# Stereoselective Syntheses of Two Constituents
Against Rice Blast Disease

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Abstract. (11S,12S,13S)-Trihydroxy-(9Z,15Z)-octadecadienoic acid **1** and methyl (11R,12S,13S)-11-hydroxy-12,13-epoxy octadecadienoate **3a** were synthesized starting from L-(+)- and D-(-)- tartaric acids, respectively.

Oxygenated metabolites of unsaturated fatty acids play various important roles in biological systems, either in animals or in plants. Recently, several oxygenated C_{18} fatty acids have been isolated from rice plants such as *Fukuyuki*, suffering from the rice blast disease[1], among these acids, **1**-**4** can act as self-defense substances against the fungus.
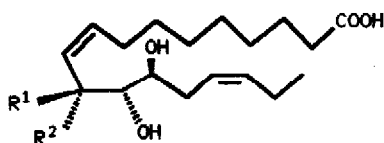
1	R^1 = OH, R^2 = H	
2	R^1 = H, R^2 = OH	
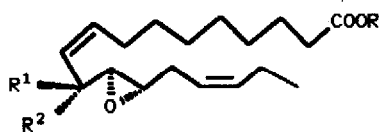
|		
3	R^1 = H, R^2 = OH,	R = H
3a	R^1 = H, R^2 = OH,	R = Me
4	R^1 = OH, R^2 = H,	R = H

In the last three years, a few individual organic syntheses of compounds **2**,**3a**,**4** have been repored[2~4], however, a general synthetic method for these structurally similar acids has not appeared in the literature yet. we have been endeavoring to develop a methodology for stereoselective synthesis of all of the four acids **1**-**4**. In this communication, we wish to report the first total synthesis of (11S,12S,13S)-trihydroxy-(9Z,15Z)-octadecadienoic acid **1** and a total synthesis of methyl (11R,12S,13S)-(9Z,15Z)-11-hydroxy-12,13-epoxy octadecadienoate **3a**, starting from L-(+)-

and D-(-)-tartaric acids, respectively.

The synthetic approach to <u>1</u> is outlined in scheme 1.

Scheme 1
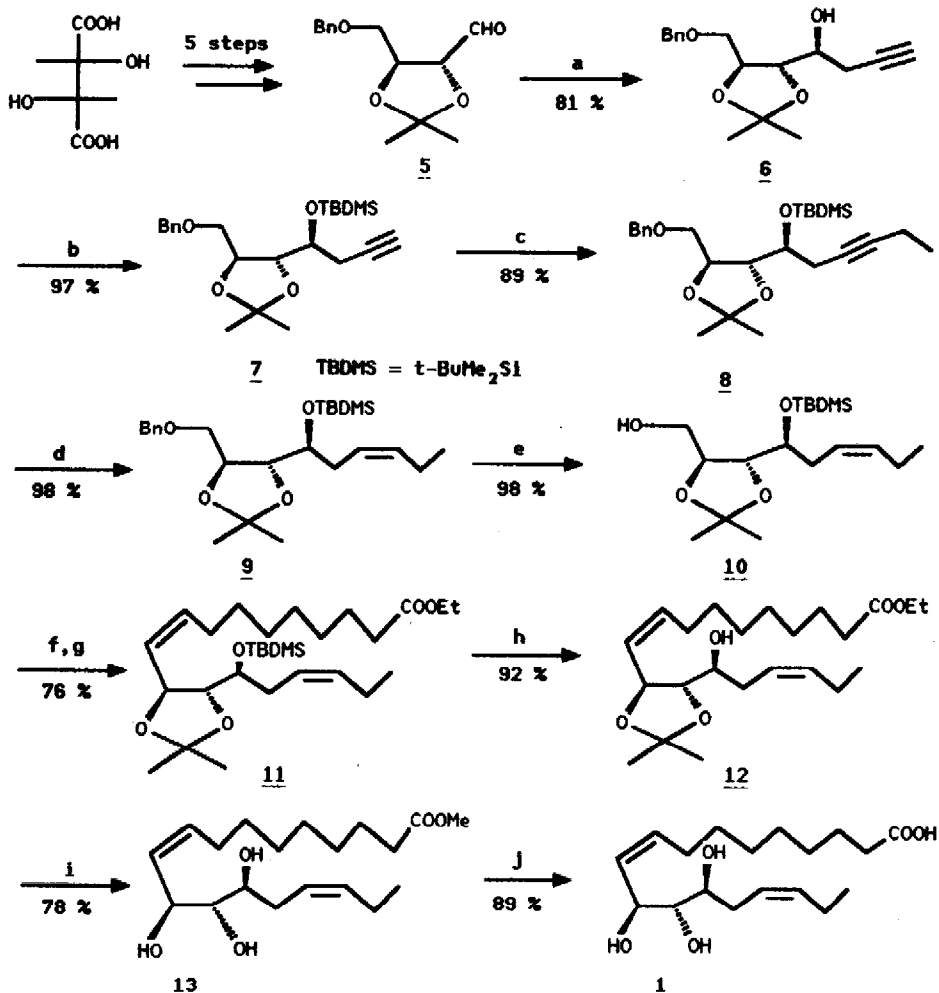
a) Zn, BrCH₂C≡CH, DMF-Et₂O(1:1)   b) TBDMSCl, imidazole   c)1.n-BuLi,
THF-HMPA, 2.BrC₂H₅   d) H₂, Pd-Pb-CaCO₃, quinoline   e) Li, liq. NH₃
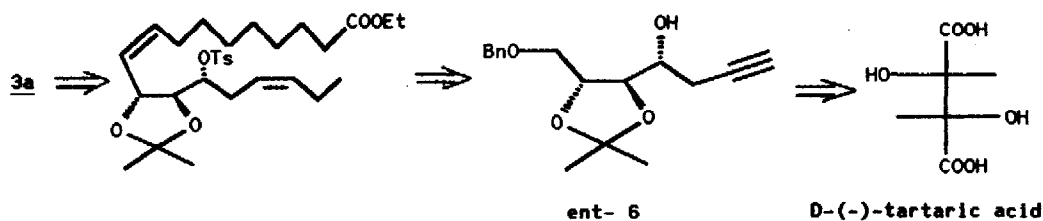f)Swern Oxd.   g)Br⁻Ph₃P⁺C₈H₁₆COOEt,t-BuOK, THF   h)n-Bu₄NF   i)PTS,MeOH
j) KOH, EtOH-H₂O

