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The Allylic Rearrangement. IV.[1] New Synthesis of 4-Hexenoic Acid

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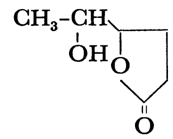
Synopsis. *trans*-4-Hexenoic acid, a useful starting material for the synthesis of racemic 4*R* : 5*S* and 4*S* : 5*R* 4,5-dihydroxyhexanoic acid γ-lactone, one component of the aroma extracts from one Californian and two Spanish flor sherries, has been conveniently prepared by the Favorskii-type rearrangement of 5-chloro-3-hexen-2-one.

The investigation of two samples of Spanish fino sherry and one sample of a California palomino flor sherry has been reported by Webb *et al.*[2] They were unable to identify two of the major high boiling components completely. Muller *et al.*[3] have isolated these components from the aroma extracts of the California palomino flor sherry, using the techniques described by Webb *et al.* and identified as (−) 4*R* : 5*R* or 4*S* : 5*S* 4,5-dihydroxyhexanoic acid γ-lactone and (+) 4*R* : 5*S* or 4*S* : 5*R* 4,5-dihydroxyhexanoic acid γ-lactone, which are diastereomeric forms of 5-(1′-hydroxyethyl)dihydro-2(3*H*)-furanone (**1**).



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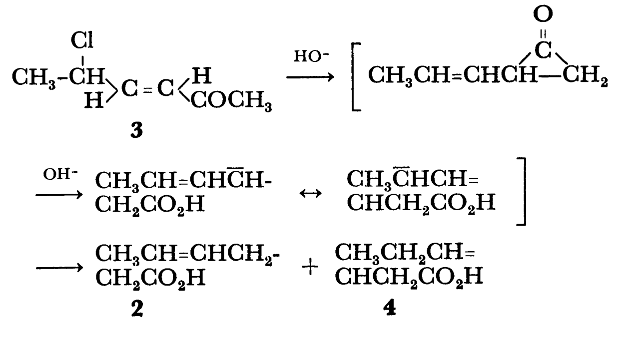
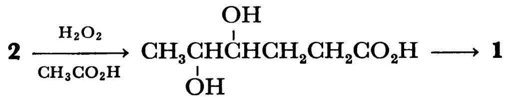
They have synthesized lactone **1** by the hydroxylation of *trans*-4-hexenoic acid (**2**), which was obtained from cyclopropyl methyl ketone *via* four steps by adaptation of the procedure reported by Julia *et al.*[4] This synthetic method of **2** seems to us less profitable for the purpose of a large scale preparation because only a mixture (approximately 1 : 1) of *trans* and *cis* isomers was obtained and gas-chromatographical fractionation was needed to isolate *trans*-**2**. We wish to report here a simple and more convenient synthesis of acid **2**, by means of the vinylogous Favorskii rearrangement[1] previously reported by us. The starting material, 5-chloro-3-hexen-2-one (**3**) was prepared by the Wittig-type reaction of 2-chloropropanal and diethylphosphonoacetone. Ketone **3** is thought to be of *trans* configuration because a large coupling constant (J=15.8 Hz) has been observed in its NMR spectrum. The treatment of ketone **3** with 15% aqueous NaOH afforded 4-hexenoic acid (**2**) in a 47% yield, with a small amount of 3-hexenoic acid (**4**). The formation of **2** can be well explained by the following mechanism involving a Favorskii-type rearrangement[1] of ketone **3**, the vinylogue of methyl α-chloroethyl ketone.



The NMR spectrum of the product **2** exhibited a complicated pattern due to the existence of acid **4**, but its IR spectrum was identical with that of *trans*-acid **2** reported by Muller *et al.* Therefore, it is suspected that the *trans*-acid **2** obtained by Muller *at al.* also may be a mixture of the acid **2** and **4**.

trans Hydroxylation of the acid **2** with peracetic acid was done according to the Muller's procedure to give a racemic mixture of 4*R* : 5*S* and 4*S* : 5*R* 4,5-dihydroxyhexanoic acid γ-lactone (**1**) in a total yield of 29%.



$$\mathbf{2} \xrightarrow[\mathrm{CH_3CO_2H}]{\mathrm{H_2O_2}} \mathrm{CH_3\overset{OH}{C}H\underset{OH}{C}HCH_2CH_2CO_2H} \longrightarrow \mathbf{1}$$

Experimental

Materials. 2-Chloropropanal was prepared by the method described by us previously.[5] Diethyl phosphonoacetone was obtained by the procedure described in the literature,[6] yield 68%: bp 101—106 °C/4 mmHg (lit.[6] bp 126 °C/9 mmHg).

