Chemistry

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Abstract

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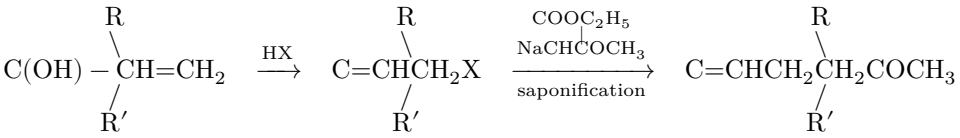
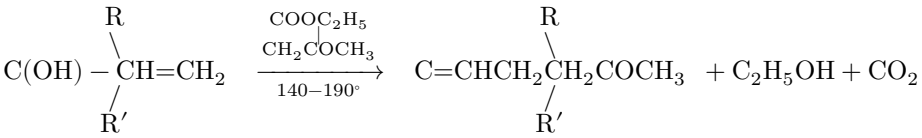
Synthesis of Analogs of Methylheptenone and Methylheptadienone

The synthesis of analogs of methylheptenone and methylheptadienone is of interest for obtaining the corresponding analogs of linalool, geraniol, citral, dehydrocitral, farnesol, ionone, and other natural isoprenoid compounds. The starting acetylenic alcohols required for the planned syntheses were obtained by the method developed in our laboratory: condensation of ketones with acetylene in the presence of powdered caustic potash under pressure ([1]). Upon selective hydrogenation in the presence of palladium on calcium carbonate, acetylenic alcohols are converted almost quantitatively into the corresponding vinyl alcohols ([2]), and the latter into the corresponding analogs of methylheptenone by three different methods, as was described in the preceding communication ([3]).

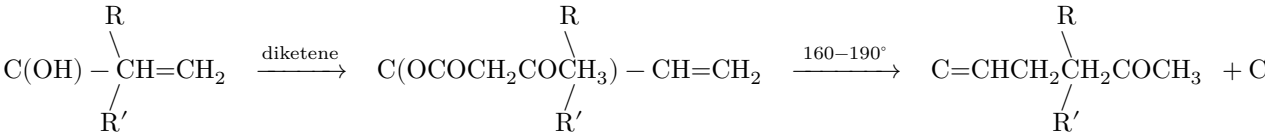
Method A. By the action of gaseous hydrogen chloride or hydrogen bromide on tertiary vinyl alcohols at a temperature of 0–20°, primary allylic-type halogen derivatives are readily formed ([4]); upon condensation of these with sodium acetoacetic ester and subsequent saponification, analogs of methylheptenone are obtained in an overall yield of 70–75% based on the vinylcarbinols taken into the reaction:



Method B. At a temperature of 140–190°, tertiary vinyl alcohols react directly with acetoacetic ester; in this process an almost theoretical amount of ethyl alcohol and carbon dioxide is liberated, and analogs of methylheptenone are formed in 60–70% yield ([5]):



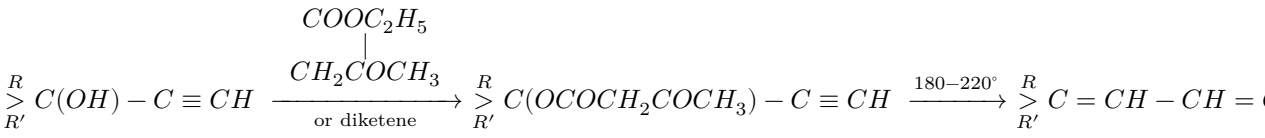
Method V. By the action of diketene on tertiary vinyl alcohols in the presence of small amounts of triethylamine or piperidine, the acetoacetic esters of these alcohols are formed in 80-90% yield (Table 2); pyrolysis of these at 160-190° also leads to the formation of analogs of methylheptenone in 70-75% yield ([6]):



The 2,3-dimethyl-2-hepten-6-one (IV) required for the synthesis of irone was obtained in 60-75% yield by all three of the methods described above.

The starting dimethylisopropenylcarbinol was obtained by the action of methyllithium on methyl methacrylate.

