

United States Patent

Leffingwell et al.

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[54] **SYNTHESIS OF ALKYL
CYCLOPENTYL KETONES**

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[21] Appl. No.: **807,120**

[52] U.S. Cl. **260/586 R, 252/522, 260/489, 260/587, 260/617 R**

[51] Int. Cl. **C07c 45/00**

[58] Field of Search **260/586 R, 587, 488 R, 489, 260/617 R**

[56]

References Cited

UNITED STATES PATENTS

| | | | |
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| 2,972,632 | 2/1961 | Bain et al. | 260/587 |
| 2,803,647 | 8/1957 | Bain et al. | 260/489 |
| 3,510,510 | 5/1970 | Kropp | 260/489 |

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Attorney—Pendleton, Neuman, Williams & Anderson

[57]

ABSTRACT

Pyrolysis of trans-1-hydroxy-2-acetoxycyclohexanes to produce alkyl cyclopentyl ketones.

5 Claims, No Drawings

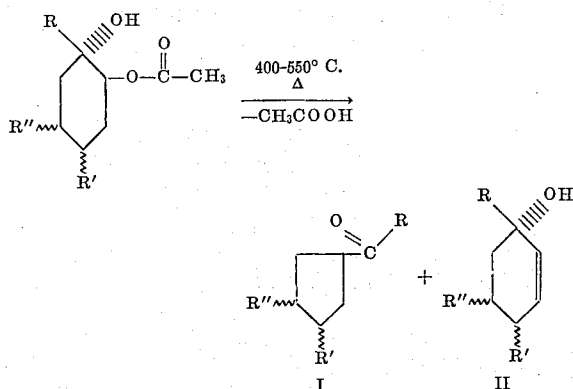
SYNTHESIS OF ALKYL CYCLOPENTYL KETONES

This invention relates to a process for producing alkyl cyclopentyl ketones.

We have found that alkyl cyclopentyl ketones are obtained by vapor phase pyrolysis of certain trans-1-hydroxy-2-acetoxycyclohexanes.

In accordance with our discovery certain trans-1-hydroxy-2-acetoxycyclohexanes are subjected to vapor phase pyrolysis at temperatures of approximately 400° C. to 550° C., preferably 425° C. to 475° C., with the formation of alkyl cyclopentyl ketones which are then recovered. The alkyl cyclopentyl ketones have desirable olfactory characteristics and can be used in compounding perfumeries. The use in perfumeries of alkyl cyclopentyl ketones of the type produced in accordance with this invention is disclosed, for example, in U.S. Pat. No. 2,946,823 which issued July 26, 1960.

The synthesis of this invention can be illustrated generally by the following reaction:



wherein

R = methyl or isopropyl;

R' = methyl, isopropyl or isopropenyl;

R'' = hydrogen; and

R' + R'' = dimethylmethylene;

with the hydroxyl and acetate groups being in trans position with respect to one another as indicated by the bonds — and —, and R' and R'' being in trans or cis position with respect to one another as indicated by the bonds ~.

As seen in the above reaction, an allylic alcohol (II) is also formed by pyrolysis. The alkyl cyclopentyl ketone (I) can be separated from the allylic alcohol by fractional distillation, chromatography and the like.

The following examples further illustrate but do not limit the present invention. All temperatures recited are in degrees centigrade and all parts are by weight unless otherwise stated.

In the following examples, the pyrolysis apparatus employed consisted of a vertical tube, 18 inch long and 1 inch diameter filled with ¼ inch glass helices, mounted in a combustion furnace. The sample was directed through the apparatus by means of a pressure equalizing funnel mounted on the top of the pyrolysis tube. The sample was carried through the pyrolysis tube by gravity and the pressure due to vaporization. The effluent pyrolyzate was condensed by means of a cold water condenser and trapped in an ice cooled vessel. The samples used in pyrolysis were 20 percent hydroxyacetates by weight in acetone (a solvent being employed for convenience but not required). A drop

rate of 0.5–2.0 drops/second was generally employed. The reaction temperatures reported are external wall temperatures of the pyrolysis tube. After pyrolyses were complete, the samples were neutralized with a sodium bicarbonate solution and extracted with either hexane or ether. Multiple vapor phase chromatographic analyses were done on each sample using a 10 foot, 10 percent diethyleneglycolsuccinate column under several conditions. Product analyses were done by comparison of the retention times and spectra with known samples, when available.

