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Reactions of 2,4,5-Trimethyl-4-hexen-3-one and 2,4,5-Trimethyl-5-hexen-3-one with Base in the Presence of Molecular Oxygen

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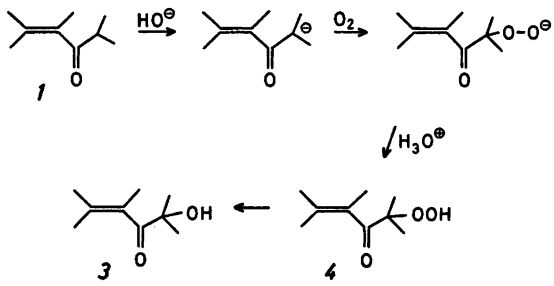
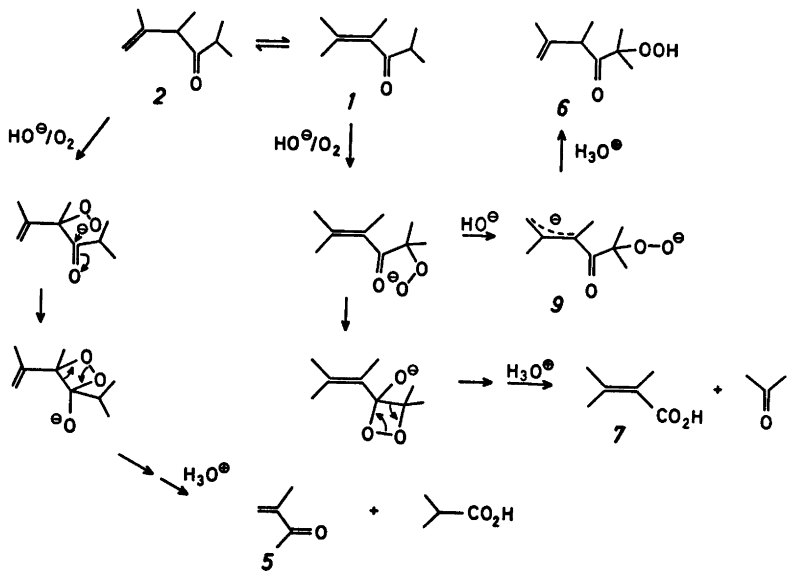
When the title compounds reacted with base under phase transfer conditions with access to air 2,4,5-trimethyl-2-hydroperoxy-4-hexen-3-one (*4*) was formed in 15 – 20 % yield. A complex reaction mixture was obtained when a similar reaction was carried out under pure oxygen, the main products being *4*, 2,4,5-trimethyl-2-hydroperoxy-5-hexen-3-one (*6*), and 2,3-dimethyl-2-butenoic acid (*7*).

When a mixture of 2,4,5-trimethyl-4-hexen-3-one (*1*) and bromoform was treated with 50 % aqueous sodium hydroxide in the presence of triethylbenzylammonium chloride (TEBA) small amounts of 2,4,5-trimethyl-5-hexen-3-one (*2*) and traces of a hydroxy enone (*3*) were isolated in addition to unreacted starting material and 1,1-dibromo-2-isobutyryl-2,3,3-trimethylcyclopropane.[1] Based on limited spectroscopic data it was assumed that the hydroxy enone was 2-hydroxy-2,4,5-trimethyl-4-hexen-3-one which under basic conditions can be formed from *1* as outlined in Scheme 1. To test this hypothesis a study of the reactions of *1* and *2* with base under phase transfer conditions was carried out.

The ketone *1* dissolved in benzene was stirred with a three-fold excess of 50 % aqueous sodium hydroxide in the presence of TEBA and under an atmosphere of air. According to GC analyses the resulting reaction mixture consisted of three products in a ratio of 8:72:20. These were separated by preparative GC and analyzed by IR and NMR spectroscopy. The main product was unreacted ketone whereas the smallest amount present turned out to be enone *2* which is formed from *1* by base-catalyzed isomerization. The IR spectrum of the third compound shows two symmetrical bands at 1365 and 1385 cm^{-1} characteristic of geminal methyl groups, a strong absorption at 1680 cm^{-1} characteristic of an α,β-unsaturated ketone, and a broad band in the 3300 – 3600 cm^{-1} region due to a hydroxyl group. Its NMR spectrum shows a singlet at δ 1.30, three partly overlapping broad singlets at 1.62, 1.73 and 1.80, and a broad singlet at 3.18 with a peak area ratio of 6:3:3:3:1, respectively. Finally, iodine was formed immediately when the compound was treated with an aqueous solution of potas-



Scheme 1.