We also studied in detail the synthesis of analogs of methylheptadienone by methods B and C. Heating tertiary acetylenic alcohols with acetoacetic ester, as well as pyrolysis of the acetoacetic esters of these alcohols obtained with diketene (Table 2), makes it possible to obtain analogs of methylheptadienone in 60-70% yield (7).



All the analogs of methylheptenone obtained by us (except ketones I-IV) and methylheptadienone are summarized in Table 1.

Allylacetone (I) (9), crotylacetone (II), and chlorocrotylacetone (III) (8) were obtained in about 70% yield only by method A—by the interaction of the corresponding halo derivatives with sodium acetoacetic ester.

It should be noted that in the case of vinylcyclopentanol the yield of the unsaturated ketone (X) by methods B and C is greatly reduced as a result of a different direction of pyrolysis of its acetoacetic ester, with formation of acetone and a hydrocarbon: (1-vinyl-Δ'-cyclopentene).

Dimethylisopropenylcarbinol. To an ethereal solution of methyllithium, prepared from 9.1 g of lithium and 91 g of methyl iodide in 400 ml of dry ether, at −10° over two hours, 25 g of methyl methacrylate in 70 ml of ether was added, and then the reaction mixture was heated for 40 min at the boiling point of ether.

The lithium alcoholate was decomposed with cooling by ice water; the ether layer was separated, dried with potash, and distilled. 20.3 g (81%) of dimethylisopropenylcarbinol was obtained, b.p. 115-116°; n_D^{20} 1.4320; d_{20}^{20} 0.8437; MR found 30.67; calculated 30.96.

Found, %:	C 72.00; H 12.00
$C_6H_{12}O$. Calculated, %:	C 72.12; H 11.95

Active hydrogens found: 1.00; 0.96.

Acetoacetate of dimethylisopropenylcarbinol. To a mixture of 15 g of dimethylisopropenylcarbinol and 5 drops of triethylamine at 60-70° over 15 min, 15 g of diketene was added. The mixture was heated for 2.5 hours at 80°, dissolved in ether, the ethereal solution was washed with 5% bicarbonate, dried with magnesium sulfate, and distilled. 26.2 g (95%) of the acetoacetate of dimethylisopropenylcarbinol was obtained, b.p. 68-69°/2 mm; n_D^{20} 1.4479; d_{20}^{20} 0.9915; MR found 49.56; calculated 49.58.

Found, %:	C 65.32; 65.25; H 8.62; 8.37
$C_{10}H_{16}O_3$. Calculated, %:	C 65.22; H 8.70

Dimethylheptenone (IV). Method A. To sodium acetoacetic ester, prepared from 1100 ml of methanol, 60 g of metallic sodium, and 365 g of acetoacetic ester, over 85 min with stirring and cooling, 415 g of 2,3-dimethyl-4-bromobutene-2 (b.p. 69-71°/40 mm), obtained by saturating 230 g of 2,3-dimethylbutadiene (without solvent) with dry hydrogen bromide at −5°, was introduced. The mixture was stirred for 3 hours at 65°, the methanol was distilled off under slight vacuum, and the residue was heated with a solution of 120 g of caustic soda in 800 ml of water for 3 hours at 70°. The reaction mass, upon cooling, was acidified with hydrochloric acid; the product was extracted with ether, dried with magnesium sulfate, and distilled. 278 g (79%) of dimethylheptenone (IV) was obtained, b.p. 78-80°/15 mm; n_D^{20} 1.4500; d_{20}^{20} 0.8688; MR found 43.33; calculated 43.30 (10). By the action of crotyl bromide on Na-acetoethyl acetate by an analogous procedure, crotylacetone (V) was obtained in 63% yield, b.p. 75–77°/60 mm; n_D^{20} 1.4292; d_4^{20} 0.8442; MR found 34.26; calculated 34.07 (11).

