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Abstract

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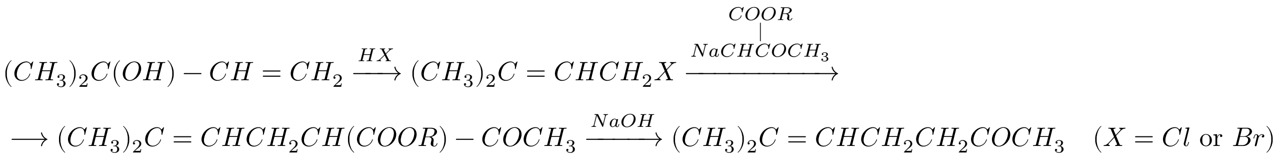
SYNTHESIS OF METHYLHEPTENONE AND METHYLHEPTADIENONE

Methylheptenone and methylheptadienone are important starting materials for the synthesis of natural fragrant substances of the isoprenoid type (linalool, geraniol, farnesol, citral, dehydrocitral, safranal, ionone). We have studied in detail the preparation of methylheptenone from dimethylvinylcarbinol or isoprene by three different methods: 1) condensation of prenyl halides with acetoacetic ester (^{1}); 2) interaction of dimethylvinylcarbinol with acetoacetic ester and 3) pyrolysis of the acetoacetic ester of dimethylvinylcarbinol (^{2}).

As was shown in our laboratory (^{3}), under the action of hydrogen halides on dimethylvinylcarbinol, the corresponding prenyl halides are formed in high yield; these readily condense with sodium acetoacetic ester and, upon subsequent saponification, give methylheptenone:

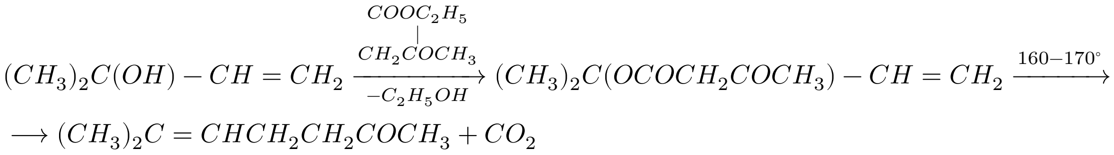


$$(CH_3)_2C(OH)-CH=CH_2 \xrightarrow{HX} (CH_3)_2C=CHCH_2X \xrightarrow{\substack{COOR\\ |\\ NaCHCOCH_3}}$$

$$\longrightarrow (CH_3)_2C=CHCH_2CH(COOR)-COCH_3 \xrightarrow{NaOH} (CH_3)_2C=CHCH_2CH_2COCH_3 \quad (X = Cl \text{ or } Br)$$

All three stages of this synthesis are expediently carried out in one operation, without isolation of intermediate products; in this way methylheptenone is obtained in a yield of 75% via prenyl bromide and 60% via prenyl chloride. The latter, as is known, can also be obtained by the action of hydrogen halides on isoprene.

The second method for the synthesis of methylheptenone consists in the direct interaction of dimethylvinylcarbinol with acetoacetic ester at a temperature of 160–170° and is illustrated by the following scheme:



$$(CH_3)_2C(OH)-CH=CH_2 \xrightarrow[-C_2H_5OH]{\substack{COOC_2H_5\\ |\\ CH_2COCH_3}} (CH_3)_2C(OCOCH_2COCH_3)-CH=CH_2 \xrightarrow{160–170^\circ}$$

$$\longrightarrow (CH_3)_2C=CHCH_2CH_2COCH_3 + CO_2$$

The yield of methylheptenone by this method is 60–70%; at the same time an almost theoretical amount of ethyl alcohol and carbon dioxide is evolved. Owing to the low boiling point of dimethylvinylcarbinol, the indicated reaction must be carried out under pressure or in the presence of high-boiling diluents (vaseline oil), using an efficient column 100–120 cm high. If this reaction is carried out at a temperature not above 140°, then as a result of transesterification an almost theoretical amount of ethyl alcohol is distilled off, but no carbon dioxide is evolved, and upon distillation of the residue in vacuo it is possible to isolate the acetoacetic ester of dimethylvinylcarbinol. The latter, at 160–170°, undergoes pyrolysis with formation of methylheptenone and carbon dioxide, which proves the reaction mechanism given above. The use of metallic sodium or other additives in this reaction is not expedient (^{4}).

