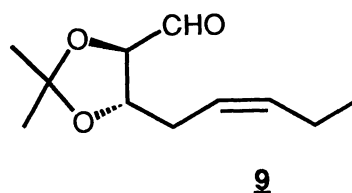
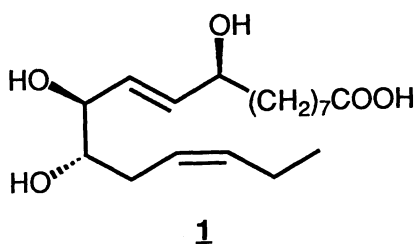


Formal Synthesis of a Unsaturated Trihydroxy C-18 Fatty Acid

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Stereoselective synthesis of (4R,5S)-2,2-dimethyl-5-[(Z)-2-pentenyl]-1,3-dioxolane-4-carboxaldehyde, a key intermediate for the synthesis of (9S, 12S, 13S)-trihydroxy-(10E, 15Z)-octadecadienoic acid starting from *cis*-butene-1,4-diol, is described.

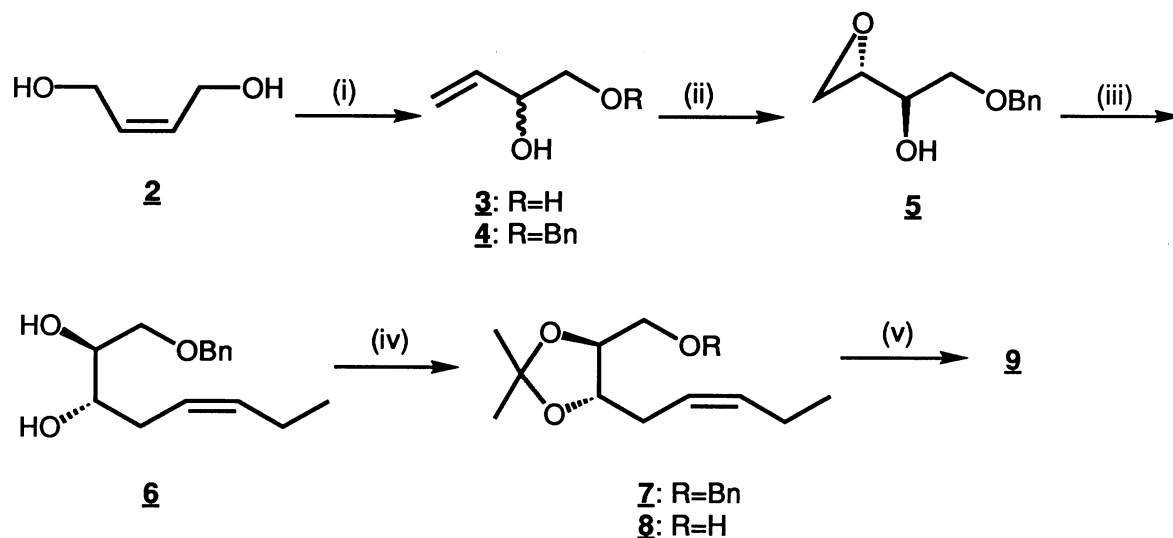
Unsaturated hydroxy fatty acids are well known to possess a wide range of biological activities in animals and in plants.^{1,2)} The synthesis of such hydroxy acids is facinating target due to their complex structures.³⁾ Kato et. al.⁴⁾ have isolated (9S, 12S, 13S)-trihydroxy-(10E, 15Z)-octadecadienoic acid **1** from rice plants suffering from rice blast disease (*Pyricularia oryzae*). The synthesis of **1** has already been achieved through the intermediate (4R,5S)-2,2-dimethyl-5-[(Z)-2-pentenyl]-1,3-dioxolane-4-carboxaldehyde **2** starting from allyl alcohol,⁵⁾ (R)-tartaric acid⁶⁾ and 1,2:5,6-di-O-isopropylidene- α -D-gulofuranose.⁷⁾ In this paper a new synthesis of intermediate **2** starting from *cis*-butene-1,4-diol **2** is reported.



Isomerisation of **2**⁸⁾ in the presence of HgSO₄-H₂SO₄-H₂O followed by distillation with a long vigreux column provided 3-butene-1,2-diol **3** in 64% yield, the primary hydroxy group of which was protected by selective monobenzoylation with one equivalent of sodium hydride and benzyl bromide in dry THF to afford **4** in 70% yield. The Sharpless asymmetric epoxidation⁹⁾ of **4** under kinetic resolution conditions with (-)-diisopropyl tartarate (DIPT) as a chiral auxiliary and *tert*-butyl hydroperoxide (TBHP) in methylene chloride at -20 °C provided **5** [(α)_D = -11.2(c, 1.16, CHCl₃), 94% ee]⁸⁾ in 52% yield. The epoxide ring opening of **5** with lithium-(Z,Z)-di-1-butenylcuprate in dry ether¹⁰⁾ occurred smoothly at -78 °C and **6** was isolated in 73% yield. The diol of

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6 was protected as acetonide using 2,2-dimethoxypropane-acetone (1:1, v/v) containing catalytic amount of PTSA furnished **7** in 78% yield. The debenzoylation of **7** in acetonitrile under went smoothly in presence of iodotrimethylsilane¹¹⁾ to afford **8** in 84% yield. Finally, **8** was oxidized under Swern oxidation¹²⁾ condition using dimethyl sulfoxide and oxalyl chloride in methylene chloride to afford **9** in quantitative yield.



(i) (a) $\text{HgSO}_4\text{-H}_2\text{SO}_4\text{-H}_2\text{O}$ (b) NaH, BnBr, THF (ii) (-)-DIPT, TBHP, CH_2Cl_2 , -20°C
 (iii) $(\text{EtCH=CH-})_2\text{CuLi}$, Et_2O , -78°C (iv) (a) $(\text{MeO})_2\text{CMe}_2$, Me_2CO , PTSA, RT, (b) Me_3SiCl , NaI, CH_3CN (v) DMSO, $(\text{COCl})_2$, CH_2Cl_2 , -60°C , Et_3N

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