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STEREOSELECTIVE SYNTHESIS OF HYDROXY OCTADECATRIENOIC ACIDS. THE SELF DEFENSIVE SUBSTANCES IN RICE PLANT

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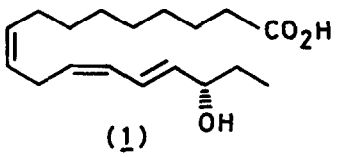
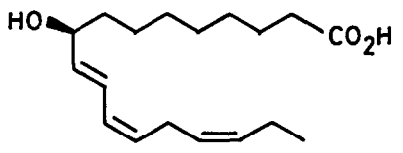
Abstract Convenient synthesis of 16-hydroxy-9Z,12Z,14E-octadecatrienoic acid (1) and 9-hydroxy-10E,12Z,15Z-octadecatrienoic acid (2) the self defensive substances in rice plant against rice blast disease are described.

Unsaturated hydroxy fatty acids play important role in biological systems. Recently Kato et al[1] isolated fatty acids,16-hydroxy-9Z,12Z,14E-octadecatrienoic acid (1) and 9-hydroxy-10E,12Z,15Z-octadecatrienoic acid (2) from resistent cultivar of rice plant FUKUYUKI (oryza sative-L) and demonstrated to act as self defensive substances against rice blast disease. 2 was also isolated[2] from rice plant leaves treated with probenzole and shown to inhibit conidial germination of Pyrichularia oryzae. In continuation of our programme on the synthesis of unsaturated hydroxy fatty acids[3], the fascinating structural features coupled with interesting biological activity, stimulated us to develop the total synthesis of 1 and 2 so that their properties can be well assessed.



(1)



(2)

The synthetic strategy for the construction of 1 is given in Scheme-1. Thus 1,4-dichloro but-2-yne(3) on treatment with sodamide in liquid ammonia and propionaldehyde in ether at -32°C and usual work up[4] gave hepta-5,6-diyn-3-ol[5] (4). The alcohol 4 on selective reduction (LAH, ether, 25°C, 12 hr) afforded (E)-hept-4-en-6-yn-3-ol (5) in 72% overall yield. Compound (5) not only serves as a handle for the elaboration of aliphatic chain but also precursor for the cis double bond at the final step to complete the synthesis of 1. 11-Bromo undec-9-ynoic acid (8) was prepared by alkylation propargyl alcohol[6] with 8-bromooctanoic acid (6) using lithium amide in liquid ammonia to give hydroxy-acid 7 followed by converting into bromo-

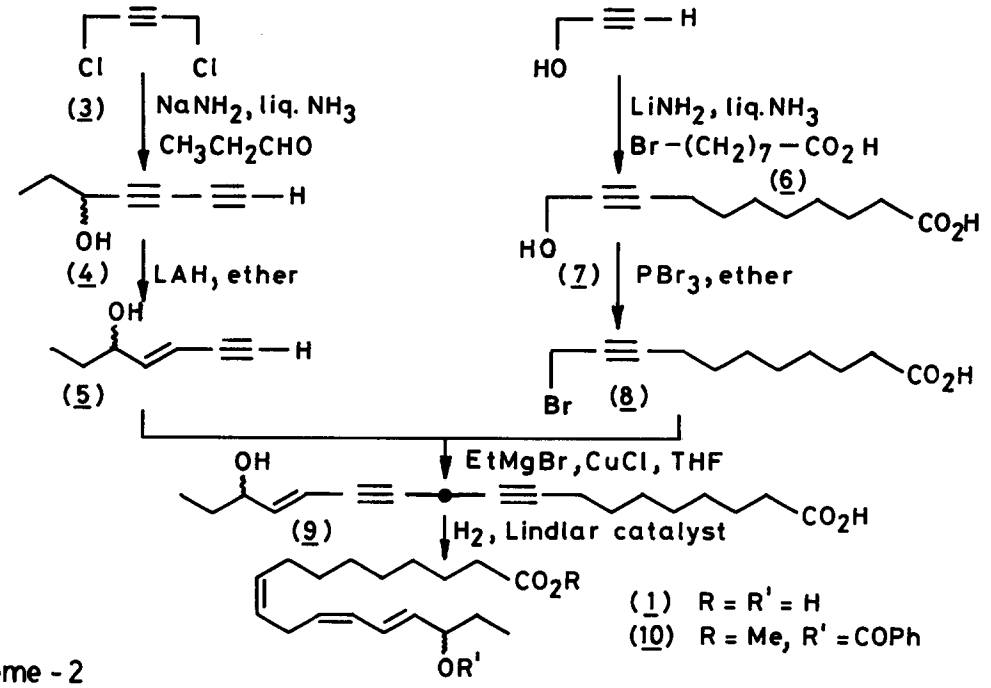
acid 8 (PBr_3, PY, ether 25°C, 6 hr) in 76% overall yield. The chain elaboration was achieved by cuprous chloride catalysed Grignard coupling reaction of 5 with magnesium bromide salt of 8 (EtMgBr 2eq, CuCl 5%, THF, 55°C, 12 hr) and chromatographic purification afforded diacetylene alcohol 9 in 55% yield. Partial hydrogenation of triple bonds in 9 was carried out by using Lindlar catalyst in the presence of quinoline to yield 1 in 90% which was converted to benzoate-methyl ester 10 which is in full agreement with the reported data[1].

