

Isomerization of Dihydromyrcene Oxide

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The application of structure-activity relationships has led to a better understanding of the olfactory recognition process. Especially, when computer assisted, this approach will become more valuable in providing insights into the search for new fragrance chemicals.¹ However, the abundant availability of α - and β -pinenes throughout the world makes it only natural to continue to look for ways to convert them into novel odorants.

Both the pinenes can be converted to a common intermediate. *cis*-Pinane [1], for the past 15 years, has provided our industry with a new route to linalool and geraniol.

cis-Pinane [1] can also be pyrolyzed to dihydromyrcene

[2], now produced in multi-ton quantities to meet the growing need for dihydromyrcenol [3]² (Scheme 1).

Experimental Details

2,2,5-Trimethyl-6-heptenal [5] Silica Alumina (Davison 135) 30 g was mixed in 2,000 g heptane. The slurry was refluxed to a Barrett trap for 15 min. Then 800 g dihydromyrcene oxide [4] was added to the refluxing mixture over 30 min. Reflux (97°C) was continued for an additional 60 min. The slurry was cooled to room temperature, filtered and the filter cake rinsed with 200 g heptane. After removal of the heptane, the product was fractionally

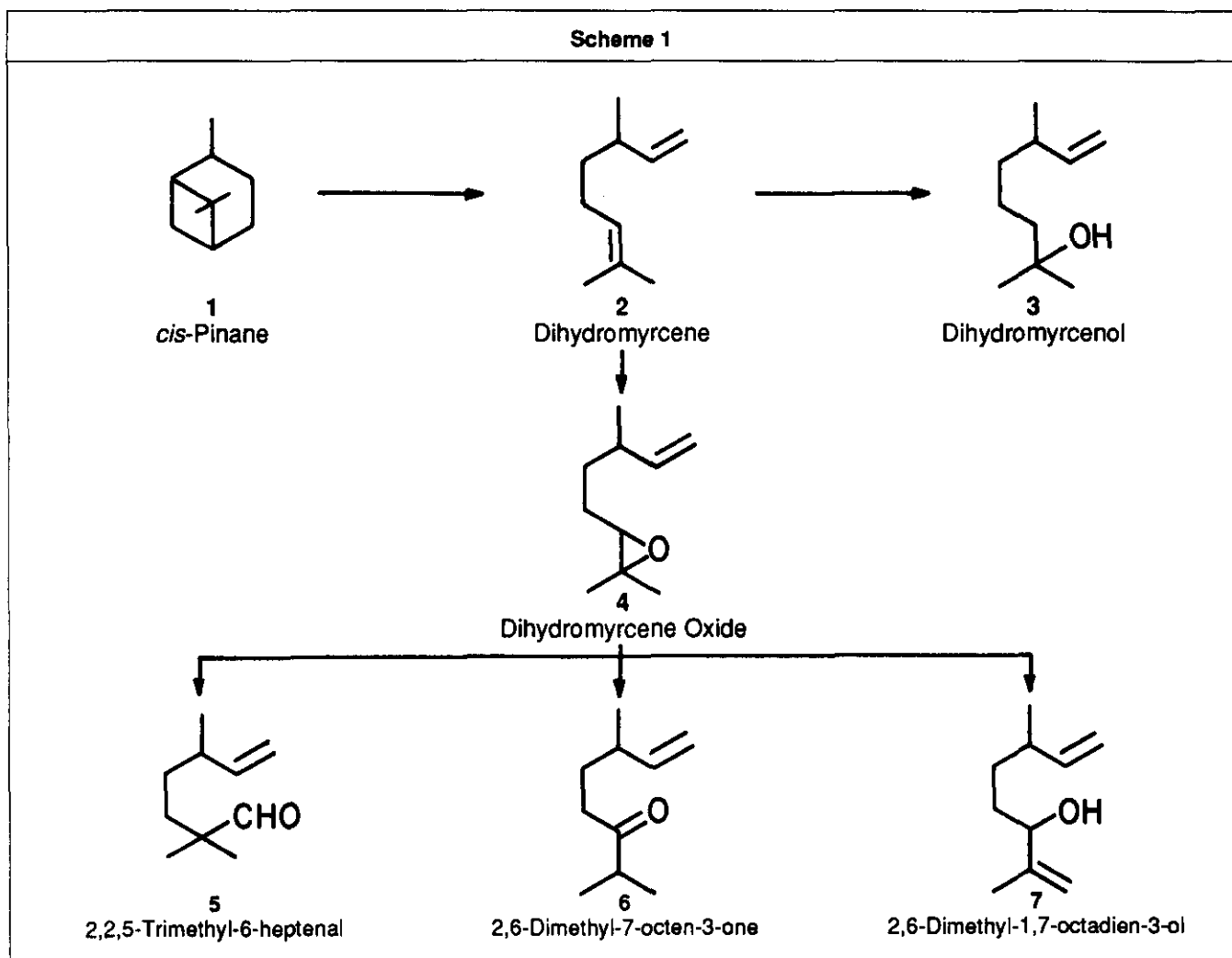


Table I. Isomerization of dihydromyrcene oxide

| Catalyst | T°C | Solvent | Hours | Conv | Selectivity | | |
|--|-----|-------------|-------|------|-------------|-----|-----|
| | | | | | [5] | [6] | [7] |
| ZnBr ₂ | 117 | toluene | 2.0 | 100 | 44 | 52 | 4 |
| Li Triflate | 150 | o-xylene | 3.0 | 100 | 7 | 46 | 47 |
| LiClO ₄ | 126 | xylene | 8.0 | 100 | 9 | 59 | 32 |
| Nafion-H | 50 | toluene | 0.1 | 100 | 6 | 80 | 14 |
| Al Isopropylate | 127 | xylene | 2.0 | 100 | - | 7 | 93 |
| SiO ₂ /Al ₂ O ₃ | 95 | heptane | 1.0 | 100 | 46 | 22 | 32 |
| Li Di-isopropyl Amide | 0 | heptane/THF | 2.0 | 100 | - | - | 100 |

distilled at 10 mm. Obtained were 302 g of the aldehyde [5], b.p. 65°C; 144 g of the ketone [6], b.p. 70°C; and 212 g of the alcohol [7], b.p. 87°C. ¹H-NMR: The ketone [6] and alcohol [7] both matched the respective spectra previously reported.^{3,6} The aldehyde [5] exhibited the following ¹H-NMR (270 MHz) spectra (CDCl₃): 0.96 (d, J=7, CH₃(5)); 1.00 (s, z CH₃(2)); 1.12-1.22 (m, CH₂(4)); 1.38-1.48 (m, CH₂(3)); 2.03 (m, CHCH₃); 4.88-5.00 (m=CH₂); 5.56-5.68 (m, CH=CH₂); 9.40 (s, CHO).

Dihydromyrcene Oxide

We have examined dihydromyrcene oxide [4], its isomerization products, and the fragrance properties of a number of their derivatives. This epoxide [4] can readily be prepared by the use of peracetic acid buffered with sodium carbonate in methylene chloride solvent.³ However, we find that the method of Venturello⁴ is more convenient in the industrial setting. This method employs dilute hydrogen peroxide and does not require chlorinated solvents and sensitive peracetic acid. Moreover, the tungsten/phosphate aqueous layer can be recycled to subsequent epoxidations. The yield of isolated 99% epoxide [4] is about 87% and compares favorably to that obtained with the peracetic acid route.

