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A FACILE SYNTHESIS OF OPTICALLY PURE VALEROLACTONE AND β-HYDROXY VALEROLACTONE FROM A COMMON SUGAR-DERIVED PRECURSOR

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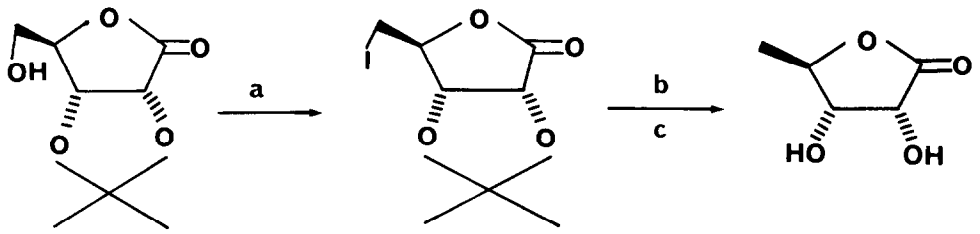
Summary. Both title compounds were obtained in four steps from 2R, 3R-dihydroxy-4R-valerolactone 5 readily available from D-ribonolactone.

Chiral γ-lactones are a common feature of many natural products. Among them, valerolactones 1 are the privileged target of a number of chiral syntheses[1]. The synthesis of optically active β-hydroxy-valerolactone 2 either from D-ribonolactone[2] or racemic 3-hydroxy-4-pentenoic acid via quinine resolution[3] have also been described recently.

We report here a new synthesis of valerolactone and β-hydroxyvalerolactone from a common sugar-derived precursor 5 in four steps with good overall yields.

The synthesis of 5 is outlined in scheme I.



3 4 5

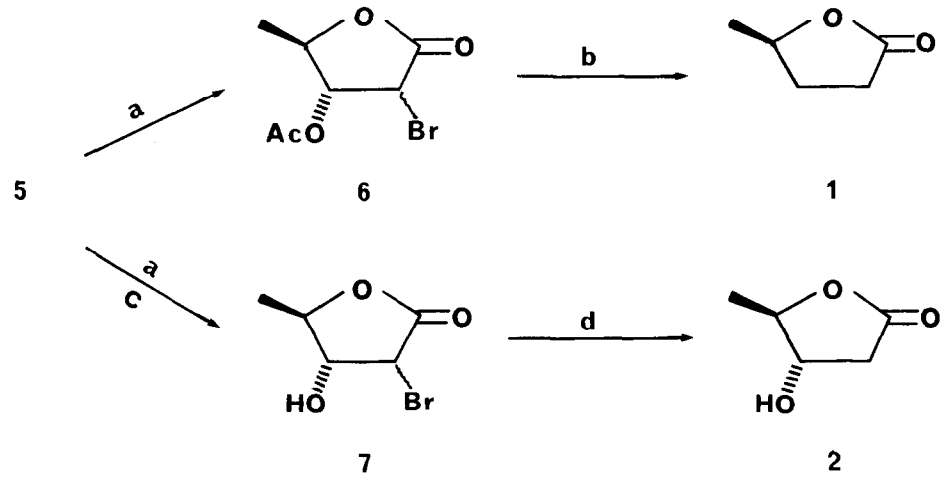
SCHEME I

a) I_2, PPh_3, imidazole ; b) Bu_3SnH, AIBN, Δ ; c) CF_3CO_2H-H_2O (9:1)

The starting material, 2,3-O-isopropylidene-D-ribonolactone 3 which is readily available from commercial D-ribonolactone[4], is converted by the method of Garegg and Samuelsson[5] into the deoxyiodo derivative 4 which is immediately treated with tri-n-butyltin hydride and left overnight. Cleavage of the isopropylidene protecting group gives the diol 5[6] in a 71 % overall yield from 3.

Compound 1 is obtained by treatment of 5 with a solution of hydrogen bromide in acetic acid[7] followed by catalytic hydrogenation of bromoacetate 6 in the presence of triethylamine[8]. (Scheme II) Loss of both β-acetoxy and α-bromo substituents can be explained by successive (or simultaneous) hydrogenolysis, known for β-acetoxy and for α-bromo groups[9,10] Two moles of hydrogen are consumed in the process.

