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Abstract -- (11S,12S,13S)-(9Z,15Z)- and (11R,12S,13S)-(9Z,15Z)-11-Hydroxy-12,13-epoxy octadecadienoic acids, self defensive substances against the rice blast disease, were synthesized enantioselectively by employing the Sharpless asymmetric epoxidation reaction of the unsymmetrical divinylcarbinol, as a key step.

Several oxygenated metabolites of unsaturated C₁₈ fatty acids, such as the compounds (1-4), were isolated by Kato and co-workers¹ from the rice plants suffering from rice blast caused by Pyricularia oryzae. These fatty acids were shown to be self-defence substances against the fungus. For example, the epoxy compounds (1) and (2) exhibit strong spore germination inhibitory action against the rice blast disease. Owing to their interesting biological activity and also to their low abundance in natural sources, much effort has been devoted to develop

![Chemical Structures](image)

1 $R^1 = OH, R^2 = H$
2 $R^1 = H, R^2 = OH$
3 $R^1 = OH, R^2 = H$
4 $R^1 = H, R^2 = OH$

Figure 1.

This paper is dedicated to the memory of the late Professor Shun-ichi Yamada.
an efficient procedure for their syntheses.\textsuperscript{2}

Recently we have established the Sharpless asymmetric epoxidation reaction of racemic unsymmetrical
divinylcarbinols, where the kinetic resolution and subsequent epoxidation have proceeded in an entirely regio-
and diastereoselective manner to give the corresponding epoxy-alcohols with high enantiomeric excesses.\textsuperscript{3,4}
This procedure has already been applied to the enantioselective synthesis of an antitumor antibiotic, (+)-asperlin, successfully.\textsuperscript{3} As an extension of this work, we became interested in an enantioselective synthesis of
defensive substances against the rice blast disease, since these natural products seem to be suitable target
compounds for applying the above synthetic strategy.

The requisite unsymmetrical divinylcarbinol (19) was synthesized as follows. Dess-Martin periodinane
oxidation\textsuperscript{5} of (Z)-3-hexen-1-ol (5) gave (Z)-3-hexenal (6), which on Wittig-Horner reaction with triethyl
phosphonoacetate afforded the dienoate (7). Reduction of the ester (7) with diisobutylaluminum hydride
(DIBAL), followed by Dess-Martin periodinane oxidation of the alcohol (8) gave the dienal (9) in 69% yield.
Addition of the lithium salt of 10-tert-butyldimethylsiloxy-1-decyne\textsuperscript{6} to the aldehyde (9) gave the alcohol (10)
in 83% yield. After protection of the secondary hydroxy group of 10 as the acetate (11), the silyl ether was
removed by treatment with tetrabutylammonium fluoride (TBAF) to provide the primary alcohol (12) in 92%
yield from 10. Successive oxidation of the alcohol (12) with Dess-Martin periodinane reagent and sodium
chlorite\textsuperscript{7} gave the acid (14) via the aldehyde (13) in 89% yield from 12. Esterification of the acid (14) with
iodomethane and potassium carbonate afforded the ester (15), which was further converted into the triethylsilyl
ether (17) by two steps involving methanolysis giving the alcohol (16) and silylation with triethylsilyl chloride
(TESCl). The formation of the (Z)-olefin from the silyl ether (17) was achieved in a usual manner by using a
catalytic reduction with the Lindlar catalyst to give the triene (18). Deprotection of the silyl group of 18 with
TBAF afforded the alcohol (19) in 89% yield from 14. With the requisite starting unsymmetrical
divinylcarbinol (19) available, a study was made of the best conditions for the Sharpless asymmetric
epoxidation to the desired epoxy-alcohol. The reaction of 19 with 0.4 equiv. of \textsuperscript{tert}-butyl hydroperoxide
(TBHP), 0.55 equiv. of L-(+)-DIET and 0.5 equiv. of Ti(O\textsuperscript{3}Pr\textsubscript{4}) in dichloromethane in the presence of calcium
hydride and molecular sieves 3A at -40°C gave the epoxy-alcohol (20) and the recovered (R)-secondary alcohol
(21), in 33% and 57% yields, respectively. None of the other products including the regioisomeric epoxide
could be isolated in this reaction. The spectroscopic data including specific rotation, \([\alpha]\textsubscript{D} +69.6° (CHCl\textsubscript{3}),
\textit{lit.}\textsuperscript{2h} [\alpha]\textsubscript{D} +72.2° (CHCl\textsubscript{3})], of the former epoxide (20) were identical with those reported,\textsuperscript{2h}
suggesting its
absolute configurations to be 11S,12S, and 13S. Its enantiomeric excess was also determined to be 94% by HPLC analysis with the chiral column CHIRALPAK AD.

It should be noted again that the kinetic resolution and subsequent epoxidation of 19 under the Sharpless asymmetric oxidation conditions proceeded in an entirely regio- and diastereoselective manner.

Finally, hydrolysis of the ester (20) with 0.5N sodium hydroxide afforded the desired acid (1), $\left[\alpha\right]_D +65.2^\circ$ (CHCl$_3$), lit.,$^{2a}$ $\left[\alpha\right]_D +39.5^\circ$ (CHCl$_3$), in 91% yield. The reported value of rotation for the natural product$^{2a}$ was much smaller than that for our synthetic compound, possibly due to sample contamination.
(11R,12S,13S)-(9Z,15Z)-11-Hydroxy-12,13-epoxy octadecadienoic acid (2), [α]D -54.2° (CHCl₃), was also synthesized from the epoxy-alcohol (20) by two steps, including Mitsunobu reaction with p-nitrobenzoic acid, and hydrolysis of the resulting p-nitrobenzoate (22) with lithium hydroxide, in 45% overall yield. The partial hydrolysis of 22 under the above reaction conditions with a shorter reaction time gave the hydroxy ester (23), [α]D -52.3° (CHCl₃), which was also converted into the acid (2).

The present work illustrates a further application of the Sharpless asymmetric epoxidation of the unsymmetrical divinylcarbinols to the synthesis of physiologically active fatty acids with high optical purity. The synthesis of the triols (3 and 4) by the ring-opening reaction of the epoxy-alcohols (1 and 2) is under investigation.

**REFERENCES**


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