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STEREOSELECTIVE SYNTHESIS OF (11R,12S,13S)-TRIHYDROXY-(9Z,15Z)-OCTADECADIENOIC ACID : A CONSTITUENT OF RICE PLANT SUFFERING FROM RICE BLAST DISEASE

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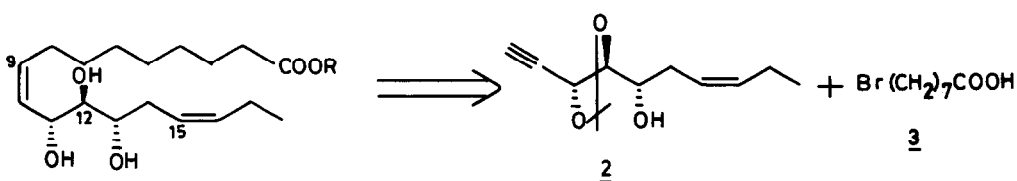
Abstract : *A highly stereoselective synthesis of the title compound from D-ribose is described.*

Research in our group has recently led [1,2] us to the development of new and highly effective protocol, where a base induced elimination of β-alkoxy chlorides derived from carbohydrates, affords potentially valuable chiral polyhydroxyl propargylic derivatives. Influenced by this felicitous results, we have now undertaken a judicious programme to utilise these chiral propargylic alcohols in the synthesis of natural products. This communication therefore deals with the first stereoconvergent synthesis of (11R,12S,13S)-trihydroxy-(9Z,15Z)-octadecadienoic acid **1**, a trihydroxy fatty acid isolated[3] as one of the highly oxygenated metabolites from the rice plant Fukuyuki, suffering from rice blast disease caused by the fungus Pyricularia oryzae from D-ribose and also substantiates its absolute configuration[3].

Scheme 1



1 R = H
1a R = Me

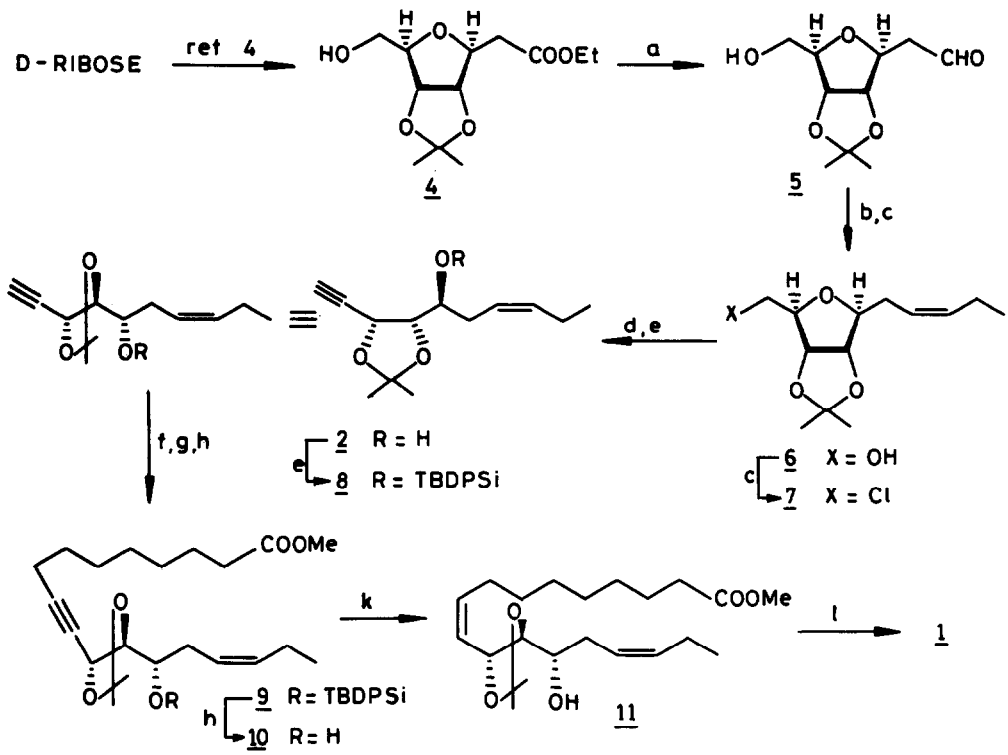
2

3

The retrosynthetic analysis (Scheme 1) for **1** indicates that **2** is the pivotal intermediate whose stereochemical centres can be correlated with those of D-ribose. The reduction of **4**, prepared by known procedure[4], with DIBAL-H gave **5** which on Wittig olefination with n-C_3H_6= PPh_3 in THF-HMPA (8:1) afforded **6** (Scheme 2). The free hydroxyl group in **6** was converted into the corresponding chloride **7** by the treatment with triphenylphosphine in refluxing CCl_4. The chloride **7** was subjected[1] to the $LiNH_2$ in liq.NH_3 to give the acetylenic derivative **2**, which was converted into the TBDPSi derivative **8**. The chain extension of **8** was accomplished by alkylation with lithium 8-bromooctanoate, prepared in situ from **3**[5], using n-BuLi in THF-HMPA (8:1). The resulting acid was characterised as its methyl ester **9**, which on treatment with pyridine-HF complex in THF gave **10**. **10** on hydrogenation over Lindlar's catalyst gave rise to **11** which on subsequent hydrolysis with PTSA furnished **1a** $[\alpha]_D$ -16° (c 0.7, $CHCl_3$). lit.[3] $[\alpha]_D$ -8.5° (c 0.6, $CHCl_3$) whose spectral data were compared with reported data for **1a** and further treatment of **1a** with KOH afforded acid **1**. $[\alpha]_D$ -16.6° (c 1.4, $CHCl_3$). ^1H NMR ($CDCl_3$) : δ 5.67 (dt, J_1=6.8 Hz, J_2=10.7 Hz, H-9), 5.58 (dt, J_1=9.8 Hz, J_2=7.2 Hz, H-16), 5.45 (dd, J_1=9.1 Hz, J_2=10.7 Hz, H-10), 5.39 (dt, J_1=9.8 Hz, J_2=5.9 Hz, H-15), 4.59 (dd, J_1=9.1 Hz, J_2=6.0 Hz, H-11), 3.64 (m, H-13), 3.45 (dd, J_1=6.0 Hz, J_2=6.2 Hz, H-12).

Thus, this novel approach for the expedient stereospecific synthesis of the trihydroxy fatty acid (1) presented here, clearly demonstrates that other structurally analogous natural products such as trioxillin, lipoxins[6] etc. could find their synthetic origin based on this methodology[7].

Scheme 2



a) DIBAL-H (2 eq), CH_2Cl_2, -78°C, .5 h, 95.%; b) n-$C_3H_7P^+Ph_3$ Br^-, $NaNH_2$, -78°, 1.5 h, 70%; c) Ph_3P, CCl_4, 6 h, 90%; d) $LiNH_2$, -33°C, .5 h, 92%; e) TBDPSiCl, imidazole, DMF, 60°C, 6h, 95%; f) n-BuLi, $Br(CH_2)_7COOLi$, -78°C, .5 h, 85%; g) CH_2N_2, ether; h) C_5H_5N-HF, THF, 25°C, 48 h, 95%; k) Pd-$CaCO_3$, H_2, EtOH, l) i. p-TSA, MeOH, 25°C, 24 h, 86%; ii. KOH-MeOH, 65%.

Acknowledgement Authors are indebted to Prof T Kato for providing spectral data for **1a**.

References and Notes

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7. All new compounds gave expected spectral data and exact mass (HRMS).

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