We also investigated in detail the pyrolysis of pure dimethylvinylcarbinol acetoacetate, readily obtained in 90% yield by the action of diketene on dimethylvinylcarbinol in the presence of small amounts of pyridine:

$$(CH_3)_2C(OH)-CH{=}CH_2 \xrightarrow{\text{diketene}} (CH_3)_2C(OCOCH_2COCH_3)-CH{=}CH_2 \xrightarrow{145\text{–}160^\circ}$$
$$\longrightarrow (CH_3)_2C{=}CHCH_2CH_2COCH_3 + CO_2$$

The pyrolysis of dimethylvinylcarbinol acetoacetate proceeds most smoothly without any additives at 145–160°, giving methylheptenone in 65–70% yield. This entire process can also be carried out in one operation without isolating the dimethylvinylcarbinol acetoacetic ester in pure form. The pyrolysis of the latter also has a side direction, in which isoprene, acetone, and carbon dioxide are formed:

$$(CH_3)_2C(OCOCH_2COCH_3)-CH{=}CH_2 \xrightarrow{t^\circ} CH_2{=}C(CH_3)-CH{=}CH_2{+}CH_3COCH_3{+}CO_2$$

In some cases, such decomposition of acetoacetates of tertiary vinyl- and ethynylcarbinols becomes the main direction of the reaction, as was established in our laboratory on a number of other examples.

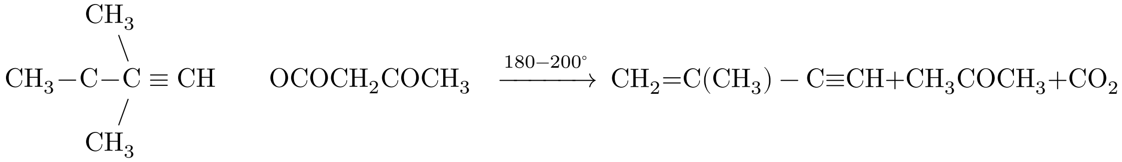
We also studied in detail methods for preparing methylheptadienone both by the interaction of dimethylethynylcarbinol with acetoacetic ester and by pyrolysis of pure dimethylethynylcarbinol acetoacetate, obtained in 90% yield by the action of diketene on dimethylethynylcarbinol in the presence of triethylamine:

$$(CH_3)_2C(OH)-C{\equiv}CH \xrightarrow[\text{or diketene}]{\substack{COOC_2H_5\\ CH_2COCH_3}} (CH_3)_2C(OCOCH_2COCH_3)-C{\equiv}CH \xrightarrow{180\text{–}200^\circ}$$
$$\longrightarrow (CH_3)_2C{=}CH-CH{=}CHCOCH_3 + CO_2$$

Below 160° no interaction occurs between dimethylethynylcarbinol and acetoacetic ester (the starting products are recovered); this reaction must be carried out at 170-180°, but the yield of methylheptadienone obtained is only about 25%.

Pyrolysis of pure dimethylethynylcarbinol acetoacetate in the liquid phase proceeds most smoothly without any additives at 180-200°,

and in this way methylheptadienone can be obtained in 55% yield. In the gas phase (Pyrex tube) this pyrolysis proceeds at an appreciable rate only at 250-300°, and methylheptadienone is then obtained in low yield (15-20%), including when vacuum is used. The introduction of inert diluents and additions of various acids, salts, and metal oxides (phosphoric and boric acids, α-naphthalenesulfonic acid, copper acetate, Cr_2O_3, Cu_2Cl_2, Hg_2Cl_2, $AlCl_3$, etc.) did not give favorable results, and in a number of cases led to complete resinification of the substance (copper acetate, boric acid, Cu_2Cl_2). Pyrolysis of the acetoacetate of dimethylethynylcarbinol is also accompanied by side processes with formation of isopropenylacetylene and acetone:



$$\mathrm{CH_3-C-\overset{\overset{CH_3}{\diagdown}}{\underset{\underset{CH_3}{/}}{C}}\equiv CH \qquad OCOCH_2COCH_3 \xrightarrow{180-200^\circ} CH_2{=}C(CH_3)-C{\equiv}CH+CH_3COCH_3+CO_2}$$

Experimental Part

Preparation of methylheptenone. a) Through 200 g of dimethylvinylcarbinol, while cooling with ice water (0°), 193 g of gaseous hydrogen bromide (3% excess) was passed over three hours. The mixture stood for 2 hours at room temperature; the aqueous layer formed (40 ml) was separated, the bromide was washed with sodium bicarbonate solution and dried with calcined magnesium sulfate. A total of 323 g of prenyl bromide was obtained, which without distillation was added (over the course of an hour) to sodium acetoacetic ester prepared from 55 g of metallic sodium and 380 g of ethyl acetoacetate in 650 ml of absolute alcohol. The reaction mixture was stirred for 5 hours at a temperature of 5-20°, then left overnight, and on the following day stirred again for 4 hours at 60°. The precipitated sodium bromide (213 g) was filtered off, the alcohol was distilled off under slight vacuum, 1100 ml of 10% caustic soda solution was added to the residue, and the mixture was stirred for 3 hours at 60-65°. After acidification with hydrochloric acid to an acid reaction to Congo, the product was extracted with ether, washed with bicarbonate solution, dried with magnesium sulfate, and distilled in vacuum on a 25-theoretical-plate column. A total of 219 g (75%) of methylheptenone was obtained, b.p. 75.5-76°/25 mm, n_D^{20} 1.4404. Its semicarbazone melted at 135.5-136°, and the 2,4-dinitrophenylhydrazone at 85.5-86° (from aqueous alcohol).