EXAMPLE I

4-Hydroxyneomenthylacetate is prepared by treating 3-menthene with an organic peroxyacid such as peracetic acid to form (±) cis and trans-3-menthene epoxides. Reaction of the cis-3-menthene epoxide with acetic acid in a sodium acetate buffered solution produces 4-hydroxyneomenthylacetate. The 4-hydroxyneomenthylacetate when subjected to vapor phase pyrolysis afforded a product mixture of isopropyl 3-methylcyclopentyl ketone and trans-2-menthene-4-ol.

In Table I there are set forth the results of vapor phase pyrolysis of 4-hydroxyneomenthylacetate at different temperatures.

TABLE I

Pyrolysis of 4-Hydroxyneomenthylacetate

| Pyrolysis Temperature | % Acetate Pyrolyzed | Product Ratio | |
|-----------------------|---------------------|---------------|--------------------|
| | | % Ketone* | % Allylic Alcohol† |
| 410° | 27.6 | 81 | 19 |
| 430° | 73 | 68 | 32 |
| 444° | 86.2 | 65 | 35 |
| 475° | 100 | 60 | 40 |

*Isopropyl 3-methylcyclopentyl ketone

†trans-2-Menthene-4-ol

The isopropyl 3-methylcyclopentyl ketone was identified from its characteristic spectral data. The infrared spectrum exhibited a ketone carbonyl at 5.83 μ. The nuclear magnetic resonance spectrum exhibited a doublet methyl at 9.01 τ (J = 7 cps, 3H); the isopropyl methyls appeared as a doublet at 8.95 τ (J = 7 cps, 6H); the isopropyl proton adjacent to the carbonyl appeared as a 5 peaked multiplet at 7.40 τ (1H) and the ring proton adjacent to the ketone carbonyl appeared as unresolved multiplet at 7.0 τ (1H). The mass spectrum gave a parent molecular ion at m/e 154. From the isotopic abundance ratio of M, M + 1 and M + 2 (11.143, 7.68, 14.50 respectively) a molecular weight of 154.1851 (calculated mol. wt. = 154.2) was determined. Major fragment peaks appeared at m/e 154, 111, 99, 83, 71, 66, 55, 43 and 41 with metastable peaks at m/e 62.1 (due to 111 → 83) and 36.4 (due to 83 → 55). Identification of trans-2-menthene-4-ol was made by spectral comparison with a known sample.

EXAMPLE II

Pyrolysis of 1-Hydroxyneocarvomethylacetate

1-Hydroxyneocarvomethylacetate is prepared by acetylation of 1-hydroxyneocarvomethylol. The results of pyrolysis thereof at different temperatures are tabulated below.

TABLE II

Pyrolysis of 1-Hydroxyneocarvomenthylacetate

| Pyrolysis Temperature | % Acetate Pyrolyzed | % Ketone* | Product Ratio Allylic Alcohol [†] |
|-----------------------|---------------------|-----------|--|
| 417° | 20 | 22 | 78 |
| 438° | 79 | 22 | 78 |
| 449° | 94 | 23 | 77 |

* 3-Isopropylcyclopentyl methyl ketone

[†] trans-2-Menthene-1-ol

Identification of the trans-2-methen-1-ol was made by comparison with a known sample. The 3-isopropylcyclopentyl methyl ketone was identified by its characteristic spectra and semicarbazone. The infrared spectrum of this ketone exhibited a saturated carbonyl absorption at 5.83 μ . The nuclear magnetic resonance spectrum had resonance signals at 9.12 τ (doublet, J \approx 6 cps, 6H), an acetyl methyl at 7.95 τ (singlet, 3H) and the ring proton adjacent to the carbonyl appeared at 7.13 τ (multiplet, 1H). The mass spectrum exhibited a molecular ion at m/e 154; other fragment peaks appeared at m/e 139, 136, 111, 96, 84, 71, 69, 55, 43, 41 and a metastable peak at 120.1 corresponding to the m/e 154 \rightarrow 136 transformation. The semicarbazone melted at 156°–158° [reported literature m.p. 156°–157°].

EXAMPLE III

Pyrolysis of 1-Hydroxyneoisocarvomenthylacetate 1-Hydroxyneoisocarvomenthylacetate (α_D^{25} –28.1°, n_D^{23} 1.4651) was prepared by acetylation of 1-hydroxyneoisocarvomenthol (5 g., m.p. 85°–86°, $[\alpha]_D^{25}$ +2.41°) with acetic anhydride.

The results of the pyrolysis are tabulated below.

