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# CONVERSION OF 2,3-*O*-CYCLOHEXYLIDENE-(D)-RIBONOLACTONE INTO 2,3-*O*-CYCLOHEXYLIDENE-(L)-RIBONOLACTONE

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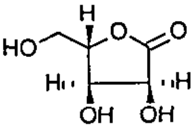
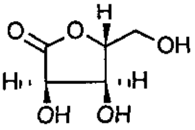
*Abstract*——A convenient method for the chirality inversion of 2,3-*O*-cyclohexylidene-D-ribonolactone to 2,3-*O*-cyclohexylidene-L-ribonolactone has been established.

D-Ribonolactone (D-**1**) is an inexpensive and commercially available abundant sugar. Because of its high functionality with contiguous chiral centers, it has been widely used as a versatile chiral building block for the construction of a variety of natural products.[1] However, its enantiomeric counterpart L-ribonolactone (L-**1**) is less available which prevents more extensive use of ribonolactone units as chiral building blocks. In this report we describe a convenient method for the conversion of 2,3-*O*-cyclohexylidene-D-ribonolactone (D-**2**) into its L-enantiomer (L-**2**) by formal inversion of total chirality.[2]

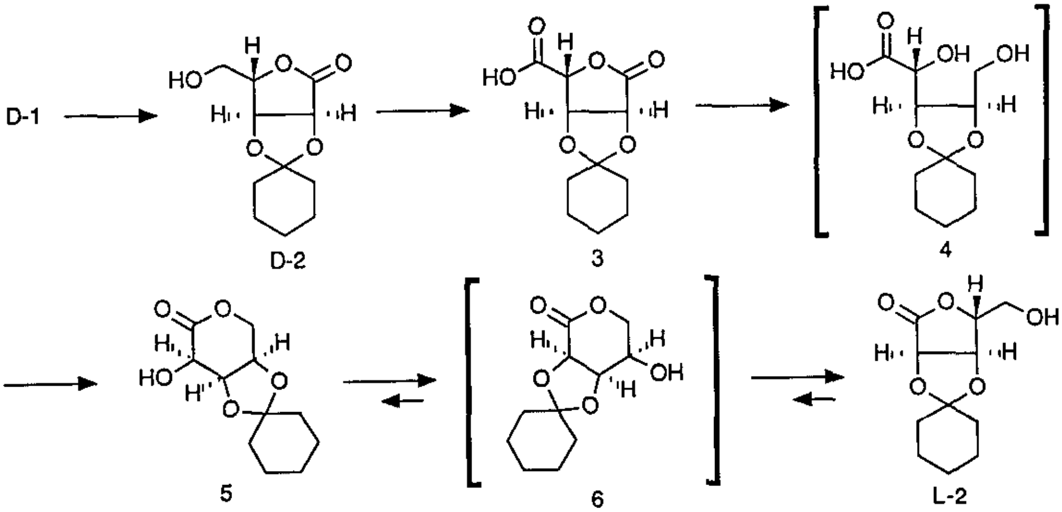


D-Ribonolactone (D-1)



L-Ribonolactone (L-1)

2,3-*O*-Cyclohexylidene-D-ribonolactone (D-**2**)[3] was oxidized with rutenium oxide[4] to give the carboxylic acid (**3**) which without purification was immediately reduced with sodium borohydride in aqueous 5% sodium hydrogen carbonate. The reaction mixture containing the reduction product (**4**) was made acidic and heated briefly at 50 °C to give the δ-lactone (**5**) in 45% overall yield from the starting γ-lactone (D-**2**) after purification by silica gel column chromatography. Although complete isomerization could not be realized, upon reflux in xylene in the presence of a catalytic amount of D-camphorsulfonic acid **5** furnished the desired 2,3-*O*-cyclohexylidene-L-ribonolactone (L-**2**) in 45% yield accompanied by the readily separable starting δ-lactone (**5**) in 40% yield which could be recycled.



## EXPERIMENTAL

Reactions were carried out under argon. Ir spectra were measured with a JASCO A-102 spectrophotometer. $^{1}$H-Nmr spectra were recorded on a JEOL-JNM 90A spectrometer. Mass spectra were measured with a JEOL-01SG-2 instrument. Optical rotations were measured with a JASCO-DIP-4 automatic polarimeter.