b) Through 86 g of dimethylvinylcarbinol at 0° over the course of 4 hours, 39.5 g of gaseous hydrogen chloride (8% excess) was passed. After a two-hour standing at room temperature, the aqueous layer (2 ml) was separated; the prenyl chloride was washed with saturated bicarbonate solution, dried with magnesium sulfate, and without distillation added dropwise (over the course of 2 hours) to a solution of sodium acetoacetic ester prepared from 34 g of metallic sodium and 190 ml of ethyl acetoacetate in 300 ml of absolute methanol. The mixture was stirred for 3 hours at a temperature of 30-40°. On the next day, the precipitate of sodium chloride was filtered off, the methanol was distilled off, 600 ml of 10% caustic soda solution was added to the residue, and the reaction mixture was stirred for 3 hours at 60-70°. After acidification with hydrochloric acid the product was extracted with ether, washed with bicarbonate solution, dried with magnesium sulfate, and distilled in vacuum. A total of 76.3 g (60%) of methylheptenone was obtained, b.p. 56-57°/9 mm, n_D^{20} 1.4403.

c) In a flask equipped with a thermometer, dropping funnel, and a column 120 cm high, 25 ml of vaseline oil was placed, and at a temperature of 210° (in the oil) a mixture of 43 g (0.5 mole) of dimethylvinylcarbinol and 72 g (0.55 mole) of ethyl acetoacetate was slowly added over the course of 6 hours, so that the temperature of the reaction mixture was main-

was maintained at not below 160-165°. Then heating at 160-180° was continued for another 3 hours until gas evolution ceased. In all, 9 l of gas was evolved in the experiment (analysis showed about 90% carbon dioxide and 10% isoprene), and 25 g of distillate with b.p. up to 78° was distilled off (ethyl alcohol with an admixture of acetone). Distillation of the residue in vacuo gave 38 g (60%) of methylheptenone with b.p. 61-62°/10 mm, n_D^{20} 1.4412, $\lambda_{\max}$ 243 mμ (in alcohol), $\lg\varepsilon$ 2.54; the semicarbazone melted at 136-137° (from alcohol).

d) To 17.2 g of dimethylvinylcarbinol (0.2 mole) was added 1 ml of dry pyridine, and 21 g of 83% diketene (0.25 mole) was added dropwise so that the temperature of the reaction mixture did not rise above 60°. After completion of the exothermic reaction, the mixture was heated at 70° for 15 min. Distillation gave 31.4 g (92%) of dimethylvinylcarbinol acetoacetate with b.p. 86-88°/10 mm, n_D^{20} 1.4410.

Found, %:	C 63.16; 63.53; H 8.19; 8.34
$C_9H_{14}O_3$. Calculated, %:	C 63.51; H 8.29

When diketene was allowed to act on dimethylvinylcarbinol in the presence of metallic sodium, as described in one of the recent patents ([2]), the acetoacetate was obtained in only 60% yield.

30 g of dimethylvinylcarbinol acetoacetate was heated in a nitrogen atmosphere at 145-160° for 2 hours, until gas evolution ceased. 2950 ml of carbon dioxide

was collected (75% of theory). Distillation of the residue in vacuo gave 13.6 g (62%) of methylheptenone with b.p. 56-58°/9 mm, n_D^{20} 1.4414.

Preparation of methylheptadienone. To 84 g of dimethylethynylcarbinol were added 2 ml of triethylamine, and 94 g of 85% diketene was introduced dropwise. The temperature of the reaction mixture was thereby maintained at not above 50°; the mixture was then heated for 30 min at 60°. Distillation in vacuo gave 152 g (90%) of dimethylethynylcarbinol acetoacetate with b.p. 85-86°/10 mm, n_D^{20} 1.4400. 84 g of the obtained dimethylethynylcarbinol acetoacetate was heated in a nitrogen atmosphere at 190-200° for 2 hours, until gas evolution ceased. 8 l of carbon dioxide was collected (72% of theory). Distillation of the residue in vacuo gave 34 g (55%) of methylheptadienone with b.p. 77-79°/8 mm, n_D^{20} 1.5300. Its semicarbazone melts at 175-176° (from alcohol).

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