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STEREOSELECTIVE SYNTHESIS OF UNSATURATED C-18 HYDROXY FATTY ACIDS THE SELF DEFENSIVE SUBSTANCES

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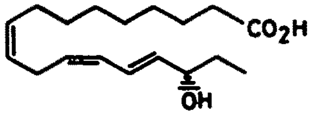
Abstract : A convenient stereoselective synthesis of 16-hydroxy-9Z,12Z,14E-octadecatrienoic acid (1), 9-hydroxy-10E,12Z,15Z-octadecatrienoic acid (2), 9-hydroxy-10E-octadecenoic acid (3) and 10-hydroxy-8E-octadecenoic acid (4), the four self defensive substances in rice plant and timothy plant are described.

Unsaturated hydroxy fatty acids occupy an important place among the natural products owing to their wide range of biological activities. Particularly, in the recent past, unsaturated C-18 fatty acids have attracted a considerable attention. For example, Kato et al.[1] isolated the fatty acids 1 and 2 from the resistent cultivar of rice plant FUKUYUKI (Oryza sative-L) and demonstrated their self defensive activity against rice blast disease while recently Koshino et al.[2] isolated 3 and 4 from timothy plant (Phleum pratense) infected by a phytopathogenic fungus Epichloe typhina and found to be acting as defensive substances against another timothy leaf spot disease pathogen Cladosporium phlei. In continuation of our programme[3] on the synthesis of unsaturated hydroxy fatty acids, herein, we report the details[4] of our studies towards the synthesis of 1 to 4 as an aid to the further biological evaluation.



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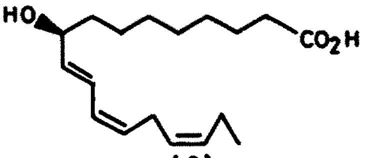

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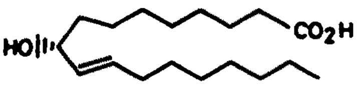

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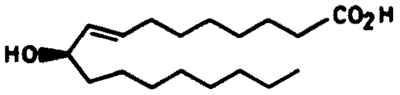
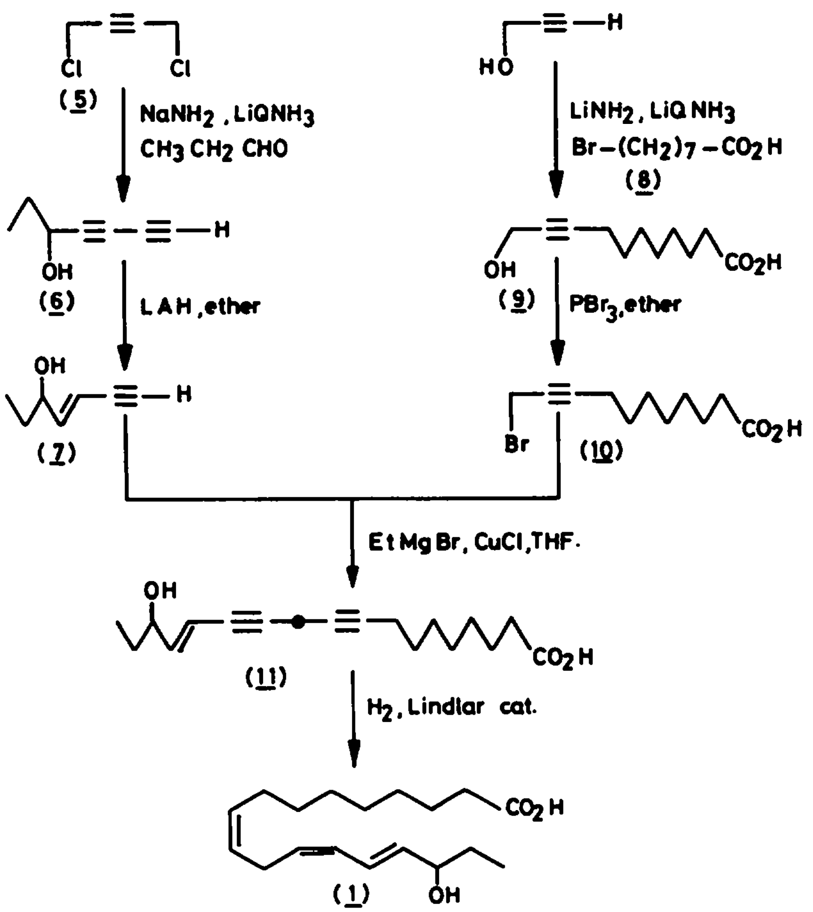


(4)

The strategy involved in the synthesis of 1 (Scheme 1) starts with 1,3-butadiyne which allows the elaboration of aliphatic chain by successive alkynylation and alkylation reactions as desired and serves as precursor for the stereoselective introduction of trans and cis double bonds.