**Conversion of 2,3-*O*-Cyclohexylidene-D-ribonolactone (D-2) into 3,4-*O*-Cyclohexylidene-L-ribonic Acid δ-Lactone (5)** To a solution of 2,3-*O*-cyclohexylidene-D-ribonolactone (D-2) (6.2 g, 27.2 mmol) in a mixture of acetonitrile, carbon tetrachloride, and water (2:2:3, 105 ml) was added ruthenium trichloride trihydrate (213 mg, 0.82 mmol) and sodium periodate (14.5 g, 68.0 mmol) at 0 °C with stirring. After stirring at the same temperature for 1 h, the mixture was further stirred at room temperature for 4 h and treated with aqueous sodium hydrogen sulfite (5%, 100 ml). The organic layer was separated and extracted with aqueous sodium hydrogen carbonate (5%, 100 ml x 3). The aqueous extracts were combined with the aqueous layer of the reaction mixture and the mixture was washed with methylene chloride (50 ml). The aqueous layer was then made acidic by careful addition of hydrochloric acid (35%, 15 ml) and extracted with ethyl acetate (70 ml x 6). The combined organic layers were dried with magnesium sulfate and evaporated under reduced pressure to give the carboxylic acid (3) (5.27 g) which was directly used for the next reaction.

To a stirred solution of the above crude acid (2.23 g) in aqueous sodium hydrogen carbonate (5%, 25 ml) was added sodium borohydride (1.02 g, 27.5 mmol) portionwise at 0 °C and the mixture was stirred for 30 min at 0°C and for 2 h at room temperature. The mixture was then made acidic with hydrochloric acid (10%, 30 ml) and stirred for 4 h at 50 °C. After cooling, the mixture was filtered through celite and extracted with ethyl acetate (30 ml x 5). The combined extracts were dried with magnesium sulfate and evaporated under reduced pressure to give a crystalline solid (1.3 g) which was chromatographed on a silica gel column (30 g) using ethyl acetate-hexane (1:1 v/v) as eluent to give the δ-lactone (**5**) (952 mg, 45% overall from D-**2**): mp154~155 °C; $[\alpha]_D^{25}$ +133.33° (*c* 1.044, MeOH); ir (Nujol) 3200~3500, 1752 cm$^{-1}$; $^1$H-nmr ($CDCl_3$) 1.13~1.80 (10H, m), 3.18~3.40 (1H, m, exchangeable with $D_2O$), 4.06~4.48 (3H, m), 4.48~4.70 (1H, m), 4.81 (1H, dd, *J*=3.4, 7.8); ms (m/z) Calcd for $C_{11}H_{16}O_5$ 228.0997, Found 228.0995.

**2,3-*O*-Cyclohexylidene-L-ribonolactone (L-2)** A solution of the above δ-lactone (**5**) (200 mg, 0.88 mmol) in xylene (3 ml) containing D-camphorsulfonic acid (20 mg, 0.088 mmol) was refluxed for 13 h. After evaporation of the solvent, the residue was chromatographed on a silica gel column (10 g) using ethyl acetate-hexane (1:2 v/v) as eluent to give the L-ribonolactone (L-**2**) (90 mg, 45%; 75% based on consumed starting material);mp 129~131.5 °C [lit. for D-**2** 128~129 °C ,[3a] 128~130 °C[3b]], $[\alpha]_D^{26}$ +52.52° (*c* 0.990, MeOH) [lit. for D-**2** -54.6° (*c* 0.986, MeOH)[3a] ]; ir (Nujol) 3455, 1790 cm$^{-1}$; $^1$H-nmr ($CDCl_3$) 1.17~1.81 (10H, m), 2.18~2.80 (1H, m, exchangeable with $D_2O$), 3.79 (1H, dd, *J*=1.7, 12.2), 4.02 (1H, dd, *J*=2.2, 12.4), 4.65 (1H, t, *J*=2.2), 4.76 (1H, d, *J*=5.6), 4.85 (1H, d, *J*=5.6); ms (m/z) Calcd for $C_{11}H_{16}O_5$ 228.0997, Found 228.0990. Using ethyl acetate-hexane (2:1 v/v) as eluent, the starting δ-lactone (**5**) (80 mg, 40%) was recovered.

## REFERENCES AND NOTES

1. A pertinent review, see: K. L. Bhat, S. -Y. Chen, and M. M. Joullie, *Heterocycles*, 1985, **23**, 691.
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3. (a) D. Beer, R. Meuwly, and A. Vasella, *Helv. Chim. Acta*, 1982, **65**, 2570. (b) A. M. Sepulchre, A. Gateau, and S. D. Gero, *Carbohyd. Res.*, 1972, **24**, 311.
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