TABLE III

Pyrolysis of 1-Hydroxyneoisocarvomenthylacetate

| Pyrolysis Temperature | % Acetate Pyrolyzed | % Ketone* | Product Ratio % Allylic Alcohol [†] |
|-----------------------|---------------------|-----------|--|
| 480° | 100 | 75 | 25 |

* 3-Isopropylcyclopentyl methyl ketone

[†] cis-2-Menthene-1-ol

Product identification was made by trapping the two product peaks via preparative gas phase chromatography. The first product peak eluting was identified as 3-isopropylcyclopentyl methyl ketone by comparison of the infrared, nuclear magnetic resonance and mass spectra with that of a sample previously identified from Example II. The second minor component was identified as cis-2-methen-1-ol from its characteristic spectra. The infrared spectrum exhibited absorptions at 2.97, 3.34, 3.40, 3.45, 6.84, 7.25, 7.33 (doublet), 7.53, 8.15–8.37, 8.58, 8.92 (strong), 9.47, 10.22, 10.58, 10.90, 11.65, 12.30, 12.45, 13.50 and 13.90 microns. The nuclear magnetic resonance spectrum exhibited doublet isopropyl methyls centered at 9.1 τ (J \approx 6 cps, 6H), a singlet methyl at 8.74 τ (3H), saturated methylene protons at 8.1–8.8 τ and an unresolved singlet for the olefinic protons at 4.38 τ (2H).

EXAMPLE IV

Pyrolysis of 3 β -Hydroxy-4 α -acetoxycarane

3 β -Hydroxy-4 α -acetoxycarane (m.p. 69.5°–70.5°) was prepared according to the procedure of Kropp "

Cyclopropyl Participation in the Carane System", J. Am. Chem. Soc., 88, 4926 (1966). The results of the pyrolysis are tabulated below:

TABLE IV

Pyrolysis of 3 β -Hydroxy-4 α -Acetoxycarane

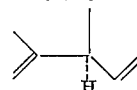
| Pyrolysis Temperature | % Acetate Pyrolyzed | % Ketone* | Product Ratio % Alcohol [†] |
|-----------------------|---------------------|-----------|--------------------------------------|
| 408° | 75 | 24 | 76 |
| 420° | 95 | 24 | 76 |
| 446° | 100 | 27 | 73 |
| 520° | 100 | 23 | 77 |

* 6,6-Dimethyl-3-acetyl-bicyclo-[3.1.0]-hexane

[†] trans-4,8-m-Menthadiene-1-ol

The two pyrolysis products were isolated by preparative gas phase chromatography and identified by their characteristic spectra. The first product peak eluting off a 10 foot 10 percent Carbowax 20M (¼ inch analytical) column was 6,6-dimethyl-3-acetyl-bicyclo-[3.1.0]-hexane, identified by its characteristic spectra. The ketone exhibited infrared absorptions at 3.31 (cyclopropyl C—H), 3.40, 3.48, 5.83 (methyl ketone carbonyl), 6.85, 7.00, 7.25, 7.35, 8.23, 8.40, 8.87, 11.87 and 12.6 microns. The nuclear magnetic resonance spectrum exhibited resonance signals at 9.05 τ (singlet, 6H) corresponding to the cyclopropyl gem methyl groups, cyclopropyl protons at 8.83 τ (multiplet, 2H) and an acetyl methyl at 7.9 τ (singlet, 3H); the ring proton adjacent to the carbonyl appeared at 7.28 as a multiplet (1H). The mass spectrum exhibited a molecular ion at m/e 152 with other fragments at m/e 137, 119, 109, 95, 93 and 91.

The second product peak eluting on preparative vapor phase chromatography solidified and, when sublimed onto a microscope slide cover, melted at 65°–66°. This material was identified as the sylvestrene derivative trans-4,8-m-menthadien-1-ol from knowledge of the configuration of the starting hydroxyacetate coupled with the observed spectral data. The infrared spectrum exhibited a strong -OH absorption at 3.05 μ and other absorptions at 3.32, 3.43, 3.50, 6.06 (strong, olefinic), 6.85, 7.26, 7.48, 7.56, 7.75, 7.85, 8.04, 8.18, 8.77, 8.93, 9.13, 9.36, 10.31, 10.55, 10.80, 11.0, 11.25 (strong), 11.70, 12.70, 13.70 and 15.05 microns. The nuclear magnetic resonance spectrum exhibited signals at 8.75 τ (singlet, 3H) corresponding to the tertiary methyl, an allylic methyl group at 8.25 τ (poorly resolved triplet, 3H), an allylic methylene at 7.85 τ (multiplet, 2H), an allylic proton at 7.15 τ corresponding to the doubly allylic ring proton



(broad multiplet, 1H); the terminal methylene protons appeared as a poorly resolved quartet at 5.20 τ (2H) and the ring olefinic protons appeared at an unresolved singlet at 4.38 τ (2H) in CDCl₃ solution. The mass spectrum exhibited a molecular ion at m/e 152 and other major fragments at m/e 137, 134, 119, 109, 94 and 79.