Scheme - 1

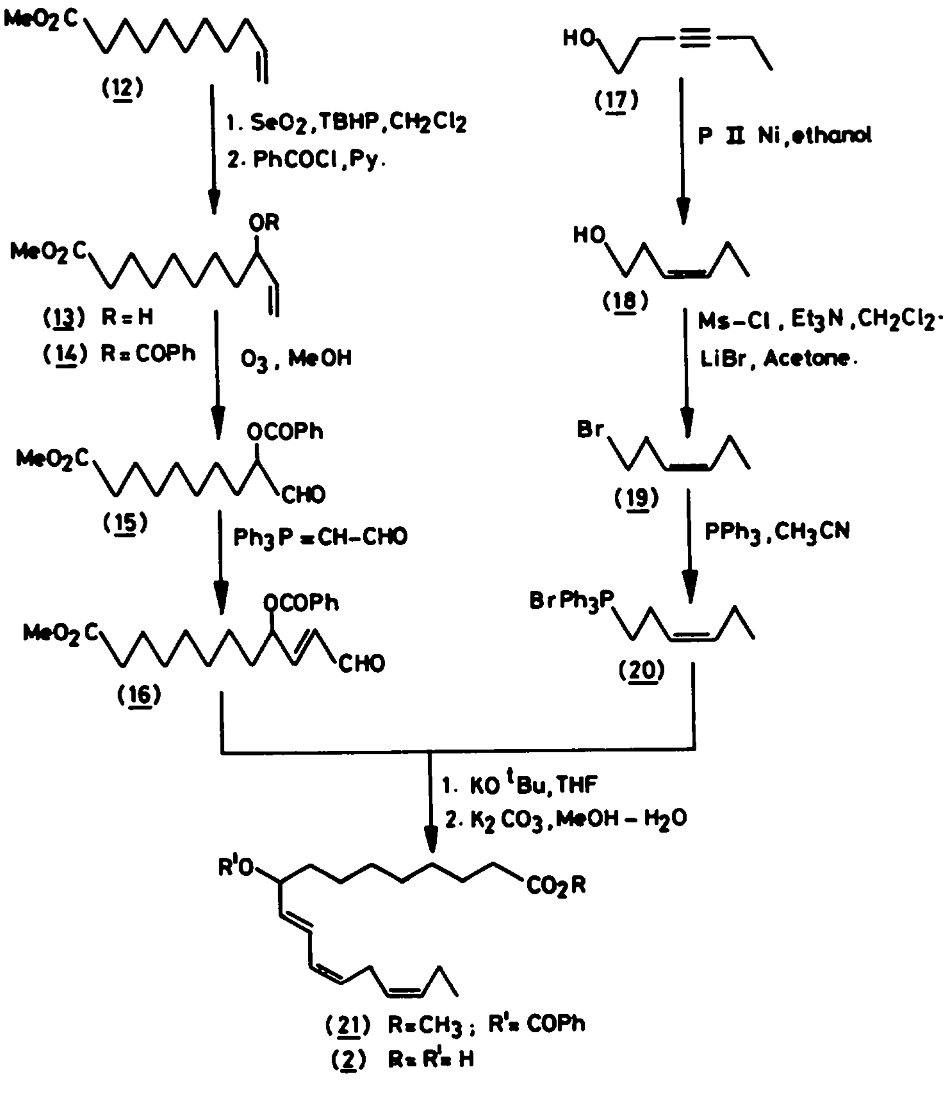


Thus, 1,4-dichloro-but-2-yne (5) on reaction with propionaldehyde[5] in the presence of sodamide in liquid ammonia gave hept-5,6-diyn-3-ol (6). The diacetylenic alcohol 6 on selective reduction with lithium aluminium hydride in ether afforded (E)-hept-4-en-6-yn-3-ol (7) in 72% overall yield. It could be noted that compound 7 not only serves as a handle for the elaboration of aliphatic chain but also as a precursor for cis double bond at the final step to complete the synthesis of 1.