Method B. 18.4 g of dimethylisopropenylcarbinol acetoacetate was heated at 170–175° for 45 min. 2330 ml of

Table 1

Nos.	Formula and constants:b.p. °C/mm; n_D^{20}; d_4^{20}	Yield, % A	Yield, % B	Yield, % C	Found, % C	Found, % H	Calc., % C	Calc., % H	Semicarbazone or 2,4-DNPH m.p., °C	N, % found	N, % calculated
V	$CH_3\backslash C$ $CHCH_2CH_2COCH_3$	73	–	62	77.18	11.34	77.08	11.51	113 – 114[3] 60 – 61[4]	21.31[3]	17.43[3] 17.49[4]
	C_2H_5/75 – 77/11; 1.4420; 0.8603										
VI	$CH_3\backslash C$ $CHCH_2CH_2COCH_3$	76	–	60	77.84	11.41	77.93	11.69	124[3] 58[4]	19.89[3]	16.96[3] 16.77[4]
	iso-C_3H_7/85 – 87/10; 1.4445; 0.8570										
VII	$CH_3\backslash C$ $CHCH_2CH_2COCH_3$	70	60	72	78.80	12.06	78.57	11.90	158 – 159[3] 94 – 96[4]	18.49[3]	16.08[3] 16.07[4]
	tert-C_4H_9/96 – 98/16; 1.4488; 0.8557										
VIII	iso-C_3H_7C = $CHCH_2CH_2COCH_3$	82	70	80	79.33	12.20	79.05	12.16	148[3] 84[4]	17.68[3]	15.75[3] 15.46[4]
	iso-C_3H_7/120/25; 1.4466; 0.8496										
IX	cyclohexyliden $CHCH_2CH_2COCH_3$	68	72	71	79.40	10.95	79.50	10.85	78[4]	16.15[4]	16.20[4]
	64 – 66/1; 1.4780; 0.9848										
X	cyclopentylidene $CHCH_2CH_2COCH_3$	40	16	73	79.19	10.56	79.00	10.50	90[4]	17.34[4]	16.85[4]
	75/2; 1.4790; 0.9250										

Nos.	Formula and constants:b.p. °C/mm; n_D^{20}; d_4^{20}	Yield, % A	Yield, % B	Yield, % C	Found, % C	Found, % H	Calc., % C	Calc., % H	Semicarbazone or 2,4-DNPH m.p., °C	N, % found	N, % calculated
XI	CH_3\C = CH—CH = CH—$COCH_3$ C_2H_5/93 – 94/10; 1.5161; 0.8943	–	–	61	78.30	10.03	78.21	10.21	164[3]	21.64[3]	21.52[3]
XII	CH_3\C = CH—CH = CH—$COCH_3$ iso-C_3H_7/103 – 104/11; 1.5166; 0.8904	–	–	59	78.92	10.48	79.89	10.59	161[3]	20.24[3]	20.08[3]
XIII	CH_3\C = CH—CH = CH—$COCH_3$ tert-C_4H_9/78 – 80/1; 1.5160; 0.8930	69	60	79.42	10.94	79.52	10.84	194[3]	18[4]	18.88[3]	18.83[3]
XIV	iso-C_3H_7\C = CH—CH = CH—$COCH_3$ iso-C_3H_7/66 – 67/0.2; 1.4925; 0.8783	56	62	80.14	11.08	79.93	11.18	147[3]	20[4]	17.83[3]	15.87[3] 15.53[4]
XV	cyclohexylidene CH—CH = CH—$COCH_3$ 98 – 100/1; 1.5290	37	38	80.31	9.61	80.50	9.75	183[4]	16.10[4]	16.27[4]	
XVI	cyclopentylidene CH—CH = CH—$COCH_3$ 75 – 77/1; 1.5258	13	14	79.80	9.26	80.00	9.33	198[4]	16.95[4]	17.27[4]	

[1] A, B, C –methods of preparation.
[2] Repeated analyses have been omitted throughout.

[3] Data refer to the semicarbazone.
[4] Data refer to the 2,4-dinitrophenylhydrazone.

carbon dioxide was evolved. The product was distilled in vacuo, giving 8.4 g (60%) of dimethylheptenone (IV), b.p. 78–80°/15 mm; n_D^{20} 1.4500.

