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# Chemoenzymatic preparation of enantiopure partial esters of conduritol E

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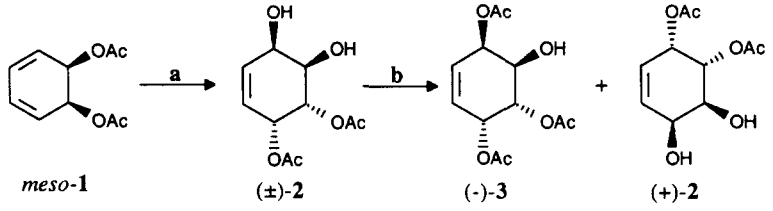
***Abstract:*** Two partial esters of conduritol E, namely (2*R*)-hydroxy-(1*R*,3*R*,4*R*)-triacetoxycyclohex-5-ene and (1*S*,2*S*)-dihydroxy-(3*S*,4*S*)-diacetoxycyclohex-5-ene, have been prepared in high chemical and optical yields from 'benzene *cis*-glycol' diacetate via $OsO_4$ catalysed dihydroxylation followed by enantioselective esterification of the resulting conduritol E diacetate in the presence of *Mucor miehei* lipase. © 1997 Elsevier Science Ltd

Enantiopure partially protected conduritols (1,2,3,4-tetrahydroxycyclohex-5-enes)[1] are potentially valuable as intermediates in the synthesis of bioactive compounds, as for instance cell mediators (inositols and aminoinositols)[2] or inhibitors of glycosidases (conduritol epoxides and aminoconduritols).[3]

As part of a work currently being carried out in our laboratory on cyclitols of biological interest,[4] we wish to report here the straightforward preparation, in high chemical and optical yields, of two previously unreported partial esters of conduritol E, namely (2*R*)-hydroxy-(1*R*,3*R*,4*R*)-triacetoxycyclohex-5-ene, (−)-**3** and (1*S*,2*S*)-dihydroxy-(3*S*,4*S*)-diacetoxycyclohex-5-ene, (+)-**2** (Scheme 1).




**Scheme 1**. **a**: NMMO/$OsO_4$ in $CH_2Cl_2$; **b**: lipase from *Mucor miehei*, vinyl acetate in *t*-BME.

Dihydroxylation of *cis*-1,2-diacetoxyclohexa-3,5-diene, *meso*-**1**, with $OsO_4$ in the presence of *N*-methylmorpholine-*N*-oxide (NMMO) occurred in a diastereoselective manner from the less-hindered face of the molecule to give quantitatively conduritol E diacetate (±)-**2**.[5] This was subjected to esterification in *t*-BME, using vinyl acetate as irreversible acylating agent in the presence of immobilised *Mucor miehei* lipase (Lipozyme IM). After 6 h conversion was ca. 48% and GC analysis of the reaction mixture showed the presence of unreacted ester (+)-**2** and a single product, (−)-**3**, which were separated by column chromatography.[6] The $^1H$ NMR spectrum of (−)-**3** contained three signals for acetyl groups and, *inter alia*, a dd signal for a hydroxymethine proton correlating with two protons both located on carbons bearing an acetoxy group, thus indicating the allylic nature of the newly-formed ester group. On the basis of this and the result of its chemical hydrolysis, which afforded (−)-conduritol E,[7] the acetylation product was assigned structure (2*R*)-hydroxy-(1*R*,3*R*,4*R*)-triacetoxycyclohex-5-ene. Chiral GC analysis of (+)-**2** and (−)-**3**, after conventional acetylation,

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indicated an ee 92% and >95% respectively. In a parallel experiment prolonged until 52% conversion the unchanged (+)-**2** was recovered enantiopure.

The chemoenzymatic procedure described here offers a practical access to two enantiopure partial acetates of conduritol E, whose use as building blocks in the synthesis of aminocyclitols with controlled stereochemistry is currently investigated in our laboratory. Obviously, these esters can also be hydrolysed to give each enantiomer of conduritol E with high enantiomeric excess.

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5. Preparation of (±)-**3**: NMMO (716 mg, 6.1 mmol) and $OsO_4$ (52 mg, 0.2 mmol) were added to a solution of **1** (1g, 5.1 mmol) in 50 mL of $CH_2Cl_2$ cooled at 0°C, and the mixture was stirred for 48 h at rt. Column chromatography (hexane/ethyl acetate 1:1 vol/vol as the eluent) of the crude product afforded *1,2-dihydroxy-3,5-diacetyloxycyclohex-5-ene* (±)-**2** (973 mg, yield 83%). $^1$H NMR: δ 2.07 (3H, s), 2.09 (3H, s), 4.14 (1H, m), 4.41 (1H, dd, *J*=4.0 and 4.4), 5.28 (1H, dd, *J*=4.0 and 9.5), 5.63 (1H, dd, *J*=4.0 and 4.7), 5.85 (1H, dd, *J*=4.7 and 9.8), 6.05 (1H, dd, *J*=4.0 and 9.8); $^{13}$C NMR: δ 20.89, 22.65, 66.34, 66.86, 67.35, 69.78, 126.00, 131.92, 170.38, 171.07. Anal. Calc. for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.30; H, 6.0.
6. In a typical experiment lipase from *Mucor miehei* (Lipozyme IM, 800 mg) and vinyl acetate (0.22 mL, 3.47 mmol) were added to a solution of (±)-**2** (400 mg, 1.74 mmol) in *t*-BME (40 mL). The reaction mixture was stirred at 45°C and 300 rpm for 6 h (conv. 48%), the suspension was then filtered and the filtrate taken to dryness. The residue was chromatographed on Si Diol (ethyl acetate/hexane 3:7 vol/vol) to give *(2R)-hydroxy-(1R,3R,4R)-triacetoxycyclohex-5-ene*, (−)-**3** (208 mg, 44% yield), ee>95%, $[\alpha]_D$ −275 (*c* 1.2, $CHCl_3$). $^1$H NMR: 2.06 (3H, s), 2.08 (3H, s), 2.11 (3H, s), 4.23 (1H, dd, *J*=4.3 and 9.7), 5.31 (1H, dd, *J*=4.1 and 9.7), 5.48 (1H, m), 5.64 (1H, m), 5.87 (1H, dd, *J*=4.4 and 10.0), 5.98 (1H, dd, *J*=4.4 and 10.0); $^{13}$C NMR: 20.80, 20.90, 66.26, 66.43, 68.93, 69.41, 128.09, 128.33, 170.16, 170.47, 170.70. The unreacted *(1S,2S)-dihydroxy-(3S,4S)-diacetoxycyclohex-5-ene*, (+)-**2** (192 mg, 48% yield) had ee 92%, $[\alpha]_D$ +200 (*c* 1.2, $CHCl_3$).
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