The required 11-bromo undec-9-ynoic acid (10) was prepared from propargyl alcohol and 8-bromo-1-octanoic acid (8). Thus, propargyl alcohol on alkylation with 8 using lithium amide in liquid ammonia[6] gave the hydroxy acid (9). The hydroxyl group in 9 was converted to the bromide (10) using PBr_3 in ether in 76% over all yield. The further chain elaboration was achieved by cuprous chloride catalysed Grignard coupling reaction. Accordingly, 7 on reaction with magnesium bromide salt of 10 using ethyl magnesium bromide as a base and cuprous chloride as catalyst in THF afforded 11 in 55% yield after chromatographic purification. Finally, the cis double bonds were introduced by the partial hydrogenation of triple bonds in 11 using Lindlar catalyst in ethanol to afford 1 in 90% yield which was characterised as its methyl ester.

The strategy for the construction of 2 (Scheme 2) involves the introduction of hydroxy group by selenium dioxide catalysed tert-butyl hydroperoxide followed by protection and cleavage of double bond to give the -hydroxy (protected) aldehyde 15 which was elaborated by successive Wittig reactions.

Scheme - 2

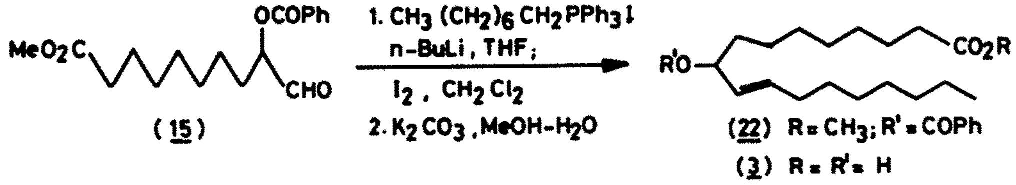


Thus, methyl-10-undecenoate on allylic hydroxylation using SeO_2 and TBHP in dichloromethane[7] afforded the hydroxy ester 13 in 60% yield. The hydroxyl group in 13 was protected by benzoylation using benzoyl chloride in pyridine to afford 14 in 95% yield. The benzoate (14) on ozonolysis in methanol at 0°C afforded the -hydroxy (protected) aldehyde 15 in 75% yield. The aldehyde 15 on treatment with formylmethylenetriphenylphosphorane in refluxing benzene for 3 h gave the , -unsaturated aldehyde (16) in 78% yield.

The required phosphonium bromide (20) was prepared starting from 3-hexyn-1-ol[8] (17). Accordingly, 17 was reduced by using PII Nickel in ethanol[9] to afford the olefinic alcohol (18) which was subsequently converted to the bromide (19) via its mesylate. The bromide (19) was treated with triphenylphosphine in refluxing acetonitrile to afford the phosphonium salt (20) in 70% overall yield. Compound 20 on Wittig reaction with the aldehyde (16) using potassium tert-butoxide in THF afforded the benzoate ester (21) after chromatographic purification. Finally, the saponification of 21 was effected using potassium carbonate in $MeOH-H_2O$ medium to give 2 in 65% yield.

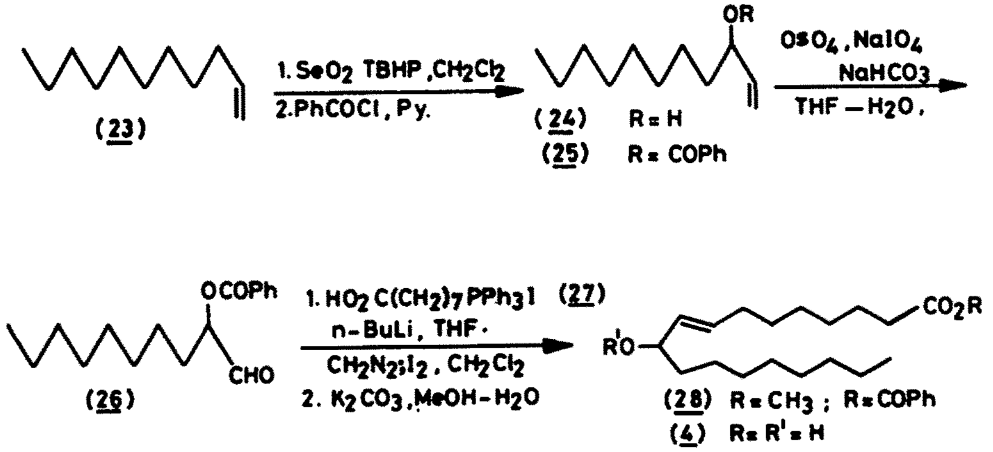
The above strategy was extended for the synthesis of 3 and 4, the two fungitoxic fatty acids. Accordingly, Wittig olefination of the aldehyde (15) using ylide (Scheme 3) generated from n-octyl triphenylphosphonium iodide followed by isomerisation of the crude with iodine in dichloromethane gave 22 in 60% yield. Compound 22, on hydrolysis using K_2CO_3, gave the acid (3) in 70% yield.