The strategy for the construction of 2 (Scheme-2) involves the introduction of hydroxyl group by SeO_2 catalysed tert-butyl hydroperoxide hydroxylation of olefine followed by ozonolysis to give the α-hydroxy aldehyde which was eloborated by Wittig reaction.

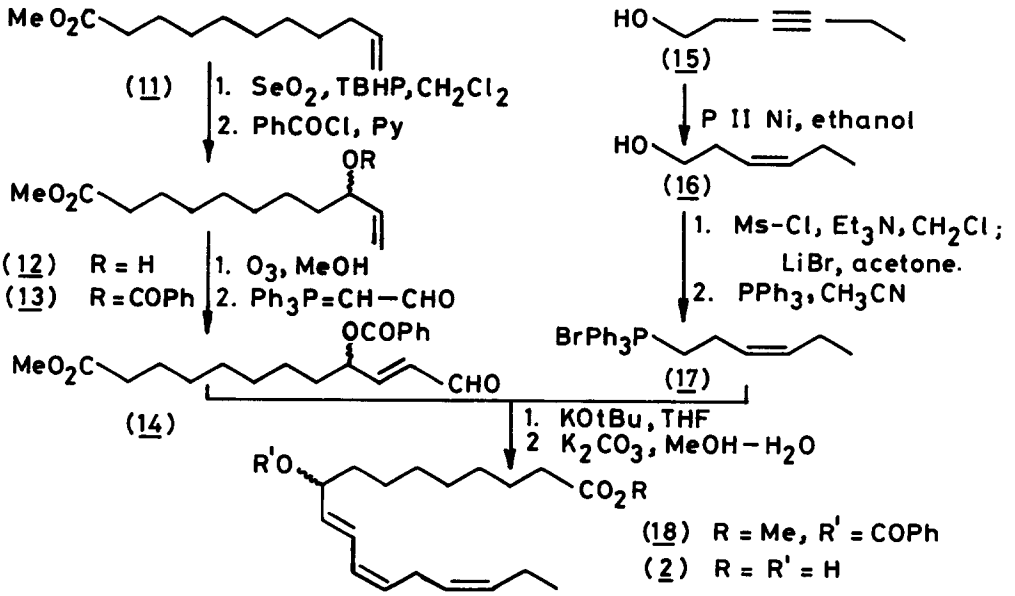
Thus Methyl 10-undecenoate (11) on allylic hydroxylation[7] (SeO_2, TBHP, CH_2Cl_2, 25°C, 36 hr) afforded hydroxy olifinic ester 12 in 60% yield. The secondary alcohol in 12 was protected by benzoylation (PhCOCl, pyridine, 25°C, 6 hr) to give 13 in 95% yield. 13 on ozonolysis (O_3, MeOH, 0°C, 15 min) gave the α-hydroxy protected aldehyde in 75% yield which on further treatment with formylmethylene triphenylphosphorane in refluxing benzene for 3 hr gave the olefinic-aldehyde 14 in 78% yield. The phosphonium salt 17 was prepared by reducing 3-Hexyn-1-ol[8] (15) with PII Nickel[9] in ethanol followed by converting into bromide (MsCl, Et_3N, CH_2Cl_2, 0°C, 2 hr; LiBr acetone, 25°C, 12 hr) which upon treatment with triphenylphosphine in refluxing acetonitrile for 36 hr in 70% overall yield. 17 on Wittig reaction with aldehyde 12 (KOtBu THF, 0°C, 12 hr) afforded benzoate-methyl ester 18 after purification in 55% yield. Saponification of 18 (K_2CO_3, MeOH : H_2O (4:1), 25°C, 12 hr) and careful acidification gave the hydroxy-acid 2 in 65% yield.[10]

The above strategies are being extended for the synthesis of other unsaturated hydroxy fatty acids showing wide variety of biological activity.

Scheme -1



Scheme - 2



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10. This work was carried out at the National Chemical Laboratory, Pune.

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