Scheme 2.

sium iodide. These results are all in accord with the structure 2,4,5-trimethyl-2-hydroperoxy-4-hexen-3-one (*4*) which is confirmed by the ^{13}C NMR spectrum. As expected *4* was not formed when the reaction was carried out under pure nitrogen.

On storage the hydroperoxy ketone *4* decomposed to the corresponding hydroxy compound 2-hydroxy-2,4,5-trimethyl-4-hexen-3-one whose spectroscopic properties were practically identical to those of by-product *3*, facts supporting the rationale sketched in Scheme 1.

Reaction of 2,4,5-trimethyl-5-hexen-3-one (*2*) with base under identical conditions in the presence of air afforded a mixture of compounds *1*, *2*, and *4* in a ratio of 78:7:15, respectively. In the absence of TEBA, however, neither of the products *1* and *4* were formed. TEBA therefore catalyzes the generation of the intermediate anion and thus the formation of ketone *1* and hydroperoxy ketone *4*.

In order to improve the yield of *4* a mixture of ketones *1* and *2* was treated with aqueous sodium hydroxide under an atmosphere of oxygen. As expected the hydroperoxy ketone was formed in higher yield but in addition the number of products increased from three to at least twelve. Ten of these were isolated by preparative GC and on the bases of spectroscopic and chemical evidence and comparison with authentic samples their structures were established. In addition to small amounts of acetone and 3-methyl-3-buten-2-one (*5*) the following products were formed (relative yield of the higher-boiling products): 2,4,5-trimethyl-5-hexen-3-one (*2*) (1 %), 2,4,5-trimethyl-4-hexen-3-one (*1*) (6 %), acetic acid (10 %), 2,4,5-trimethyl-2-hydroperoxy-5-hexen-3-one (*6*) (13 %), isobutyric acid (7 %), 2,4,5-trimethyl-2-hydroperoxy-4-hexen-3-one (*4*) (44 %), 2,3-dimethyl-2-butenoic acid (*7*) (16 %), and 2,4-dihydroxy-2,4,5-trimethyl-5-hexen-3-one (*8*) (3 %). In accordance with an accepted mechanism for the reaction of an enolate anion with molecular oxygen [2-4] the hydroperoxy ketones and most of the cleavage products can be rationalized as outlined in Schemes 1 and 2. However, an alternative pathway of fragmentation involving nucleophilic addition of hydroxide anions to the carbonyl groups of *4* and *6* followed by intramolecular rearrangements [5] also accomodates the results. Acetic acid probably originates from acetone which forms some of this acid when exposed to the same reaction conditions in a separate experiment. The cleavage of acetone probably takes place by

a reaction similar to those outlined in Scheme 2; however, no formaldehyde or formic acid was detected.

The precursor of dihydroxy ketone *8*, however, is still uncertain. Analogous to the formation of *3* (Scheme 1) one may imagine *8* resulting from decomposition of the dihydroperoxy compound [6,7] formed by reaction of dianion *9* with molecular oxygen.

EXPERIMENTAL

General. The apparatus employed have been described elsewhere.[8]

Starting materials. 2,4,5-Trimethyl-4-hexen-3-one (*1*) and 2,4,5-trimethyl-5-hexen-3-one (*2*) were prepared as described by Colonge and Mostafavi [9] and separated by distillation through an efficient spinning band column.

Reaction of ketones with base; general procedure. A mixture of 3 mmol of ketone, 0.2 g of triethylbenzylammonium chloride (TEBA), 9 mmol of 50 % aqueous sodium hydroxide, and 8 ml of benzene was stirred vigorously at room temperature for 16 h. Hydrochloric acid (10 mmol) was added and the products were extracted with ether; the combined organic fractions were dried ($MgSO_4$). Evaporation of the solvent left a pale yellow residue which was analyzed by GC prior to distillation.

The following reactions were carried out according to this procedure.

Reaction of 2,4,5-trimethyl-4-hexen-3-one (1) with base under an atmosphere of air. GC analyses (20 % SE 30, 100 – 120 °C) revealed three compounds in a ratio of 8:72:20 and these were separated by preparative GC (same conditions). The product formed in lowest yield had physical properties identical with those of 2,4,5-trimethyl-5-hexen-3-one (*2*) whereas the predominant compound was unreacted *1*.

The third product, b.p. 93 °C/9 mmHg, was assigned the structure 2,4,5-trimethyl-2-hydroperoxy-4-hexen-3-one (*4*). ^{13}C NMR [15.0 MHz, CCl_4]: δ 16.1 (CH_3), 19.6 (CH_3), 22.6 (CH_3), 27.4 (2 CH_3), 76.5 (1 C, tertiary), 129.2 (1 C, olefinic), 131.8 (1 C, olefinic), 212.6 (C=O).