Scheme - 3



Similarly, in order to synthesise acid (4), 1-undecene (23) was hydroxylated (Scheme 4) using selinium dioxide and TBHP in dichloromethane to give the hydroxy-alkene (24) in 70% yield. The hydroxyl group in 24 was protected as the benzoate (25). Compound 25, upon treatment with OsO_4 followed by $NaIO_4$ cleavage, gave the aldehyde (26) in 75% yield. The aldehyde (26) was coupled with ylide

Scheme-4



generated from triphenylphosphine salt of 8-iodooctanoic acid (27) followed by esterification and iodine catalysed isomerization gave the compound 28 in 55% yield. Finally, the ester 28 was saponified using K_2CO_3 in MeOH-H_2O to afford 4 in 75% yield.

Thus, compounds 1 to 4 have been synthesized using strategies that have a good potential for making similar biologically active compounds. Currently, the above strategies are being extended for the synthesis of other unsaturated hydroxy fatty acids showing wide variety of biological activity.

Experimental

IR spectra (ν_{max} in cm^{-1}) were recorded in nujol or neat on a Perkin Elmer Model 683 spectrometer with sodium cloride optics. ^{1}H-NMR spectra were obtained on Varian T-60 or Varian FT-80 or Bruker WH-90 spectrometer in $CDCl_3$ or CCl_4 solutions containing TMS as an internal standard with chemical shifts (δ) expressed in PPM down field from TMS. Mass spectra were run on AEI MS 30 double beam mass spectrometer or CEC 21-110 B spectrometer. All solvents and reagents were purified and dried by standard techniques. Column chromatography was performed using silica gel (60-120 mesh Acme). Progress of the reactions was checked by TLC on 0.2 mm layers of silica gel using iodine chamber for visualisation.

Hept-5,6-diyn-3-ol (6)

To a stirred suspension of sodamide (prepared from 13.8 g, 0.6 g atom of sodium) in liquid ammonia (300 ml) was added 1,4-dichloro-2-butyne (**5**) (24.6 g, 0.2 mol) carefully over a period of 15 min. Then propionaldehyde (11.6 g, 0.2 mol) in ether (100 ml) was added and stirred for further 6 hr at -33°. Reaction mixture was quenched with ammonium chloride and excess ammonia was allowed to evaporate. The compound was extracted with ether. The combined etherial layer was washed with water, dried (Na_2SO_4), concentrated and distilled carefully to give **6** (6.91 g) in 32% yield. b.p. 61-62°/1 mm (lit.[5] 57°/0.05 mm).

(E)-Hept-4-en-6-yn-3-ol (7)

To the ice cooled solution **6** (2.7 g, 0.025 mol) in ether (50 ml) was added LAH (0.466 g, 0.0125 mol) in portions and stirred at room temperature for 6 hr. The reaction mixture was poured over ice and extracted with ether. The ether extracts were washed with water, dried (Na_2SO_4) and concentrated to give **7** (2.69 g) in almost quantitative yield. IR (Neat) : 3400 (OH), 3290 ($C\equiv C$-H), 2160 ($C\equiv C$), 965 cm^{-1} (trans double bond); PMR ($CDCl_3$) : δ 1.00 (t, 3H, CH_3), 1.60 (m, 2H, $C\underline{H}_2$), 2.95 (d, 1H, $C\equiv C$-H), 4.10 (m, 1H, $C\underline{H}OH$), 5.25-6.40 (m, 2H, olefinic); Mass : 110 (M^+); Analysis calculated for $C_7H_{10}O$: C, 76.36; H, 9.09; Found : C, 76.28; H, 9.12%.

Undec-11-ol-9-ynoic acid (9)

To the freshly prepared suspension of lithium amide (prepared from lithium 2.8 g, 0.4 g atom) in liquid ammonia (350 ml) was added propargyl alcohol (11.2 g, 0.2 mol) over 15 min and stirred for 1 hr. Then 8-bromo-1-octanoic acid (**8**)[3c] (22.2 g, 0.1 mol) in THF (50 ml) was added and reaction mixture was stirred for additional 8 hr at -33°. Ammonia was allowed to evaporate, the crude reaction mixture was acedified with dilute HCl and extracted with chloroform. The organic layer was washed with water, dried (Na_2SO_4) and concentrated to afford **9** (18.6 g) in almost quantitative yield. m.p. 56.0-56.5° (lit.[6] 56.5-57.0°).