The dihydromyrcene [2] is not enantiomerically pure when the starting material is α -pinene isolated from the turpentine of the southeastern part of the United States. If the more expensive β -pinene is the starting point, then the optical purity is quite high. The dihydromyrcene oxide [4] prepared in this work was made from (+)-dihydromyrcene [2] having an enantiomeric excess of about 30%. The diastereoisomers of the oxide, as a result, are seen to separate in the gas chromatogram into two peaks having a ratio of 65 to 35.

Isomerization Studies

Dihydromyrcene epoxide [4] can be catalytically isomerized chiefly to three compounds: an aldehyde, 2,2,5-trimethyl-6-heptenal [5]; a ketone, 2,6-dimethyl-7-octen-3-one [6]; and a secondary allylic alcohol, 2,6-dimethyl-1,7-octadien-3-ol [7] (see Scheme 1).

These transformations are analogous to similar transformations of tri-substituted epoxides which have been reported using various Lewis Acid catalysts. The methyl ketone which would be obtained by methyl migration to the 6-carbon was not observed in our studies, nor was it seen by Yamamoto⁵ in his studies using the silyl ether of epoxy citronellol.

The selectivity to each of these compounds depends on the nature of the isomerization catalyst employed. The results of a brief screening of several

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Table II. Odor characteristics of aldehyde [5] derivatives

| | | |
|--|----|--|
| | 5 | Intense green note with a citronellal connotation, also ozony woody background. |
| | 8 | Powerful floral note - very diffusive and fresh. In the family of hydroxy citronellal/lyral odor. White flowers - magnolia, etc. |
| | 9 | Clean citronella-citrus note with a woody orris character - powerful. |
| | 10 | Very citrusy note - lime orangey floral. Very fresh. |
| | 11 | Powdery floral woody balsamic. Dry - Weak floral powdery. Fresh - Sweet floral, powdery woody balsamic - strong. |
| | 12 | Weak leathery green fatty note. |
| | 13 | Green vegetable - peppery cuminic - cucumber note. Dry - Slight fatty cuminic note. Fresh - Weak oily green peppery. |
| | 14 | Spicy green - musky-fruity powerful and lasting over 24 h. Dry - Spicy - green angelica like-amber fruity powerful. Fresh - Spicy green floral - fatty - fruity green. |

Table III. Odor characteristics of ketone [6] derivatives

| | | |
|--|----|--|
| | 6 | Sharp ketonic lavender citrus grapefruit note - very powerful - top note green lavender. |
| | 15 | Very fresh green vegetable - green peas - green beans - with a citrus note. |
| | 16 | Musty woody camphor - green note. |
| | 17 | Citrus/floral camphoraceous - piney background. |

catalysts are presented in Table I.