trans-*5-Chloro-3-hexen-2-one (**3**).* To a stirred solution of 0.96 g (0.04 mol) of sodium hydride in 60 ml of dry ether was added 7.7 g (0.04 mol) of diethyl phosphonoacetone at 0 °C. After evolution of hydrogen gas ceased, 3.7 g (0.04 mol) of freshly distilled 2-chloropropanal was added dropwise. The mixture was stirred for 30 min and then poured into a large amount of water. The ethereal extract of the organic layer was washed with water and dried over $MgSO_4$. After removal of the solvent, the residue was distilled to give 1.7 g (32%) of **3**: bp 65—70 °C/5 mmHg; IR (neat) 1695 (cisoid C=O), 1670 (transoid C=O), 1625 (C=C), 980 cm^{-1} $\left({}^{\mathrm{H}}\!\!>\!\mathrm{C{=}C}\!<_{\mathrm{H}}\right)$; NMR ($CCl_4$) δ 1.65 (d, 3H, J=7 Hz, $\mathrm{C\underline{H}_3CHCl}$–), 2.20 (s, 3H, CH_3CO), 4.60 (doublet of quartet, 1H, J=7 Hz, $\mathrm{CH_3C\underline{H}Cl}$–), 6.08 (d, 1H, J=15.8 Hz, –CH=C$\underline{\mathrm{H}}$CO–), 6.68 ppm (double d, 1H, J=7 and 15.8 Hz, –C$\underline{\mathrm{H}}$=CHCO–); MS (70 eV) *m/e* (rel. intensity) 132 (40, M^+, 1Cl), 117 (100, M^+-CH_3), 97 (84, M^+-Cl), 89 (75, M^+-COCH_3), 53 (75), 43 (84, $COCH_3$).

Found: C, 54.05; H, 6.81%. Calcd for C_6H_9ClO: C, 54.36; H, 6.84%.

trans-*4-Hexenoic Acid (**2**).* Ketone **3** (1.5 g, 0.011 mol) was added slowly to 15 ml of 15% aqueous NaOH with stirring at 50—55 °C. The mixture was stirred for 15 min, and washed with ether to remove neutral materials. The aqueous layer was treated with active charcoal, and then acidified with dilute hydrochloric acid. After the organic layer was extracted several times with ether, the combined etheral extract was dried over $MgSO_4$. Removal of the solvent left 0.59 g (crude yield 47%) of crude **2**. Tlc analysis[7] showed one clean spot at R_f value of 0.58: IR (neat)[8]

3500—2500 (COOH), 1710 ($C=O$), 1411, 1210, 1172, 968 cm^{-1} $\left({}^{H}\!\!>C=C<_{H}\right)$; NMR ($CDCl_3$)[9] δ 1.00 (t, 0.6H, $C\underline{H}_3CH_2-$ of **4**), 1.63 (broad d, 3H, $C\underline{H}_3CH=$), 2.09 (m, 0.4H, $CH_3C\underline{H}_2-$ of **4**), 2.37 (m, 4H, $-CH_2CH_2-$), 3.10 (m, 0.4H, $-C\underline{H}_2CO_2H$ of **4**), 5.50 (m, 2H, $-CH=CH-$), 9.57 ppm (broad s, 1.2H, CO_2H of **2** and **4**); MS (70 eV) *m/e* (rel. intensity) 114 (68, M^+), 99 (13, $M^+—CH_3$), 96 (13, $M^+—H_2O$), 68 (71), 55 (100).

Racemic Mixture of 4R : 5S and 4S : 5R *4,5-Dihydroxyhexanoic Acid γ-Lactone (**1**).* Trans hydroxylation of **2** was carried out by the modification of the procedure of Muller *et al.*[3] A solution of 0.28 g of 30% H_2O_2 in 0.50 g of glacial acetic acid was heated for 30 min at 75 °C, and then cooled. The peracid solution was added dropwise to 0.21 g (0.0018 mol) of **2** with stirring. The solution was then heated at 40 °C for 30 min, cooled, and extracted with ether. The etheral solution was dried over $MgSO_4$, and then the solvent was removed. The residue (clean oil, 0.18 g) was analyzed by glpc.[10] The peaks, retention times (min), and integrated percentages are as follows: 1, 1.3, 11%; 2, 3.7, 37%; 3, 4.8, 12%; 4, 9.7, 40%. Component 2 was identified as the starting material **2** by comparison of the retention time. Component 4 was collected by preparative glpc and identified as **1** (yield 29%): IR (neat) 3440 (OH), 1760 (lactone $C=O$), 1415, 1190 cm^{-1}; NMR ($CDCl_3$) δ 1.20 (d, 3H, $J=7$ Hz, $-CH_3$), 2.0—3.0 (m, 4H, α- and β-H), 3.42 (s, 1H, OH), 4.10 (m, 1H, $CH_3C\underline{H}(OH)-$), 4.42 ppm (m, 1H, γ-H). Its IR and NMR spectra were identical with those of the lactone **1** reported by Muller[3]: IR (neat) 3436, 1762, 1415, 1192 cm^{-1}; NMR ($CDCl_3$) δ 1.20 (m, 3H), 2.0—3.0 (m, 4H), 3.00 (s, 1H), 4.10 (m, 1H), 4.42 ppm (m, 1H). Components 1 and 3 were not further investigated.

References

1) Preceding paper: A. Takeda and S. Tsuboi, *J. Org. Chem.*, **38**, 1709 (1973).

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4) M. Julia, S. Julia, and S. Y. Tchen, *Bull. Soc. Chim. France*, **1961**, 1849.

5) A. Takeda, S. Tsuboi, S. Wada, and H. Kato, This Bulletin, **45**, 1217 (1972).

6) A. N. Pudovik, *Zhur. Obschei. Khim.*, **25**, 2173 (1955).

7) Condition of tlc: support, silica gel GF_{254}, 0.1 mm thickness; developer, benzene-methanol-acetic acid (10 : 1 : 1, v/v).

8) IR spectrum was identical with that of an authentic sample.[2]

9) Spectral intensity shows the existence of **2** and **4** in a ratio of 5 : 1.

10) Condition of glpc: column, 10% polyneopentyl glycol succinate on Chromosorb W, 190 °C; carrier gas, He, 20 ml/min; detector, TCD.