11-Bromo undec-9-ynoic acid (10)

The hydroxy-acid **9** (2.98 g, 0.02 mol) was taken in ether (20 ml) pyridine (5 drops) was added and cooled to 0°. Then PBr_3 (2.98 g, 0.044 mol) in ether (5 ml) was added slowly and stirred for further 3 hr at room temperature. Reaction was quenched with ice and extracted with ether. The etherial layer was washed with water, dried (Na_2SO_4) and concentrated to afford **9** (3.85 g) in 76% yield. IR (Neat) : 3350 br. (COOH); 2210 ($C\equiv C$), 1710 cm^{-1} (C=O); PMR ($CDCl_3$) : δ 1.20-1.80 (m, 10H, 5 x CH_2), 1.95-2.40 (m, 4H, $C\equiv CCH_2$, $C\underline{H}_2$, $C\underline{H}_2CO_2H$), 3.90 (t, 2H, CH_2Br), 9.50 (br.s, CO_2H, exchanges with D_2O); Mass : 261 (M^+); Analysis calculated for $C_{11}H_{17}O_2Br$: C, 50.57; H, 6.51; Br, 30.65; Found : C, 50.45; H, 6.45; Br, 30.50%.

(E)-Octadec-14-en, 16-ol-9,12-diynoic acid (11)

To the stirred suspension of ethyl magnesium bromide [prepared from magnesium (0.72 g, 0.03 g atom) and ethyl bromide (3.27 g, 0.03 mol) in THF (15 ml)] was added alcohol **7** (1.65 g, 0.015 mol) in THF (3 ml) and stirred at room temperature for 3 hr. Then freshly prepared cuprous chloride (0.11 g, 7 mole %) was added and stirred for 15 min. To the resulting yellow coloured suspension, a magnesium bromide salt **10** [prepared from ethyl magnesium bromide (0.120 g, 0.005 g atom of magnesium and ethyl bromide (0.55 g, 0.005 mol) in THF (8 ml) and bromo-acid **10** (1.91 g, 0.005 mol)] in THF (5 ml) was added and stirred the reaction mixture at 55° for 10 hr. The reaction was quenched with aqueous ammonium chloride and extracted with ethyl acetate. The organic layer was washed with water, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to afford **10** (0.780 g) in 55% yield which was characterized as its methyl ester. IR (Neat) : 3440 (OH), 2200 and 2220 ($C{\equiv}C$), 1710 ($C{=}O$), 960 cm^{-1} (trans double bond); PMR ($CDCl_3$) : δ 0.90 (t, 3H, $C\underline{H}_3$), 1.15-1.80 (m, 12H, 6 x CH_2), 2.00-2.42 (m, 4H, $C{\equiv}CCH_2$, $C\underline{H}_2CO_2Me$), 3.27 (m, 2H, $C{\equiv}CCH_2C{\equiv}C$), 3.65 (s, 3H, OCH_3), 4.05 (m, 1H, $C\underline{H}OH$), 5.25-6.20 (m, 2H, olefinic); Mass : 304 (M^+); Analysis calculated for $C_{19}H_{28}O_3$: C, 75.00; H, 9.21; Found : C, 75.05; H, 9.15%.

16-Hydroxy-9Z,12Z,14E-octadecatrienoic acid (1)

A mixture of hydroxy-acid **11** (0.290 g, 0.001 mol) and Lindlar's catalyst (0.100 g) in ethanol (8 ml) containing 2 drops of quinoline was subjected to hydrogenation at atmospheric pressure. After absorption of the required amount of hydrogen (44.8 ml), the suspension was filtered and washed with ethanol. The ethanol was removed, residue was dissolved in ethyl acetate, washed with 2% cold HCl, water dried (Na_2SO_4) and concentrated to afford **1** (0.264 g) in 90% yield which was characterised as its methyl ester. IR (Neat) : 3440 (OH), 1710 ($C{=}O$), 960 and 750 cm^{-1} (olefinic); PMR ($CDCl_3$) : δ 0.90 (t, 3H, CH_3), 1.15-1.75 (m, 12H, 6 x CH_2), 1.90-2.35 (m, 4H, $C{=}CCH_2$, $C\underline{H}_2CO_2Me$), 2.90 (m, 2H, $HC{=}CHC\underline{H}_2CH{=}CH$), 3.65 (s, 3H, OCH_3), 4.05 (m, 1H, $C\underline{H}OH$), 5.15-6.65 (m, 6H, olefinic); Mass : 308 (M^+); Analysis calculated for $C_{19}H_{32}O_3$; C, 74.02; H, 10.38; Found : C, 73.95; H, 10.25%.

