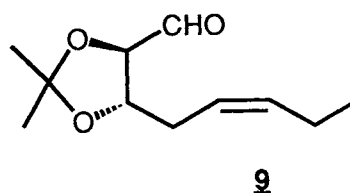
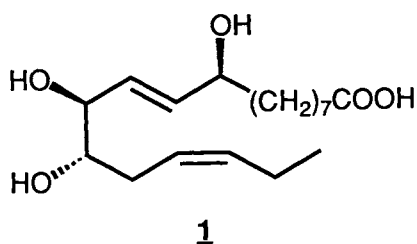


Formal Synthesis of a Unsaturated Trihydroxy C-18 Fatty Acid

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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.

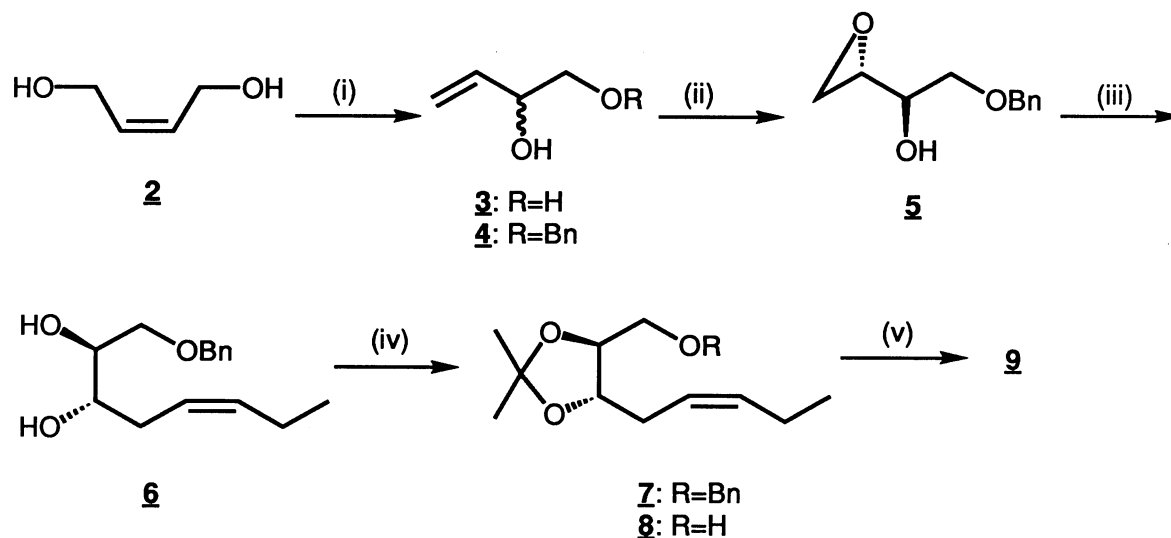
Unsaturated hydroxy fatty acids are well known to possess a wide range of biological activities in animals and in plants.^{1,2)} The synthesis of such hydroxy acids is fascinating target due to their complex structures.³⁾ Kato et. al.⁴⁾ have isolated (9S, 12S, 13S)-trihydroxy-(10E, 15Z)-octadecadienoic 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

References

- 1) C.N. Serhan, M. Hamberg and B. Samuelsson, *Natl. Acad. Sci. USA*, **81**, 5335 (1984).
- 2) A.V.R. Rao, E.R. Reddy, G.V.M. Sharma, P. Yadagiri and J.S. Yadav, *Tetrahedron Letts.*, **26**, 465 (1985).
- 3) T. Kato, Y. Yamaguchi, T. Hirano, T. Yokoyoma, T. Uyehara, T. Namai, S. Yamanaka and N. Hirada, *Chem. Letts.*, **1984**, 409; J.S. Yadav, P.K. Deshpande and G.V.M. Sharma, *Pure & Appl. Chem.*, **62**, 1333 (1990).
- 4) T. Kato, Y. Yamaguchi, S. Ohnuma, T. Uyehara, T. Namai, M. Kodama and Y. Shiobara, *J. Chem. Soc. Chem. Commun.*, **1986**, 743 and ref. cited therein.
- 5) M.K. Gurjar and A.S. Reddy, *Tetrahedron Letts.*, **31**, 1783 (1990).
- 6) H. Suemune, T. Harabe and K. Sakai, *Chem. Pharm. Bull.*, **36**, 3632 (1988); B. Gosse-Kabo, P. Mosset and R. Gree, *Tetrahedron Letts.*, **30**, 4235 (1989).
- 7) G.V.M. Sharma and S.M. Rao, *Tetrahedron Letts.*, **33**, 2365 (1992).
- 8) A.V.R. Rao, D.S. Bose, M.K. Gurjar and T. Ravindranathan, *Tetrahedron*, **45**, 7031 (1989).
- 9) V.S. Martin, S.C. Woodard, T. Katsuki, Y. Yamada, M. Ikeda and K.B. Sharpless, *J. Am. Chem. Soc.*, **103**, 6237 (1981); B.E. Rossiter "Asymmetric Synthesis" ed by J.D. Morrison, Academic Press, New York (1985), Vol 5, p. 193.
- 10) M. Gardette, A. Alexakis and J.F. Normant, *Tetrahedron*, **41**, 5887 (1985).
- 11) T. Morita, Y. Okamoto and H. Sakuri, *J. Chem. Soc. Chem. Commun.*, **20**, 874 (1978).
- 12) A.J. Mancuso, S-L. Huang and D. Swern, *J. Org. Chem.*, **43**, 2480 (1978).

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