldehyde **17c** is characterized by the floral-fatty odor, typical of branched aldehydes C_{10} , whereas aldehyde **17a**, containing two double bonds at the cyclopentane ring, has an odor similar to that of cinnamic aldehyde. It is, most probably, due to substantial differences in shapes of molecules of these aldehydes. Saturated aldehyde **17c** has extended steric structure while its unsaturated analogue has a flat one, resembling that of cinnamic aldehyde.

In our opinion, some cyclopentane derivatives described in this work exhibit interesting odor properties for perfumery and could enrich the assortment of odoriferous synthetics.

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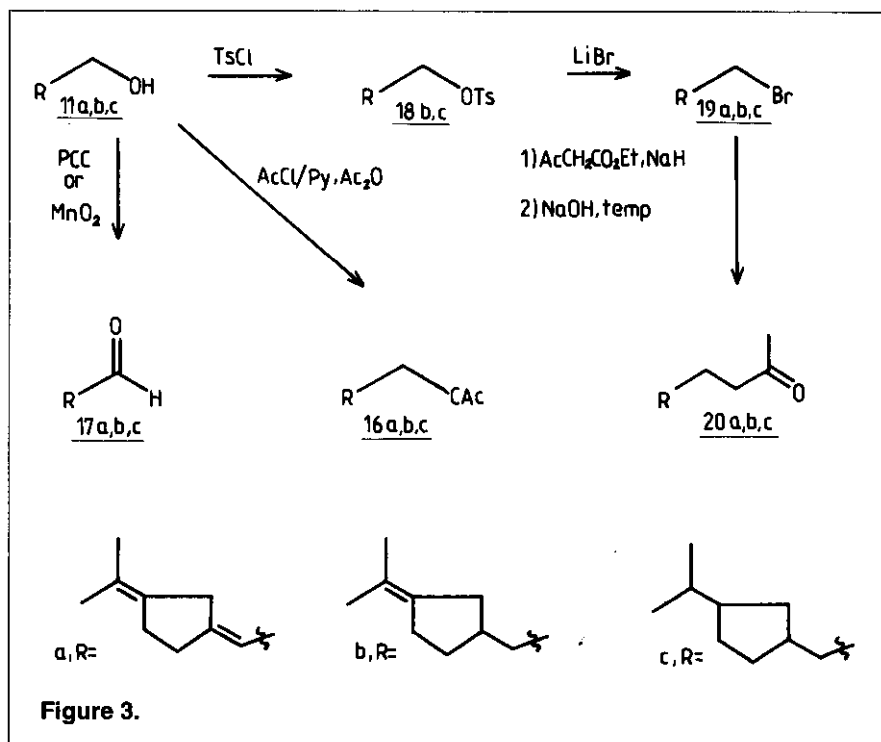


Figure 3.

Table I. Odor Characteristic of Some Cyclopentane Derivatives

R			
-CO ₂ Et	10 C ₁₂ H ₁₈ O ₂ medium-intensive, agreeable, fruity, with wine yeast (brandy) note	14 C ₁₂ H ₂₀ O ₂ medium-intensive, agreeable, fruity, China quince fruit-like	15 C ₁₂ H ₂₂ O ₂ medium-intensive fruity with peach note, agreeable
-CH ₂ OH	11a C ₁₀ H ₁₆ O agreeable, floral with cyclamen note, not geraniol-like	11b C ₁₀ H ₁₈ O medium-intensive, agreeable, floral, sweet, linalool-like	11c C ₁₀ H ₂₀ O medium-intensive fatty-floral, n-decanol-like
-CH ₂ OAc	16a C ₁₂ H ₁₈ O ₂ medium-intensive, fresh, fruity-floral, elder-fruit-like	16b C ₁₂ H ₂₀ O ₂ medium-intensive, fresh, fruity-floral with elder-fruit note	16c C ₁₂ H ₂₂ O ₂ medium-intensive fruity-floral, sweet with stock flower note
-CHO	17a C ₁₀ H ₁₄ O medium-intensive, sweet, coumarin with cinnamon note (dessicated-hay-like)	17b C ₁₀ H ₁₆ O very intensive, penetrating, fresh floral-fatty with marked almond note	17c C ₁₀ H ₁₈ O very intensive penetrating, fatty with floral note n-decanol-like but more floral and fresh
-CH ₂ CH ₂ Ac	20a C ₁₃ H ₂₀ O intensive, fresh, fruity with marked apple note, damascone-like, more intensive than geranylacetone	20b C ₁₃ H ₂₂ O agreeable, fruity delicate with dessicated-apple note	20c C ₁₃ H ₂₄ O medium-intensive fruity, fresh with cucumber note