Methyl-9-ol-10-undecenoate (13)

A mixture of selenium dioxide (1.1 g, 0.01 mol), *tert*-butyl hydroperoxide (9.76 ml, 0.04 mol) in dichloromethane (40 ml) was stirred at room temperature for 1/2 hr. Then, methyl undecenoate (**12**) (3.96 g, 0.02 mol) in dichloromethane (10 ml) was added dropwise over 10 min at 10-15° and reaction mixture was stirred at room temperature for 48 hr. Dichloromethane was removed, water added and extracted with benzene. The organic layer was successively washed with water, brine, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to afford **13** (2.54 g) in 60% yield. IR (Neat) : 3440 (OH), 1720 cm^{-1} ($C{=}O$); PMR ($CDCl_3$) : δ 1.15-1.75 (m, 12H, 6 x CH_2), 1.95 (br.s, 1H, OH, exchanges with D_2O), 2.25 (t, 2H, $C\underline{H}_2CO_2Me$), 3.65 (s, 3H, OCH_3), 4.05 (m, 1H, $C\underline{H}OH$), 5.05-6.05 (m, 3H, olefinic); Mass : 214 (M^+); Analysis calculated for $C_{12}H_{22}O_3$: C, 67.28; H, 10.28; Found : C, 67.15; H, 10.12%.

Methyl-9-benzoyloxy-10-undecenoate (14)

The compound **13** (2.14 g, 0.01 mol) in dry pyridine was cooled to 0°, benzoyl chloride (1.75 g, 0.0125 mol) was added and stirred for 6 hr at room temperature. The reaction was quenched with ice and extracted with benzene. The combined organic layer was washed successively with cold 5% aqueous HCl, 5% aqueous $NaHCO_3$, brine and dried (Na_2SO_4). Concentration of the solution afforded **14** (2.86 g) in 90% yield. IR (Neat) : 1720 cm^{-1} br. ($C{=}O$); PMR ($CDCl_3$) : δ 1.15-1.75 (m, 12H, 6 x CH_2), 2.25 (t, 2H, $C\underline{H}_2CO_2Me$), 3.65 (s, 3H, OCH_3), 5.00-6.05 (m, 4H, olefinic and $C\underline{H}OBz$), 7.25-7.55 (m, 3H, Ar-H), 7.95-8.20 (m, 2H, Ar-H); Mass : 318 (M^+); Analysis calculated for $C_{19}H_{26}O_4$: C, 71.69; H, 8.17; Found : C, 71.55; H, 8.10%.

Methyl-9-benzoyloxy-9-formylnonanoate (15)

To the cooled solution of **14** (1.5 g, 0.005 mol) in methanol (15 ml) ozone was passed for 20 min. The reaction mixture was quenched with dimethylsulphite (5 ml). Solvent was removed, water was added and extracted with benzene. The organic layer was washed with water, dried (Na_2SO_4) and concentrated to give **15** (0.8 g) in 50% yield. IR (Neat) : 1730 cm^{-1} br. ($C{=}O$); PMR ($CDCl_3$): δ 1.15-1.75 (m, 12H, 6 x CH_2), 2.25 (t, 2H, $C\underline{H}_2CO_2Me$), 3.65 (s, 3H, OCH_3), 5.20 (br. t, 1H, $C\underline{H}OBz$), 7.25-7.60 (m, 3H, Ar-H), 7.95-8.20 (m, 2H, Ar-H), 9.65 (d, 1H, CHO); Mass : 320 (M^+); Analysis calculated for $C_{18}H_{24}O_5$: C, 67.50; H, 7.50; Found : C, 67.42; H, 7.41%.