The known four-carbon building block, 4-O-benzyl-2,3-O-isopropylidene-
-ᴸ-threose (<u>5</u>) , readily available from L-tartaric acid[5], was treated with
propargyl bromide in the presence of zinc dust[6,7] to afford the   erythro-
product[8] <u>6</u>   after   column   chromatography. HPLC analysis showed that the
ratio of erythro to threo isomer was ca. 30 : 1. Silylation   of   the   free

hydroxy group of **6** with TBDMSCl followed by alkylation of the terminal alkyne with C_2H_5Br provided compound **8** . After partial hydrogenation of **8** over Lindlar catalyst and removal of the benzyl group , the corresponding primary alcohol **10** was obtained. Swern oxidation[9] of **10** followed by Wittig reaction of the resulting crude aldehyde with ethyl 9-(triphenyl-phosphorylidene)-nonanoate under cis olefination conditions afforded the (Z)-unsaturated ester **11** (Z/E > 95/5) in 76 % yield in two steps.
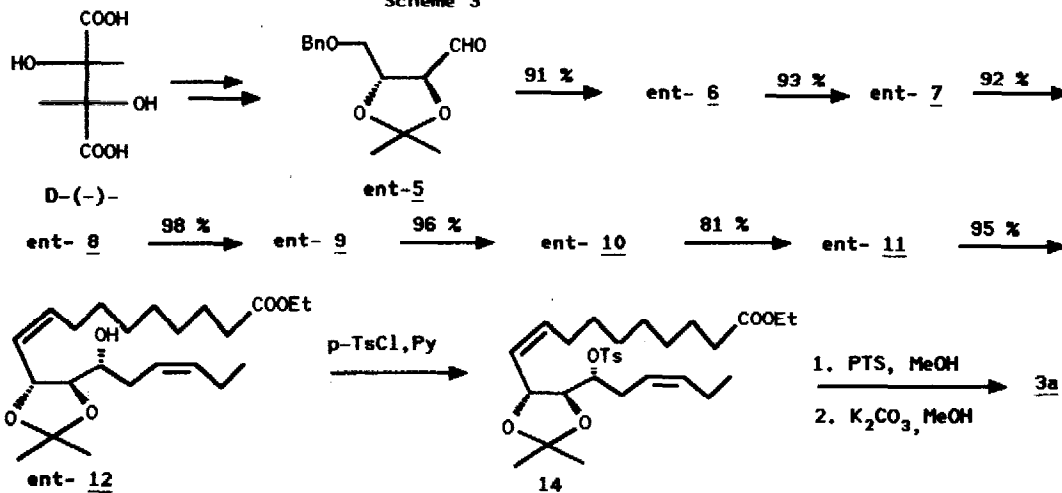
The silyl ether **11** was converted to **13** by a standard two-step sequence(n-Bu$_4$NF and then TsOH in aqueous CH$_3$OH), it is of interest to note that ester exchange (from ethyl ester to methyl ester) was complete under these acid conditions. The ^{1}H NMR spectra of **13** was identical to that reported[1a]. Finally, saponification of **13** with KOH in aqueous ethanol produced the natural acid **1**[10] ,the overall yield from the known carbohydrate-derived precursor being as high as 33 %.

The epoxide ester **3a** can be prepared from ent-**6** by the same strategy followed by inversion at C-13 during closure of the epoxide (scheme 2).

