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ALIEN PROPERTY CUSTODIAN

PROCESS OF MANUFACTURING CYCLOPENTENONEDERIVATIVES

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The processes having become known up to now for the manufacture of cyclopentenonederivatives can be divided into two groups. In the one thereof the process starts from a finished cyclopentene-nucleus or cyclopentane-nucleus respectively. There is thus, obtained for instance, alkylcyclopentenones from the nitrosochlorides of the alkylcyclopentenes when these are treated with potassium acetate and acetic acid. This process is, however, not generally applicable, as the use of dialkylcyclopentenes in which the double bond lies between the substituted nucleus-carbon atoms is not possible. The process presupposes, furthermore, the indifference of the selected alkyl groups with respect to nitrosylchloride and the like. Besides, the yield is in most cases not satisfying.

The other of the above mentioned two groups starts from linear compounds. There is, thus, obtained, for instance, methyl-alkyl-cyclopentenones if esters from laevulic acid and esters from α-halogenfatty-acids are used as starting materials (compare, for instance, Helv. Chim. Act. VII, pages 256/257, 1924). Also this process is subjected to similar restrictions as that for the manufacture of alkylcyclopentenones from alkylcyclopentenes. A particularly grave drawback connected therewith in this case is the comparatively slight yield. Thus, Staudinger and Ruzicka have obtained only about 1½ grams of methyl-amyl-cyclopentenone from 318 grams of ethyl-α-bromenanthate and 182 grams of ethyl-laevulinate (see also Treff and Werner, Berichte 68, pages 642/643, 1935).

Also the reaction found by Blaise, according to which ethyl-methyl-cyclopentenone can be obtained from dipropionyl-ethane shall be mentioned.

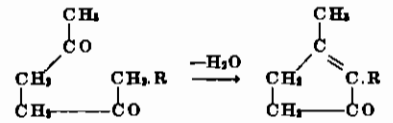
The ring closure of the acetonyl-acetone instead of the dipropionyl-ethane is not possible. In this case dimethylfurane or resinous products are obtained but by no means the desired methyl-cyclopentenone. This behaviour has been taken over, as is known, into the text-book literature as a classical example for the reaction of the aliphatic γ-dicetones. It seems, therefore, that the presence of methyl-groups in a position adjacent to the CO-groups excludes the formation of a cyclopentenone nucleus.

I have discovered that, in a surprising contrast to the hitherto usual opinion, the γ-dicetones are able to form a cyclopentenone nucleus if a methyl-group is in a position adjacent to one of the two CO-groups but a methylene-group in a position adjacent to the other of the CO-groups, that is to say, if the γ-dicetones correspond to the formula

$$CH_3.CO.C(R_1R_2).C(R_3R_4).CO.CH_2.R_5$$

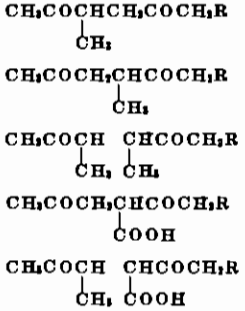
In this formula R_1 R_2 R_3 R_4 denote hydrogen or any other desired univalent group, f. i. methyl, carboxyl or the like. R_5 is an univalent aliphatic or aromatic or a substituted group.

The ring closure itself is a very simple operation. In many cases one obtains a practically quantitative yield, if the procedure is carried out in the presence of alkaline or—with poor yields—acid condensation-agents. The ring closure takes place according to the following formula:



Thus, cyclopentenonederivates are obtained when the following compounds are used as starting materials:

$CH_3.CO.CH_2.CH_2.CO.CH_2.C_4H_9$ (C_4H_9=butyl)
$CH_3.CO.CH_2.CH_2.CO.CH_2.C_5H_9$ (C_5H_9=pentenyl)
$CH_3.CO.CH_2.CH_2.CO.CH_2.CH_2.COOH$
$CH_3.CO.CH_2.CH_2.CO.CH_2.CH_2.COOR$
(R=methyl, ethyl etc.)
$CH_3.CO.CH_2.CH_2.CO.CH_2.CH_2.CH_2.CH_2OH$
$CH_3.CO.CH_2.CH_2.CO.CH_2.CH_2.CH_2.CH_2OR$
(R=methyl, ethyl etc.)
$CH_3.CO.CH_2CH_2.CO.CH_2.CH_2.CH_2.CH_2Br$ (Cl, J)



etc.

Concerning the condensation agents it is most suitable to the object in view to make use of an aqueous, alcoholic or methyl-alcoholic potassium hydroxide solution, sodium-hydroxide or barium hydroxide solution, furthermore of a solution of alkali-alcoholates, alkaline earth hydroxides, alkali-carbonate or alkali-bicarbonate or of a solution of a similar substance, but it is as well possible to employ occasionally aqueous or non-

aqueous acids or solutions of acids, salts or the like. Finally, it is possible to carry out the reaction in the gas-phase, the vapor of the dicetone being then subjected to the action of heat, may be with the simultaneous use of dehydrating agents.

