Synthesis of (3*S*)-[3-Hydroxy-(*E*)-prop-1-enyl]cyclopentanone, Potential Versatile Chiral Synthon for Natural Products from (*R*)-1,2-Isopropylideneglyceraldehyde

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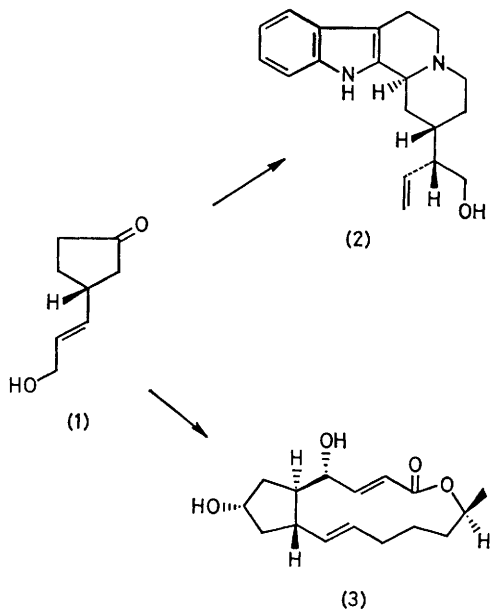
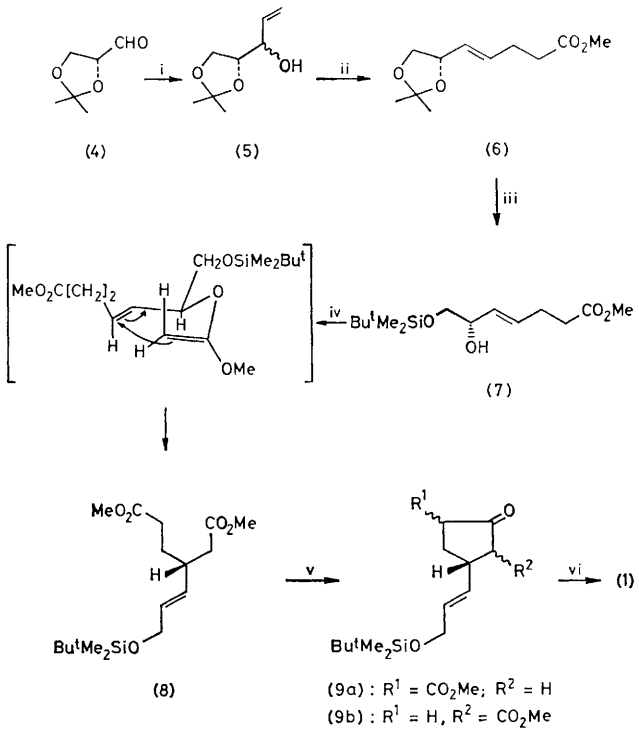
(3*S*)-[3-Hydroxy-(*E*)-prop-1-enyl]cyclopentanone (**1**) has been synthesised from an easily available chiral starting material, (*R*)-1,2-isopropylideneglyceraldehyde (**4**), through orthoester Claisen rearrangement of (**5**) and (**7**).

(*R*)-1,2-Isopropylideneglyceraldehyde (**4**)[1] has been used as a chiral starting material for a number of biologically active compounds such as prostaglandins,[2] brefeldin A,[3] ipsdienol,[4] prestalotin,[5] and leukotriene A_4.[6] In connection with our work on the use of sugars as chiral synthons, we required a synthesis of (3*S*)-[3-hydroxy-(*E*)-prop-1-enyl]cyclopentanone (**1**), a potential intermediate leading to antirhine (**2**)[7] and brefeldin A (**3**) (Scheme 1).[3,8] We have examined the synthesis of (**1**) from (*R*)-1,2-isopropylideneglyceraldehyde (**4**), and report here our successful results (Scheme 2).



Scheme 1



Scheme 2. *Reagents:* i, vinylmagnesium bromide, CH_2Cl_2, 0 °C; ii, $MeC(OMe)_3$, propionic acid catalyst, 140 °C, 82.8%; iii, 10% H_2SO_4, MeOH, room temp., 100%; Bu^tMe_2SiCl, imidazole, dimethylformamide, room temp., 83.1%; iv, $MeC(OMe)_3$, propionic acid catalyst, 145 °C, 84.6%; v, $KOBu^t$, dry tetrahydrofuran, room temp., 82.8%; vi, $MgCl_2.6H_2O$, Me_2SO, 110 °C, 82.4%.

The vinyl alcohol (**5**), prepared in 45.8% yield *via* (*R*)-1,2-isopropylideneglyceraldehyde (**4**)[1] from D-mannitol [a, acetone, $ZnCl_2$; b, $Pb(OAc)_4$; c, vinylmagnesium bromide], was subjected to orthoester Claisen rearrangement[9] to provide the methyl ester (**6**), b.p. 105—108 °C (1 mmHg), $[\alpha]_D$ + 27° (c = 0.23, $CHCl_3$).† Acetonide cleavage, followed by protection of the primary alcohol as the t-butyldimethylsilyl ether[10] gave the monoprotected allylic alcohol (**7**), $[\alpha]_D$ + 7.3° (c = 0.41, $CHCl_3$). Chirality transfer of the secondary allylic alcohol from C–O to C–C was also done by orthoester Claisen rearrangement[9] to give (**8**), $[\alpha]_D$ + 7.0° (c = 0.23, $CHCl_3$), possessing the required chirality at the C-4 position. Dieckmann condensation of the dimethyl ester (**8**), followed by demethoxycarbonylation and simultaneous deprotection of the protecting group of (**9a**) or (**9b**), $[\alpha]_D$ + 25.5° (c = 0.33, $CHCl_3$) under neutral condition[11] gave the key intermediate (**1**) {$[\alpha]_D$ + 94.4° (c = 0.22, $CHCl_3$), m/z: found, 140.0831 (M^+); calc. 140.0836} which should lead to optically active antirhine (**2**) and brefeldin A (**3**); their enantioselective syntheses are currently being studied.

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† Optical rotations were measured with a JASCO-DIP-4 automatic polarimeter.