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SYNTHESIS OF (R)-1-BENZYLOXY-3-BUTEN-2-OL - A POTENTIAL CHIRAL SYNTHON FROM L-(+)-TARTARIC ACID: ITS APPLICATIONS IN NATURAL PRODUCT SYNTHESES

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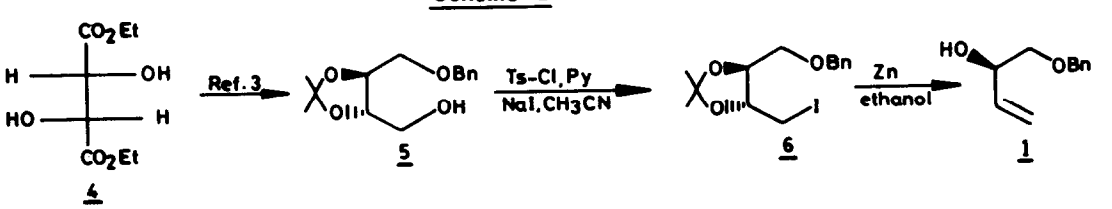
Abstract *A practical synthesis of (R)-3-butene-1,2-diol derivatives from (R,R)-tartaric acid and their applications for the syntheses of (R)-ethyl-5-benzoyloxy-5-formyl pentanoate (2), a useful synthon for the preparation of arachidonic acid metabolites and (R)-γ-caprolactone (3), a pheromone of Trogoderma species, are described.*

Chiral building blocks[1] play an important role in the synthesis of natural products especially when they are derived from cheap and abundantly available small molecules such as lactic acid, tartaric acid, carbohydrates, amino acids etc. We recently required[2] an economical preparation of a similar yet novel bifunctional chiral building block which can be conveniently used for our programme on the synthesis of chiral pheromones and unsaturated hydroxy fatty acids with useful biological activity. Indeed, we prepared a multipurpose chiral synthon (R)-1-benzyloxy-3-buten-1-ol (1) from L-(+)-tartaric acid whose practical preparation and applications are described in this communication.

The strategy for the synthesis of chiron 1 (Scheme-1) takes advantage of C_2-symmetry present in the tartaric acid. Accordingly, diethyl-(2R,3R)-tartrate (4) was transformed to monobenzyl ether 5 according to the known procedure[3]. Compound 5 was converted to iodide 6[4]

Scheme - 1



via its tosylate in 90% yield. The iodide 6 on interaction with activated zinc in refluxing ethanol underwent a facile elimination to afford (R)-1-benzyloxy-3-buten-2-ol (1) $[\alpha]_D$ + 6.2 (c, 1.6, $CHCl_3$) in quantitative yield[5,6]. The utility of allylic alcohol 1, as a chiral building block

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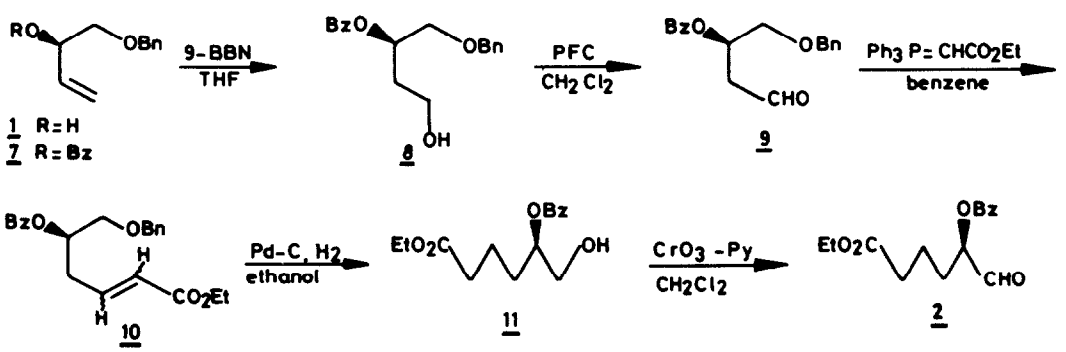
for natural products synthesis could prove to be interesting because of the presence of different functionalities at both ends of the molecule. Consequently, advantage could be taken to functionalise one end in the presence of the other. The antipode of **1** can in fact be synthesized starting from (S,S)-tartaric acid using similar sequence of reactions. The ready accessibility of **1** has prompted us to explore its transformations to an α-hydroxy aldehyde[7] **2** and (R)-γ-caprolactone (**3**)[8].