Methyl-(E)-9-benzolyloxy-11-formyl-10-undecenoate (16)

A mixture of aldehyde **15** (0.320 g, 1 m.mol) and formylmethylenetriphenylphosphorane (0.3 g, 1.1 m.mol) in dry benzene (10 ml) was refluxed for 6 hr. The reaction mixture was cooled and passed through a silica gel column to afford **16** (0.276 g) in 80% yield. IR (Neat) : 1720 (br.) and 1690 (C=O), 960 cm^{-1} (trans double bond); PMR ($CDCl_3$) : δ 1.10-1.95 (m, 12H, 6 x CH_2), 2.25 (t, 2H, $C\underline{H}_2CO_2Me$), 3.65 (s, 3H, OCH_3), 5.7 (m, 1H, $C\underline{H}OBz$), 6.05-6.95 (m, 2H, olefinic), 7.25-7.60 (m, 3H, Ar-H), 7.95-8.20 (m, 2H, Ar-H), 9.55 (d, 1H, CHO); Mass : 346 (M^+); Analysis calculated for $C_{20}H_{26}O_5$: C, 69.36; H, 7.51; Found : C, 69.25; H, 7.45%.

(Z)-3-Hexen-1-ol (18)[19]

To the freshly prepared PII Nickel [prepared from Nickel acetate (6.25 g, 0.025 mol), 1M ethanolic sodium borohydride solution (25 ml, 0.025 mol) and ethylenediamine (4.50 g, 0.075 mol)] in ethanol (75 ml) was added alcohol **17** (1.96 g, 0.02 mol) and subjected to hydrogenation at atmospheric pressure. After absorbing the required amount of hydrogen gas (480 ml), the reaction mixture was filtered over charcoal bed. The filtrate was concentrated and the residue was dissolved in ether, washed with water and dried (Na_2SO_4). Concentration of the solution afforded **18** (1.5 g) in 75% yield.

(Z)-1-Bromo-2-hexene (19)

To a cooled mixture of alcohol **18** (1.0 g, 0.01 mol) and triethylamine (2.9 g, 0.02 mol) in dichloromethane (10 ml) was added methanesulfonyl chloride (1.5 g, 0.015 mol) and stirred for 2 hr at room temperature. Reaction was quenched with ice, extracted with dichloromethane, washed with water, dried (Na_2SO_4) and concentrated.

The above crude mesylate was taken in acetone (25 ml), lithium bromide (2.6 g, 0.03 mol) was added and stirred for 12 hr at room temperature. Acetone was removed, residue was dissolved in water and extracted with ether. The combined etherial layer was washed with water, dried (Na_2SO_4) and concentrated to afford bromide **19** (1.23 g) in 76% overall yield. PMR (CCl_4) : 1.02 (t, 3H, CH_3), 1.70-2.20 (m, 2H, $C\underline{H}_2CH_3$), 2.4-2.8 (m, 2H, CH_2), 3.01 (t, 2H, CH_2Br), 4.95-5.60 (m, 2H, olefinic).

(Z)-1-Hex-2-en triphenylphosphonium bromide (20)

A mixture of bromide **19** (0.815 g, 5 m.mol) and triphenylphosphine (1.44 g, 5.5 m.mol) in dry benzene (10 ml) was refluxed for 36 hr. Benzene was removed and the residue was repeatedly washed with dry ether to afford **20** (2.1 g) in quantitative yield as a glassy material.

Methyl (10E,12Z,15Z)-9-benzoyloxy octadecatrienoate (21)

To a cooled (-5°) suspension of Wittig salt **20** (0.425 g, 1 m.mol) in dry THF (10 ml) was added potassium tert. butoxide (0.112 g, 1 m.mol) and stirred for 10 min. To the resulting yellow coloured suspension, aldehyde **16** (0.115 g, 0.33 m.mol) in THF (3 ml) was added and stirred the reaction mixture at 20° for 8 hr. Then, the reaction was quenched with ammonium chloride and extracted with benzene. The organic layer was washed with water, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to afford **21** (0.076 g) in 55% yield. IR (Neat) : 1720 br. (C=O), 960 and 750 cm^{-1} (olefinic); PMR ($CDCl_3$) : δ 0.90 (t, 3H, CH_3), 1.10-1.95 (m, 12H, 6 x CH_2), 2.05-2.40 (m, 4H, 2 x CH_2), 2.85 (m, 2H, $CH{=}CHC\underline{H}_2CH{=}CH$), 3.65 (s, 3H, OCH_3), 5.20-6.80 (m, olefinic [6 protons], $C\underline{H}OBz$), 7.30-7.60 (m, 3H, Ar-H), 7.95-8.20 (m, 2H, Ar-H); Mass : 412 (M^+); Analysis calculated for $C_{26}H_{36}O_4$: C, 75.72; H, 8.73; Found : C, 75.60; H, 8.61%.