EXAMPLE V

Pyrolysis of 1-Hydroxyneodihydrocarvylacetate

1-Hydroxyneodihydrocarvylacetate was passed

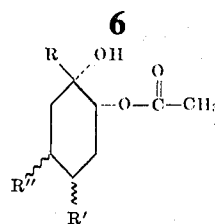
(neat) through the pyrolysis column described above at about 480° C. with a drop rate of ~0.5/sec. The pyrolyzate obtained was ~40 percent pyrolysis products and ~60 percent unpyrolyzed hydroxyacetate. Distillation gave a fraction boiling at 60°-72 L/1.5 millimeters of mercury which consisted of the main pyrolysis products. Vapor phase chromatography showed only a single peak on several different columns, but the infrared spectrum exhibited a significant carbonyl at 5.83 μ indicating the presence of a ketone. Nuclear magnetic resonance spectral analysis indicated the sample to be a mixture of ~65-70 percent 2,8-menthadien-1-ol and ~30-35 percent of a ketone which was identified as 3-isopropenylcyclopentyl methyl ketone.

It will be understood that in practicing the present invention optically active products are obtained from optically active starting materials and racemic products from racemic starting materials.

Those modifications and equivalents which fall within the spirit of the invention are to be considered a part thereof.

We claim:

1. A process which comprises pyrolyzing at a temperature of from about 400° C. to 550° C. in vapor phase a compound of the formula



wherein

R = methyl or isopropyl;

R' = methyl, isopropyl or isopropenyl;

R'' = hydrogen; and

R' + R'' = dimethylmethylene; treating the pyrolysis products with a base to effect neutralization of acidic components and recovering an alkyl cyclopentyl ketone from said products.

2. A process in accordance with claim 1 wherein 4-hydroxyneomenthylacetate is pyrolyzed and isopropyl 3-methylcyclopentyl ketone is recovered.

3. A process in accordance with claim 1 wherein 1-hydroxyneocarvomenthylacetate is pyrolyzed and 3-isopropylcyclopentyl methyl ketone is recovered.

4. A process in accordance with claim 1 wherein 1-hydroxyneoisocarvomenthylacetate is pyrolyzed and 3-isopropylcyclopentyl methyl ketone is recovered.

5. A process in accordance with claim 1 wherein 3 β -hydroxy-4 α -acetoxycarane is pyrolyzed and 6,6-dimethyl-3-acetyl-bicyclo-[3.1.0]-hexane is recovered.

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UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,689,562 Dated September 5, 1972

Inventor(s) John C. Leffingwell and Ronald E. Shackelford

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 2, line 37, in the table under the heading "% Ketone", "60" should be directly under "65"

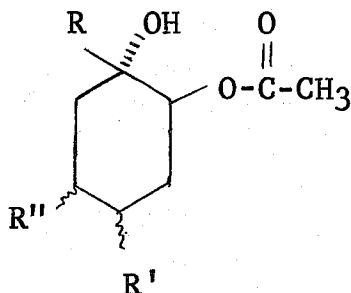
Column 3, line 5, the last column heading in the table, before "Allylic" insert -- % --

line 7, "78" appearing under the heading "% Ketone" should be under the column heading "Allylic Alcohol" directly in line with the numbers "78" and "77"

lines 27 and 28, "157°]" should all be on the same line.

Column 5, lines 5 and 6, "60°-72L/1.5" should be -- 60-72°/1.5 --

Column 6, lines 1-7, the formula should read as follows:



line 12, "diemthylmethylene" should be
-- dimethylmethylene --

line 26, "hydroxy-4 α acetoxycarane" should be
-- hydroxy-4 α -acetoxycarane --

Signed and sealed this 23rd day of January 1973.

(SEAL)
Attest:

EDWARD M. FLETCHER, JR.
Attesting Officer

ROBERT GOTTSCHALK
Commissioner of Patents