Reaction of 5 in the hydrogen bromide-acetic acid solution for 4h at room temperature followed by deacetylation with methanol gives the bromoalcohol 7 in 70 % yield. Debromination of the latter with tri-n-butyltin hydride leads to compound 2.[11] The overall yield from the starting lactone 3 is 46 %.[12]



SCHEME II

a) HBr-AcOH ; b) Pd(C), H_2, Et_3N ; c) MeOH ; d) Bu_3SnH, AIBN, Δ

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6) Synthesis of 5-deoxy-D-ribonolactone 5.
To a dry toluene solution (50 mL) of 4.6g (15 mmol) of 4 under argon, were added 20mg AIBN and 4.9g (16.5 mmol) tri-n-butyltin hydride. The resulting mixture was heated at 100°C overnight and the toluene evaporated. The crude was cooled to 0°C and treated for 1h with a 9:1 solution of CF_3CO_2H-H_2O (20mL). Removal of the solvents under vacuum followed by addition of 30mL ether gave a yellowish precipitate which was filtered and washed with ether (2X10mL) to ensure complete removal of tri-n-butyltin iodide. Yield : 2.0g (quantitative).
$[\alpha]_D$ = +17.0 (c 1.0 MeOH) ; m.p. 127° ; IR 3390, 1798 cm^{-1}
^{1}H-NMR (D_2O) 1.30 (3H, d, $J_{5,4}$ = 6.8) ; 4.22 (1H, d, $J_{2,3}$ = 5.0) ; 4.50-4.90 (2H, m)
Combustion analysis : Calc. for $C_5H_8O_4$ C 45.45 ; H 6.06 Found C 45.50 ; H 6.08

7) K. Bock, I. Lundt, C. Pedersen, Carbohydr. Res. 90, 17 (1981)

8) β-Acetoxy pentonolactones are easily deacetylated by Pd (C) hydrogenation. See also : K. Block, I. Lundt, C. Petersen, Acta Chim. Scand. B 35, 155 (1981)

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10) Selected physical data :

4 $[\alpha]_D$ = -31.8 (C 1.33 acetone) ; m.p. 92° ; IR 1793 cm^{-1}
^{1}H-NMR ($CDCL_3$) 1.40 (3H,s) ; 1.47 (3H,S) ; 3.41 and 3.46 (2H, AB part of an ABX, $J_{5,4}$ = 5.04 and $J_{5',4}$ = 3.50) ; 4.59-4.66 (2H,m) ; 4.99 (1H, d, $J_{2,3}$ = 6.07)

6 $[\alpha]_D$ = +23.3 (C 2.10 acetone) ; IR 1793, 1745 cm^{-1}
^{1}H-NMR ($CDCL_3$) 1.52 (3H,d, $J_{4,5}$ = 6.0) ; 2.09 (3H, s) ; 4.10 - 4.67 (3H,m)

7 $[\alpha]_D$ = +16.1 (C 1.80 acetone) ; m.p. 83° ; IR 3390, 1797 cm^{-1}

^{1}H-NMR ($CDCL_3$) 1.63 (3H,d, $J_{5,4}$ = 6.1) ; 3.50 (1H, broad s, D_2O exchangeable) ;

4.20 - 4.73 (3H,m)

11) Synthesis of hydroxy-valerolactone 2

A mixture of 2.0g (10.2 mmol) of compound 7,15mg AIBN and 6.0g (20.5 mmol) tri-n-butyltin hydride in 100mL dry toluene under argon were heated at 100°C overnight. The solvent was then removed under vacuum and 25mL water were added. The aqueous layer, containing all of compound 2, was continously extracted with ethyl acetate. Evaporation of the solvent followed by silica gel columm chromatography (eluent : ether) afforded 1.16g (10.0 mmol, 98%) pure 2.

12) Compounds 1 and 2 were identified by comparing their physical constants with reported data from the literature. (ref. 1a for 1 and 2b for 2)

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