α-Hydroxy aldehydes[7] are useful precursors for oxiranes, allylic alcohols, 1,2 diols and more importantly for the synthesis of various arachidonic acid metabolites. Though a variety of α-hydroxy aldehydes with varied chain length could be prepared from **1**, a practical approach to a representative aldehyde **2**, which has been utilised for the synthesis of 5-HETE[9], LTB_4[10] and lipoxin-B[11] is illustrated here to demonstrate the usefulness of **1**.

Thus, **1** was protected (Scheme-2) as its benzoate **7** (PhCOCl, Py, 6 hr) in 95% yield, which on hydroboration (9-BBN, THF, NaOAc, H_2O_2) afforded the alcohol **8** in 55% yield. The alcohol **8** on oxidation[12] (pyridinium fluorochromate, CH_2Cl_2, 2 hr) gave the aldehyde **9** in 73% yield which on two carbon homologation ($Ph_3P{=}CHCO_2Et$, benzene, 80°, 4 hr) afforded the unsaturated ester **10** as a E/Z-mixture. Hydrogenation of **10** over palladised charcoal in ethanol effected the reduction of the double bond and debenzylation simultaneously to give the alcohol

Scheme - 2

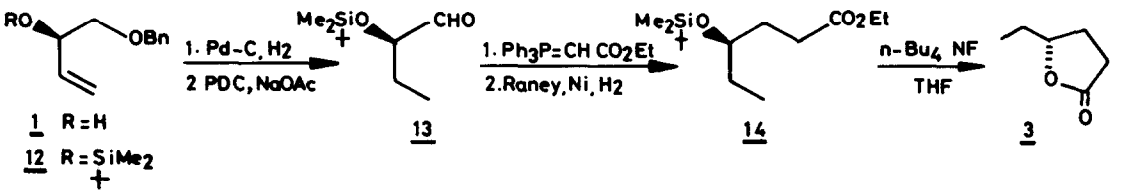


11 in 60% yield. Oxidation of **11** with CrO_3-Py. in CH_2Cl_2 afforded the aldehyde **2** in 60% yield, $[\alpha]_D$ + 34.1 (c, 2.7, $CHCl_3$), Lit.[9] $[\alpha]_D$ + 35.0 (c, 2.0, $CHCl_3$) and whose spectroscopic properties were comparable with those of the reported values[13].The S enantiomer of **2**, which is used for the preparation of natural 5-HETE, LTB_4 and lipoxin-B, could be synthesized from (S,S)-tartaric acid using the above strategy.

In addition, **1** was also exploited for the synthesis of (R)-γ-caprolactone (**3**)[8], a pheromone of the Trogoderma species, **1** was therefore protected (Scheme-3) as its silyl ether **12** (TBDMSCl, Imidazole, DMF) which on hydrogenolysis (Pd-C, H_2, ethyl acetate) and oxidation (PDC, NaOAc, CH_2Cl_2) afforded aldehyde **13** in 45% yield. **13** on two carbon homologation

(Ph_3P= $CHCO_2Et$, benzene 80°, 5 hr) and hydrogenation (Raney Nickel, ethanol) afforded the ester **14** in 65% yield. The ester **14** on treatment with tetra-n-butyl ammonium flouride in

Scheme - 3



THF afforded the lactone **3** in 55% yield $[\alpha]_D$ + 50 (c, 2.0, MeOH) Lit.[8] $[\alpha]_D$ + 53 (c, 1.3, MeOH).

The further utility of **1** for the synthesis of natural products is under investigation.

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4. All the new compounds showed consistent spectral data and gave satisfactory elemental analysis.
5. (R)-3-Butene-1,2-diol has been prepared in an impractical yield from (R,R)-tartaric acid with contamination of variable amounts of 2-butene-1,4-diol, whose purification requires tedious chromatographic separation. Further, to make this intermediate operationally useful, a difficult selective protection of one of the hydroxyl groups is required.
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