Cyclohexylideneheptanone (IX). Method B. 207 g of vinylcyclohexanol and 224 g of ethyl acetoacetate were heated for 7 h with a gradual rise in temperature from 134 to 198°. 28.7 l of carbon dioxide was evolved, and 89.7 g of ethyl alcohol distilled off with an admixture of 1-vinyl-Δ^1-cyclohexene, b.p. 72–78°. On distillation of the residue

in vacuo gave 194 g (72%) of 1-cyclohexylidenepentan-4-one, b.p. 64-66°/1 mm; n_D^{20} 1.4770.

tert-Butylheptadienone (XIII). Method B. A mixture of 12.6 g of methyl-tert-butylethynylcarbinol (b.p. 141-142°) and 13 g of acetoacetic ester was heated for 3 h at 190-220°. 2200 ml of carbon dioxide was evolved, and 6.9 ml of liquid, b.p. 70-77°, was distilled off.

Table 2

Nos.	RR'	B.p., °C/mm	n_D^{20}	d_4^{20}	MR^*, found	MR^*, calc.	Found, %, C	Found, %, H	Calc., %**, C	Calc., %**, H	Yield, %
XVII	CH , C H	62-63/0.5	1.4429	0.9809	49.78	49.58	65.48	8.59	65.19	8.75	82
XVIII	CH , iso-C H	70-72/0.5	1.4478	0.9760	54.36	54.20	66.88	9.32	66.64	9.15	81
XIX	CH , tert-C H	90-91/4	1.4552	0.9736	59.10	59.42	68.00	9.67	67.92	9.43	83
XX	iso-C H , iso-C H	87-88/1.5	1.4586	0.9773	63.37	63.43	69.28	9.97	69.00	9.80	80
XXI	(CH)	100-103/1	1.4730	–	–	–	68.41	8.72	68.60	8.58	89
XXII	(CH)	87/1	1.4571	–	–	–	67.42	8.17	67.40	8.16	78
XXIII	CH , C H	73-74/1	1.4488	1.0150	48.11	48.04	65.97	7.54	65.91	7.74	85
XXIV	CH , iso-C H	77-78/1	1.4511	1.0046	52.61	52.66	67.43	8.13	67.33	8.22	87
XXV	CH , tert-C H	90-91/4	1.4560	0.9940	57.42	57.21	68.40	8.74	68.57	8.57	82

Nos.	RR'	B.p., °C/mm	n_D^{20}	d_4^{20}	MR^*, found	MR^*, calc.	Found, %, C	Found, %, H	Calc., %**, C	Calc., %**, H	Yield, %
XXVI	iso-C H , iso-C H	89–90/1.5	1.4616	0.9970	61.91	61.83	69.52	8.97	69.61	8.98	82
XXVII	(CH)	99–100/1	1.4785	–	–	–	69.05	7.72	69.25	7.70	84
XXVIII	(CH)	90–91/1	1.4782	–	–	–	68.12	7.52	68.00	7.22	92

Acetoacetates of vinylcarbinols of the general formula

$$\begin{array}{c} \mathrm{OCOCH_2COCH_3} \\ | \\ \mathrm{R\backslash C - CH{=}CH_2} \\ \mathrm{R'/} \end{array}$$

Acetoacetates of ethynylcarbinols of the general formula

$$\begin{array}{c} \mathrm{OCOCH_2COCH_3} \\ | \\ \mathrm{R\backslash C - C{\equiv}CH} \\ \mathrm{R'/} \end{array}$$

* MR is in all cases calculated for the ketone form.
** Duplicate analyses are omitted throughout.

After distillation of the residue in vacuo, 11.5 g (69%) of tert-butylheptadienone (XIII) was obtained, b.p. 77–80°/1 mm; n_D^{20} 1.5160.

Method C. 9.6 g of the acetoacetate of methyl-tert-butylethynylcarbinol (b.p. 90–94°/4 mm) was heated for 1.5 h at 200–220°. 1020 ml of carbon dioxide was evolved. After distillation of the residue in vacuo, 4.5 g (60%) of tert-butylheptadienone (XIII) was obtained, b.p. 83–85°/4 mm; n_D^{20} 1.5160.

In an analogous manner, the other compounds listed in Tables 1 and 2 were obtained.

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Note: Figure translations are in progress. See original paper for figures.