Derivatives of the Aldehyde

The aldehyde [5] was prepared in 37.8% yield by isomerization of the epoxide [4] with silica alumina catalyst and isolated in high purity by fractional distillation.

The odor characteristics of the derivatives prepared from the aldehyde [5] are presented in Table II.

The aldehyde [5] was readily reduced with sodium borohydride in ethanol to yield 2,2,5-trimethyl-6-hepten-1-ol [8]. Reaction with hydroxylamine led to the oxime which, upon dehydration with acetic anhydride, yielded the corresponding nitrile [9], 2,2,5-trimethyl-6-heptenyl nitrile in 90% yield. The aldehyde was easily converted to two Grignard products, 3,3,6-trimethyl-7-octen-2-ol [10] and 3,6,6-trimethyl-1-nonen-7-ol [11]. Oxidation of the aldehyde in the presence of nickel chloride in methanol solution was unsuccessful; instead the dimethyl acetal [12] was isolated.

The aldehyde [5] reacted readily under aldol conditions with both acetone and butanone to give the correspond-

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ing products [13] and [14]. Steric crowding of the aldehyde resulted in the exclusive attack upon carbon one of the butanone. A brief attempt was made to cyclize [13] with sulfuric acid, but no clean product formation was observed.

Ketone Derivatives

The ketone [6] was first prepared from the epoxide by Naef and coworkers³ and has also been identified in the air-oxidation products of dihydromyrcene. Several simple derivatives were prepared from the ketone [6] and their fragrance properties are described in Table III. Reduction of the ketone with sodium borohydride in ethanol led to the alcohol [15]. Also, it was reacted with methyl and ethyl magnesium bromide to give the corresponding alcohols [16] and [17].

Alcohol Derivatives

Eschinasi⁶ first reported the isomerization of dihydromyrcene oxide [4] to the alcohol, 2,6-dimethyl-1,7-octadien-3-ol [7]. It has also been seen among the air oxidation products of dihydromyrcene. The odor characteristics of several derivatives prepared from the alcohol are described in Table IV.

The alcohol [7] was converted to its acetate [18] and hydrogenated to the saturated alcohol [19]. Isomerization with tri-isobutyl vanadate⁷ led to the formation of the primary allylic alcohol 2,6-dimethyl-2,7-octadien-1-ol [20]. This material was hydrogenated to yield the saturated alcohol [21] reported by Japanese researchers⁸ to be an effective attractant for the insect *Tribolium confusum* J., commonly found in cereal.

Conclusion

Structure activity relationships have been used in recent years to design new fragrance molecules. In spite of this new trend, there still remains a need to identify useful fragrance compounds based on readily available raw materials.

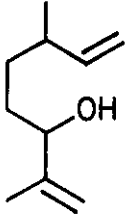
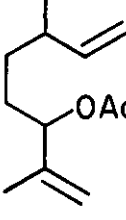
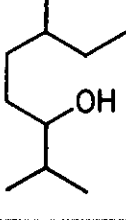
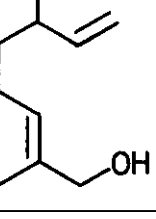
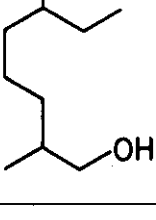
Dihydromyrcene is produced in multi-ton quantities by the pyrolysis of pinane. Its epoxide is readily prepared in high yield and selectivity. This epoxide can be isomerized to either 2,2,5-trimethyl-6-heptenal, 2,6-dimethyl-7-octen-3-one or 2,6-dimethyl-1,7-octadien-3-ol. Good selectivities for each of these products can be obtained by the proper choice of reaction conditions. Each has been converted to several new derivatives.

In the search for new odorants, the isomerization of dihydromyrcene oxide was explored. A new aldehyde was identified and several of its derivatives were prepared. No doubt, new, interesting C₁₀ molecules will continually be made from the pinenes.

References

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Table IV. Odor characteristics of alcohol [7] derivatives

| | | |
|--|----|---|
|  | 7 | Fresh green vegetation with a fruity note - green pear/apple odor. |
|  | 18 | Spicy fruity woody - Some cumin/coriander character - linalyl acetate - terpinyl acetate notes - with spicy peppery background. |
|  | 19 | Green privet odor - green bean fresh, very natural odor. |
|  | 20 | cis is more lavender, mushroomy than trans, more citrus reminiscent of myrcenol slightly fatty floral - with a piney back note. |
|  | 21 | Fresh, green, berry/green bean note, refreshing. |

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