Storage of *4* gave 2-hydroxy-2,4,5-trimethyl-4-hexen-3-one (*3*). The latter compound gave no iodine when shaken with an aqueous solution of potassium iodide. Its IR and NMR spectra were almost identical to those of *4*. MS [IP 70 eV; *m/e* (% rel. int.)]: 141 (1, [M – CH_3]), 138 (3, [M – H_2O]), 98 (49, [M – acetone]), 97 (85, [M – C_3H_7O]), 83 (7, [98 – CH_3]), 69 (73, [97 – CO]), 59 (100, [$(CH_3)_2C=OH^+$]), 41 (72, [69 – ethylene]), 39 (17, [41 – H_2]). Found: C 68.74; H 10.07. Calc. for $C_9H_{16}O_2$: C 69.19; H 10.32.

Reaction of 1 with base under pure nitrogen. When the reaction was carried out under an atmosphere of nitrogen *1* was transformed to a mixture of *1* and *2* in a ratio of 90:10, respectively, according to GC analyses (20 % SE 30, 115 °C).

Reaction of 2,4,5-trimethyl-5-hexen-3-one (2) with base under an atmosphere of air gave a reaction mixture consisting of *1*, *2* and *4* in a ratio of 78:7:15, respectively, according to GC analyses (conditions as above).

Reaction of a mixture of 1 and 2 with base under pure oxygen. When 4.2 g of a 1:1 mixture of ketones *1* and *2* reacted with base under an atmosphere of oxygen, distillation afforded, besides 0.2 g of a lower-boiling fraction, 3.85 g of a complex mixture of products, b.p. 68 – 93 °C/9 mmHg. The lower-boiling fraction contained small amounts of acetone and 3-methyl-3-buten-2-one (*5*) according to spectroscopic examinations. GC analyses (10 % PEG 4000, 140 – 150 °C) revealed that the higher-boiling fraction consisted of eight products and these were separated by preparative GC (same conditions). Their structures were assigned as listed below in order of increasing retention time (relative yield in parenthesis).

2 (1 %). *1* (6 %). Acetic acid (10 %).

2,4,5-Trimethyl-2-hydroperoxy-5-hexen-3-one (*6*) (13 %) which immediately oxidized iodide to iodine. IR (CCl_4): 3510 (w), 3080 (w), 1710 (s), 1645 (m), 1388 (s), 1368 (s), 1165 (s), 908 (s) cm^{-1}. ^1H NMR (60 MHz, CCl_4): δ 1.25 (3 H, d, *J* 7 Hz), 1.38 (3 H, s), 1.41 (3 H, s), 1.80 (3 H, m), 3.78 (1 H, q, *J* 7 Hz), 4.66 (1 H, broad s), 4.87 (2 H, m). ^{13}C NMR [15.0 MHz, CCl_4]: δ 16.8 (CH_3), 20.0 (CH_3), 26.2 (CH_3), 26.9 (CH_3), 46.8 (1 C, tertiary), 76.7 (1 C, tertiary), 113.1 (1 C, olefinic), 144.0 (1 C, olefinic), 213.0 (C=O).

Isobutyric acid (7 %). *4* (44 %).

2,3-Dimethyl-2-butenoic acid (*7*) (16 %), m.p. 68 – 69 °C from CCl_4 (lit.[10] m.p. 70 – 71 °C).

2,4-Dihydroxy-2,4,5-trimethyl-5-hexen-3-one (*8*) (3 %) which did not oxidize iodide. IR (CCl_4): 3590 (w), 3495 (m), 1722 (s), 1642 (m), 1385 (s); 1370 (s), 1195 (s), 1145 (s), 1120 (s), 1030 (m), 960 (w), 910 (m) cm^{-1}. ^1H NMR (60 MHz, CCl_4): δ 1.37 (3 H, s), 1.40 (6 H, s), 1.75 (3 H, m), 4.35 (2 H, broad s), 4.95 (2 H, m). ^{13}C NMR [15.0 MHz, CCl_4]: δ 18.4 (CH_3), 24.4 (CH_3), 28.2 (2 CH_3), 79.6 (1 C, tertiary), 82.7 (1 C, tertiary), 110.8 (1 C, olefinic), 148.1 (1 C, olefinic); the carbonyl carbon was not detected due to noise. MS [IP 70 eV; *m/e* (% rel. int.)]: 157 (1, [M – CH_3]), 114 (13, [M – acetone]), 113 (4, [M – C_3H_7O]), 86 (47), 85 (39), 59 (100, [$(CH_3)_2C=OH^+$]), 43 (91).

Reaction of acetone with base under pure oxygen. A reaction carried out with acetone according to the general procedure gave an 8 % yield of acetic acid.

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