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Synthesis of 2-Hydroxy-3-alkyl-2-cyclohexen-1-ones

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A flavoring material in roasted coffee, 2-hydroxy-3-methyl-2-cyclohexen-1-one (**1a**) and its homologs (**1b**, **1c**, and **1d**) were synthesized through the acyloin condensation for corresponding diethyl 2-alkyladipates. The flavor property of the 3-methyl diketone (**1a**) was burnt sugar-like, while that of the ethyl homolog (**1b**) was strong burnt sugar-like with sweet overtones. The isopropyl derivative (**1c**) possessed a fresh grass odor and the benzyl derivative (**1d**) a wood-like odor with phenolic overtones.

Five enolizable cyclic 1,2-diketones including 2-hydroxy-3-methyl-2-cyclopentenone (cyclopentenone) and 2-hydroxy-3-methyl-2-cyclohexenone (**1a**) had been isolated as important principles in the aroma complex of roasted coffee.¹⁾ Many reports concentrated on the synthesis of cyclopentenone and its analogs,^{2), 3)} while there was little attention for the synthesis of (**1a**) and its analogs.³⁾ In the present work, six-membered ring 1,2-diketone (**1a**) and its homologs (**1b**, **1c**, and **1d**) were synthesized in two steps with relatively good yields starting from easily obtainable diethyl 2-alkyladipates through the acyloin condensation in the presence of chlorotrimethylsilane. This would be a more direct and convenient approach to such six-membered ring 1,2-diketones in comparison with other methods, which were somewhat complicated and suffered from the inaccessibility of starting materials.³⁾

For the synthesis of (**1a**), diethyl 2-methyladipate (**2a**) which was derived from diethyl methylmalonate through reaction with ethyl 4-iodobutylate, was treated with sodium in the presence of chlorotrimethylsilane, and the bis(trimethylsilyl) ether (**3a**) was obtained as a colorless liquid. The acid-catalyzed hydrolysis of (**3a**) was followed by the oxidation with copper (II) acetate giving the desired diketone (**1a**) as a white needle.

Scheme-1

Similarly, three different 2-alkyladipates (**2b**, **2c**, and **2d**) prepared from the corresponding alkylmalonates underwent an acyloin condensation to give the bis(trimethylsilyl) ethers (**3b**, **3c**, and **3d**) as a colorless or pale yellow liquid, respectively. The same treatment of the ethers as described above gave the diketones (**1b**, **1c**, and **1d**) as a white needle or a pale yellow liquid.

The 3-methylcyclohexanedione (**1a**) had a burnt sugar-like odor, while the odor of its ethyl homolog (**1b**) was strong burnt sugar-like with sweet overtones. The isopropyl diketone (**1c**) showed a fresh grass odor and the benzyl diketone (**1d**) a wood-like odor with phenolic overtones.

Experimental

Column chromatographies were carried out with 70~230 mesh silica gel (Merck Kieselgel 60 Art 7734). All boiling points and melting

* Studies on Cyclopentenone and Its Related Compounds. Part VIII. For Part VII, Y. Naoshima, T. Nakayama, H. Kondo, S. Hayashi, and H. Ueda, *Agric. Biol. Chem.*, **48**, 1123 (1984), "Synthesis of ω -Chain-modified Analogs of 7-Oxaprostaglandins".

points were uncorrected. IR spectra were recorded on a Hitachi 260-10 spectrometer, and ^1H NMR spectra were measured on a Hitachi R-24 B spectrometer in CDCl_3 solutions by using Me_4Si as an internal standard. Mass spectroscopy was performed on a JEOL JMS-D 300 double focusing instrument operating at a 70 eV ionization potential.

General reaction procedures for the synthesis of (1a)~(1d). All of the acyloin condensation, acid-catalyzed hydrolysis, and oxidation were carried out according to the method described previously.^{2a)}

1, 2-Bis(trimethylsiloxy)-3-methylcyclohexene (3a) was isolated in 68% yield by distillation: bp $74\sim 76^\circ\text{C}/1.4\text{ mmHg}$; IR $\nu_{\text{max}}^{\text{neat}}$: 1680 cm^{-1} ; ^1H NMR δ : 0.15 (18 H, s), 1.00 (3 H, d, $J=7.0\text{ Hz}$).

1, 2-Bis(trimethylsiloxy)-3-ethylcyclohexene (3b) was isolated in 65% yield by distillation: bp $52\sim 53^\circ\text{C}/0.17\text{ mmHg}$; IR $\nu_{\text{max}}^{\text{neat}}$: 1680 cm^{-1} ; ^1H NMR δ : 0.15 (18 H, s), 0.75~0.95 (3 H, m).

1, 2-Bis(trimethylsiloxy)-3-isopropylcyclohexene (3c) was isolated in 56% yield by distillation: bp $61\sim 62^\circ\text{C}/0.23\text{ mmHg}$; IR $\nu_{\text{max}}^{\text{neat}}$: 1680 cm^{-1} ; ^1H NMR δ : 0.15 (18 H, s), 0.75 (3 H, d, $J=7.0\text{ Hz}$), 0.85 (3 H, d, $J=7.0\text{ Hz}$).

1, 2-Bis(trimethylsiloxy)-3-benzylcyclohexene (3d) was used in the next step without further purification, since it tended to decompose during distillation: IR $\nu_{\text{max}}^{\text{neat}}$: $1680, 1600\text{ cm}^{-1}$.

2-Hydroxy-3-methyl-2-cyclohexen-1-one (1a) was isolated by both column chromatography with n -hexane-ether (10 : 1) and recrystallization from n -hexane in 57% yield: mp $59\sim 60^\circ\text{C}$ (lit.^{1b)} $60\sim 62^\circ\text{C}$).

2-Hydroxy-3-ethyl-2-cyclohexen-1-one (1b) was isolated by both column chromatography and recrystallization in 52% yield: mp $24\sim 26^\circ\text{C}$ (lit.^{3b)} $22\sim 23^\circ\text{C}$).

2-Hydroxy-3-isopropyl-2-cyclohexen-1-one

(1c) was isolated by column chromatography in 55% yield. The product solidified during storage in refrigerator^{3b)}.

2-Hydroxy-3-benzyl-2-cyclohexen-1-one (1d) was isolated from (2d) in a 24% yield by column chromatography.

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2-ヒドロキシ-3-アルキル-2-シクロ

ヘキセン-1-オン類の合成

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コーヒー豆のほう(焙)焼性香気成分である 2-ヒドロキシ-3-メチル-2-シクロヘキセン-1-オンとそのエチル、イソプロピル及びベンジル同族体を、相当する 2-アルキルアジピン酸ジエチルのアシロイン縮合を通じて合成した。3-メチル体は焦げた砂糖様の香りを有し、エチル同族体はさらに強い香気と共に甘さが感じられた。イソプロピル体は若草様の香りを持ち、ベンジル体はフェノール臭を含む木様香気を示した。