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(2S,3R)-1,2-EPOXY-3-BUTANOL. A USEFUL SYNTHON FOR THE PREPARATION OF CHIRAL 1,2-DIOLS.

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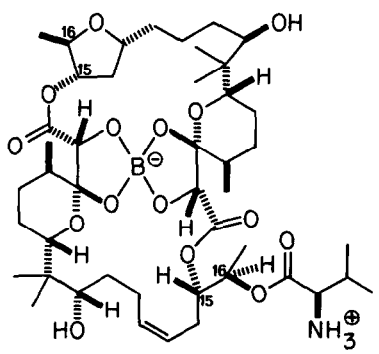
Summary: Enantioselective epoxidation of 3-butene-2-ol in the presence of D-(-)-tartrate gave (2S,3R)-1,2-epoxy-3-butanol, which was employed in chiral syntheses of 2,5-dideoxyribose and a segment of the ionophoric antibiotic boromycin.

The enantioselective epoxidation of racemic allylic alcohols mediated by optically active tartrate esters represents a powerful method for the synthesis of chiral, polyhydroxylic systems.[1] In connection with studies directed towards the total synthesis of boromycin (1),[2] we required a synthon incorporating the C(15,16) diol function of this antibiotic which possessed the natural (15S,16R) configuration. We describe herein the asymmetric synthesis of (2S,3R)-1,2-epoxy-3-butanol (3), an independent proof of its configuration, and its tranformation to 2,5-dideoxyribose and to a segment corresponding to C(11)-C(17) of 1.



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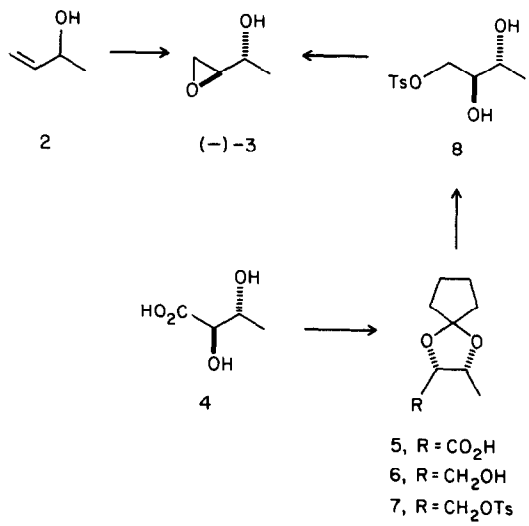
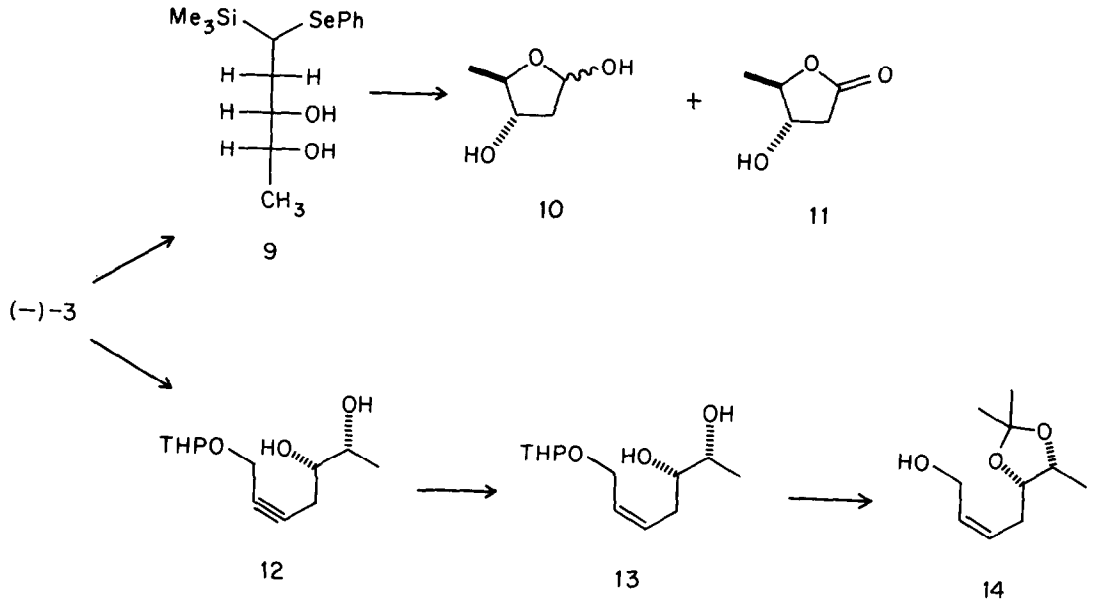
Epoxidation of 3-butene-2-ol (2) with t-butyl hydroperoxide and titanium tetraisopropoxide in the presence of D-(-)-diisopropyl tartrate, followed by distillation, afforded 3 [bp 50°C, 15 mm Hg; $[\alpha]_D^{22}$ - 16.3° (c 0.97, MeOH)] in 54% yield. Although precedence suggested that the 3R enantiomer of 2 should be the faster-reacting antipode,[1] yielding predominantly the erythro epoxide in which attack had occurred selectively from the si face,[3] an unambiguous proof of this stereochemistry was desired.