The process constituting the present invention is more fully described in detail in the following examples:

First example

5,9 grams of 2,5-nonane-dione (b. $p._{15}$=112–114°) are heated to boiling temperature together with 76 grams of 2%-aqueous sodium hydroxide solution, the mixture being kept at that temperature for several hours. There are obtained 4.15 grams of 3-methyl-2-propylcyclopentene-2-one-1, which are 80% of the theoretical yield.

b. $p._{11,5}$=94,5°
Semicarbazone: m. p. 212°

Second example

4,4 grams of 2,5-decandione (b. $p._{17}$=132–134°) are heated with 52 grams of 3%-aqueous potassium hydroxide solution to boiling, the mixture being maintained boiling for some time. The oily layer is taken up by means of ethyl ether and is distilled in vacuo after the ether has been evaporated. There are obtained 2,9 grams, viz. 74% of the theoretical yield, of 3-methyl-2-butylcyclopentene-2-one-1 which is a liquid with an agreeable smell.

b. $p._{12}$=107°
Semicarbazone: m. p.=193–193.5°

Third example

In a similar manner as in the first and in the second example there are obtained from 9,2 grams undecandione (b. $p._{14}$=141°, m. p.=33°) 7,6 grams, viz. 92% of the theoretical yield of 3-methyl-2-n-amylcyclopentene-2-one-1. This product is dihydrojasmone, as appears from its analysis and its physical constants.

f.: H=10.96 C=79.28
calc.: H=10.92 C=79.45

The boiling point of the ketone purified by the semicarbazone is 120–121.5° at 12 mm. The semicarbazone did not show any fusing point depression together with a dihydrojasmonesemicarbazone manufactured according to Duden and Freitag.

Fourth example

If 6 grams of 2-methyldecandione-6,9 (b. $p._{13}$=128–132°) are heated together with 65 grams of a 2% aqueous sodium solution to boiling temperature for 24 hours, there are finally obtained, after the process has been finished, 4,4 grams, viz. 82% of the theoretical yield, of 3-methyl-2-i-amylcyclopentene-2-one-1, which is a liquid having an odour resembling that of jasmine.

b. $p._{12}$=114,5–118,5°
Semicarbazone: m. p.=181–182°

With higher molecular γ-dicetones it is recommendable to make use of somewhat stronger condensation agents, viz. an addition of alcohol, more concentrated solutions, solid alkali- or earthalkali-hydroxides, and the like. But the use of such stronger condensation agents is not a condition, as the success is the same by heating for a longer period with dilute solutions.

Fifth example

2,2 grams of 2,5-dodecandione (b. $p._{12}$=148°, m. p.=39,5–40,5°, semicarbazone: m. p.=187°) are stirred with 11 grams of hot 3%-potassium hydroxide solution for several days. After cooling and extracting with ethyl-ether there are obtained 1,6 grams, viz. 80% of the theoretical yield, of 3-methyl-2-hexylcyclopentene-2-one-1.

b. $p._{18}$=142–144°
Semicarbazone: m. p.=163,5–164,5°

Sixth example

A mixture of 3,6 grams of 2.5-tetradecandione (m. p.=50–51°), 20 ccm. of a 10%-potassium hydroxide solution and 30 ccm. of alcohol is heated to boiling and maintained at this temperature for 2 hours, whereafter the alcohol is distilled-off and the oily layer is taken up by ethyl-ether. Yield: 2,7 grams of 3-methyl-2-octylcyclopentene-2-one-1, which are 81,4% of the theoretical yield.

Liquid of flowery odour; b. $p._{12}$=157–160°
Semicarbazone: m. p.=159–159,5°

Seventh example

A solution of 4,9 grams of 2,5-octadecandione (m. p.=70,5°) in 30 ccm. of alcohol is heated to boiling together with 20 ccm. of a 50%-aqueous potassium hydroxide solution, this temperature being maintained for 1 hour. There are obtained 3,1 grams of 3-methyl-2-dodecylcyclopentene-2-one-1, which are 68% of the theoretical yield.

m. p.=34–35,5°
b. $p._{2,5}$=171–173°
Semicarbazone: m. p.=151,5–152,5°

Eighth example

When 11-methoxy-2,5-undecandione is heated with a mixture of 40 ccm. of a 5%-aqueous sodium hydroxide solution and 10 ccm. of alcohol 3-methyl-2-(ε-methoxyamyl)-cyclopentene-2-one-1 is obtained.

b. $p._{14}$=146–148°
Semicarbazone: m. p.=150–150,5°

Ninth example

11,5 grams of 7-methyl-4,7-diketoheptoic acid (m. p.=76–78°) are dissolved in 200 ccm. of 4%-potassium hydroxide solution, the mixture being then heated to boiling for 2 hours. The originally colorless solution becomes somewhat darker. The mixture is cooled and neutralised with an amount of sulphuric acid accurately equivalent to the amount of the potassium hydroxide solution. Then the aqueous solution is concentrated by evaporation and the residue is extracted with ethyl-acetate. After the ethyl-acetate has evaporated there are obtained 10 grams instead of, theoretically, 10,3 grams of 3-methyl-cyclopentene-2-one-1-acetic-acid-2. After the recrystallisation of this product from ethyl acetate this acid forms stout crystals of m. p.=108,5–110,5°