Scheme 2

ent- **6**   D-(-)-tartaric acid

Scheme 3

ent-**5**

$$D-(-)-$$

ent- **6** $\xrightarrow{93\ \%}$ ent- **7** $\xrightarrow{92\ \%}$

ent- **8** $\xrightarrow{98\ \%}$ ent- **9** $\xrightarrow{96\ \%}$ ent- **10** $\xrightarrow{81\ \%}$ ent- **11** $\xrightarrow{95\ \%}$

ent- **12**   p-TsCl,Py   **14**   1. PTS, MeOH 2. K$_2$CO$_3$,MeOH   **3a**

Starting from D-(-)-tartaric acid, application of the same reaction sequences employed in scheme 1 to the ent-<u>5</u> led to trihydroxy ester ent-<u>12</u> in good overall yield, the spectral data of all of intermediates are in agreement with those of their enantiomers. Tosylation of ent-<u>12</u> with p-TsCl-pyridine followed by removal of the acetonide group with TsOH-aqueous methanol and treatment with potassium carbonate in methanol afforded the epoxy alcohol <u>3a</u> (methyl ester of natural product <u>3</u>), $[a]_D=$ -79.5⁰ (c 0.6, $CHCl_3$), its spectral properties are identical with that reported[1][b]

References and Notes.

1. a) Kato,T.; Yamaguchi,Y.; Ohnuma,S.; Uyehara,T.; Namai,T.; Kodama,M.; Shiobara,Y.*Chemistry Lett.*, 1986, 577.
   b) Kato,T.; Yamaguchi,Y.; Ohnuma,S.; Uyehara,T.; Namai,T.; Kodama,M.; Shiobara,Y.*J.Chem.Soc.Chem.Commun.*, 1986, 743.

2. Rama Rao,A.V.; Radha Krishna,P.; Yadav,J.S.*Tetrahedron Lett.* 1989,30, 1669.

3. Yadav,J.S.; Chander,M.C.*Tetrahedron Lett. 1990*, 31, 4349.

4. Haynes,R.K.; Vonwiller,S.C.*J.Chem.Soc.Chem.Commun.1990*, 1102.

5. Mukaiyama,T.; Suzuki,K.; Yamada,T.; Tabusu,F.*Tetrahedron* 1990, 265.

6. Fuganti,C.; Servi,S.; Zivotti,C.*Tetrahedron Lett.*,1983, 24, 5285.

7. Shono,T.; Iahifune,M.; Kashimoro,S.*Chem. Lett.*, *1990*, 449.

8. Satisfactory spectral data (IR, ^{1}H NMR, MS) were obtained for all new compounds using chromatographically homogeneous samples. $[a]_D$ values, (20 ⁰C, $CHCl_3$, g/100ml) <u>6</u>: -5.7⁰(0.7), ent- <u>6</u> : +2.7⁰(0.8); <u>7</u>: +19⁰(0.4), ent- <u>7</u>: -17.8⁰(0.8); <u>8</u>: +22.4⁰(0.6), ent- <u>8</u>: -21.2⁰(1.0); <u>9</u>: +24.4⁰(0.7), ent- <u>9</u>: -24.4⁰(0.7); <u>10</u>: +34.2⁰(1.0), ent- <u>10</u>: -42⁰(1.0); <u>11</u>: +10.0⁰(0.5), ent- <u>11</u>: -10.7⁰(0.5); <u>12</u>: +21.3⁰(0.8), ent- <u>12</u>: -22.4⁰(0.7).

9. Mancuso,A.J.; Swern,D.*Synthesis*, *1981*, 165.

10. Spectroscopic data for <u>1</u> : ^{1}H NMR (600 MHz, $CDCl_3$) 0.98(t, J= 7.5Hz, 3H) , 1.25-1.70(m, 10H), 2.0-2.2(m, 4H), 2.38(t,J=7.3 Hz, 2H), 2.62 (m,2H), 3.48(m, 1H), 3.76(m, 1H), 4.67(m, 1H), 5.39(m, 1H),5.55-5.65 (m, 3H). EIMS 311, 293, 275, 213.
   For <u>3a</u> : ^{1}H NMR (600 MHz, $CDCl_3$) 0.97(t,J=7.5Hz, 3H), 1.3-1.70(m, 10H), 2.0-2.2(m, 4H), 2.30(t,J=7.5Hz,2H), 2.41(m,2H), 2.83(dd,J=5.2, 2.2Hz, 1H), 2.97(dt, J=2.2,5.5Hz, 1H), 3.67(s, 3H), 4.29(dd, J=8.7, 5.2Hz,1H), 5.33(dt, J=10.8,7.4Hz, 1H), 5.47(dd,J=11.0,8.7Hz, 1H), 5.53(dt, J=10.8,7.3Hz,1H), 5.61(dt, J=11.0,7.4Hz, 1H). EIMS 325, 307(100 %), 289, 275, 213.