To this end, (±)-erythro-2,3-dihydroxybutyric acid (4), prepared by hydroxylation of trans-crotonic acid,[4] was resolved via its quinine salt.[5,6] Optical rotatory dispersion studies have established that (-)-4 possesses (2R,3R) absolute configuration.[7] Protection of (-)-4 as its ketal derivative 5 (91%) with cyclopentanone and a catalytic quantity of p-toluenesulfonic acid in benzene, followed by reduction with lithium aluminum hydride in THF gave the primary alcohol 6 in 87% yield. Conversion of this substance to its tosylate 7 (95%; mp 41-43°C) with p-toluenesulfonyl chloride in pyridine and removal of the cyclopentylidene residue with methanol and a catalytic quantity of p-toluenesulfonic acid gave the diol 8 (73%; mp 69-71°C). Treatment of 8 with sodium hydride in THF containing a trace of DMSO produced 3 [72%; $[\alpha]_D^{20}$ - 17.9° (c 1.16, MeOH)],[8] which was identical by both spectroscopic and gas chromatographic comparison with the material obtained from 2. From this result it was ascertained that asymmetric epoxidation of 2 had afforded a 91% enantiomeric excess of the (2S,3R) epoxy alcohol 3.

The utility of 3 as a precursor to chiral 1,2-diols was first examined in the context of a deoxypentose synthesis, where alkylation at the epoxide terminus with a formyl anion equivalent was required. The reaction of (-)-3 with

the anion of phenylselenomethyltrimethylsilane[9] (2 equiv LDA, THF, -78°C→25°C, 12h) gave 9 as a C(1) epimeric mixture in 80% yield. This mixture was subject-



ed to a Pummerer rearrangement with 30% H_2O_2 in THF-ether (4:6) to yield 2,5-dideoxyribofuranose (10, 40%),[10] accompanied by the deoxyribonolactone 11 [24%, $[\alpha]_D^{18}$ + 21.0° (c 0.67, $CHCl_3$)].

For construction of the erythro-dihydroxyheptenyl segment, corresponding to C(11)-C(17) of 1, alkylation of (-)-3 was effected with the anion of propargyl tetrahydropyranyl ether, prepared with n-butyllithium in THF, to furnish 12 in 90% yield. Semihydrogenation of the acetylenic linkage over 10% $Pd/BaSO_4$ in the presence of quinoline afforded a 98% yield of the cis olefin 13 as an epimeric mixture at the tetrahydropyran center. Treatment of 13 with methanol containing p-toluenesulfonic acid and then, following evaporation of the volatiles, with acetone-benzene (1:1), gave 14 [$[\alpha]_D^{20}$ - 22.5° (c 4.92, $CHCl_3$)] in 74% yield after chromatography.

This substance embodies the functionality and absolute configuration of an important structural component of 1 and provides a convenient starting point for elaborating the "southern" half of this macrodiolide.

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(6) (-)-Erythro-2,3-dihydroxybutyric acid showed $[\alpha]_D^{20}$ - 10.78° (c 1.17, H_2O) [lit[7] $[\alpha]_D^{20}$ - 9.50° (c 1.0, H_2O)].

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(8) ^1H NMR of 3: δ ($CDCl_3$) 3.96 (d of q, J=7,3 Hz, 1H), 3.00 (q, J=3 Hz, 1H), 2.78 (bd, J=3 Hz, 2H), 2.30 (bs, 1H, exchanged with D_2O), and 1.23 (d, J=7 Hz, 3H).

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