Semicarbazone: m. p.=213,5–216° (decomposition)

Tenth example

From 11-methyl-4,7-diketoundecanoic acid methylester (b. p.=163–165°, m. p.=31–32°) is obtained the methyl ester of the 3-methyl-cyclopentene-2-one-1-(-5-caproic acid)-2, a liquid of b. $p._{1}$=136–142°. The condensation agent to be used in this case is preferably a solution of

sodium methylate in dry methyl-alcohol. After the saponification the free acid of b. $p._{.1}$=182–184° is obtained.

m. p.=63–65°
Equivalent weight=212 instead of 210.

Eleventh example

The condensation product of sodium salt of propionyl-acetic-acid-ester and bromoacetone is heated for some time together with an excess of 2%-sodium solution. The ester forms the correspondend γ-dicetone and this reacts by ring closure similarly to that described in the preceding example. There is obtained 2,3-dimethyl-cyclopentene-2-one-1.

Liquid of b. $p._{18}$=75–78°
Semicarbazone: m. p.=247,5° (decomposition).

Twelfth example

25 grams of α-capronyl-laevulic acid-ethyl-ester are gradually heated with 1 liter of 2% sodium hydroxide solution to boiling, neutralised after a short period of boiling and then extracted with ethyl-ether. There are obtained 10,7 grams, equal to 73,3% of the theoretical yield, of 3-methyl-2-butylcyclopentene-2-one-1 of

b. $p._{10}$=102–107°
Semicarbazone: m. p.=192°

Thirteenth example

In correspondence with the description concerning the preceding example 42,5 grams of α-heptene-(4)-oyl - laevulic acid-ethyl-ester are heated together with a 2%-sodium hydroxide solution to boiling. A sufficient quantity of acid is added and the product extracted with ethyl-ether. There are obtained 17,6 grams=65% of the theoretical yield of 3-methyl-2-(penten-2-yl) - cyclopentene-2-one - 1. b. $p._{9}$=122°. The product is identical with the natural Jasmone.

In a similar manner it has been possible to obtain the corresponding hexylcyclopentenonederivates from the α-enanthoyl- and the α-caprylyl-laevulic acid ethyl-ester.

Fourteenth example

25 grams of α-capronyl-β-methyl-laevulic acid-ethyl-ester have been treated in the manner described in the twelfth example. There has been obtained the 3,4-dimethyl-2-butylcyclopentene-2-one-1. Liquid of b. $p._{14}$=114–115°. Semicarbazone: m. p.=230–232° (decomposition).

There have, furthermore, been obtained from α-capronyl-α-methyl-laevulic acid-ethyl-ester the 3,5 dimethyl-2-butylcyclopentene - 2-one-1. Liquid of b. $p._{11}$=104°.

Fifteenth example

9,2 grams of 2,5-undecandione are dissolved in a 2%-methyl-alcoholic sodium hydroxide solution and heated to 60° for some time. The dehydration is then finished and the liquid has a dark color. After the methanole has been distilled-off the residue is acidulated and extracted with ethyl ether. One obtains a yield of 87% of dihydrojasmone with the constants stated in the third example.

Sixteenth example

2,5-undecandione is slowly distilled over silicagel containing a little alkalihydroxide and alkalisilicate and heated to a temperature little above the boiling point of the undecandione. The silicagel assumes a dark color during this time. The distillate contains dihydrojasmone and a small quantity of unchanged undecandione.

Instead of the katalysator just described there may be used other dehydrating katalysators, f. i. aluminium-silicate, titaniumdioxyde and the like.

Seventeenth example

A mixture of 50 grams of cold saturated potassium-carbonate solution, 30 ccm of alcohol and 4 grams of 2,5-dodecandione is heated under shaking in a sealed tube for at least one day to 120 to 140°. After settling of the process there are obtained about 80%, of the theoretical yield of 3-methyl-2-hexylcyclopentene-2-one-1.

Eighteenth example

4 grams of dodecandione are dissolved in 50 ccm of $\frac{1}{10}$ n methyl-alcoholic barium hydroxide solution and are kept boiling for 2 or 3 hours. There is obtained a yield of 64% of 3-methyl-2-hexyl-cyclopentene-2-one-1.

b. $p._{15}$=135–137°.

Nineteenth example

2 grams of sodium metal are dissolved in 40 grams of anhydrous methanol, whereafter 17 grams of acetic ester and 4 grams of dodecandione are added. The acetic ester is partially saponified by the water split off during the reaction. In this case sodium methylate is the condensation agent. There are obtained 2,8 grams, viz. 77% of the theoretical yield, of 3-methyl-2-hexylcyclopentene-2-one-1.

The products obtained by the present improved process are intended for use as perfumes, means for annihilating plant lice and other noxious animals etc. for the synthesis of curatives etc. and the like.

HEINZ HUNSDIECKER.