9-Hydroxy-10E,12Z,15Z-octadecatrienoic acid (2)

A mixture of **21** (0.103 g, 0.25 m.mol) and potassium carbonate (0.207 g, 1.5 m.mol) in methanol-water medium (10 ml, 4:1) was stirred for 12 hr at room temperature. Then the reaction mixture was carefully acedified with methanolic acetic acid and extracted with ethylacetate. The organic layer was washed with water, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to afford **2** (0.047 g) in 65% yield which was characterised as its methyl ester. IR (Neat) : 3440 (OH) and 1720 cm^{-1} (C=O); PMR ($CDCl_3$) : δ 0.90 (t, 3H, CH_3), 1.15-1.85 (m, 12H, 6 x CH_2), 2.05-2.40 (m, 4H, $C\underline{H}_2CH{=}CH$, $C\underline{H}_2CO_2Me$), 2.85 (m, 2H, $CH{=}CHC\underline{H}_2CH{=}CH$), 5.15-6.75 (m, 6H, olefinic); Mass : 308 (M^+); Analysis calculated for $C_{19}H_{32}O_3$: C, 74.02; H, 10.38;

Found : C, 73.97; H, 10.24%.

Methyl-9-benzoyloxy-10E-octadecaenoate (23)

To the stirred suspension of n-octyltriphenylphosphonium iodide (1.3 g, 2.5 m.mol) in THF (15 ml) was added solution of n-butyl lithium (1.1 ml, 2.1 M hexane, 2.34 m.mol) at -78° and the mixture was stirred for 20 min at that temperature. Solution of the aldehyde (15) (0.500 g, 1.5 mmol) in THF (10 ml) was added for a period of 5 min and reaction was allowed to warm to room temperature and stirred for additional 3 hr. Then the reaction was quenched with ammonium chloride and extracted with benzene. The organic layer was washed with water, dried (Na_2SO_4) and concentrated. The crude product was dissolved in dichloromethane (20 ml) and after addition of iodine (50 mg), the mixture was irradiated with lamp for 1 hr. The mixture was washed with saturated hypo solution. The organic layer was dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to afford **23** (0.3 g) in 60% yield. IR (Neat) : 1735, 1725 (C=O), 760 cm^{-1} (trans double bond); PMR ($CDCl_3$) : δ 0.9 (t, 3H, CH_3), 1.10-1.85 (m, 22H, 11 x CH_2), 2.00-2.40 (m, 4H, $C=CHC\underline{H}_2$, $C\underline{H}_2CO_2Me$) 3.65 (s, 3H, OCH_3), 5.25-6.00 (m, 3H, olefinic, $C\underline{H}OBz$), 7.30-7.60 (m, 3H, Ar-H), 7.95-8.15 (m, 2H, Ar-H); Mass : 416 (M^+); Analysis calculated for $C_{26}H_{40}O_4$: C, 75.00; H, 9.61; Found : C, 75.15, H, 9.55%.

9-Hydroxy-10E-octadecenoic acid (3)

To the solution of compound **23** (0.100 g, 0.24 m.mol) in methanol-water (10 ml, 4:1) was added K_2CO_3 (0.17 g, 0.4 m.mol) and the mixture was stirred for 8 hr at room temperature. Methanol was removed under reduced pressure. The residue was acidified with 5% HCl and extracted with ether. The combined etherial layer was washed with water, dried (Na_2SO_4) and concentrated. The crude product upon chromatographic purification gave **3** (0.050 g) in 70% yield. IR (Neat) : 3440 (OH, COOH), 1710 cm^{-1} (C=O); PMR ($CDCl_3$) : δ 0.90 (t, 3H, CH_3), 1.20-1.80 (m, 22H, 11 x CH_2), 2.10-2.40 (m, 4H, $C=CHC\underline{H}_2$, $C\underline{H}_2CO_2H$), 4.15 (m, 1H, $C\underline{H}OH$), 5.10-5.50 (m, 2H, olefinic); Mass: 298 (M^+); Analysis calculated for $C_{18}H_{34}O_3$: C, 72.48; H, 11.41; Found : C, 72.35; H, 11.25%.

3-Hyderoxy-1-undecene (24)

A mixture of selenium dioxide (0.275 g, 2.5 m.mol), tert-butyl hydroperoxide (2.5 ml, 10 m.mol) in dichloromethane (10 ml) was stirred at 25° for 1/2 hr. 1-Undecene (**23**) (0.77 g, 5 m.mol) in dichloromethane (5 ml) was added dropwise at 10-15° and reaction mixture was stirred at room temperature for 24 hr. Dichloromethane was evaporated, water added and extracted with benzene. The benzene layer was successively washed with water, brine, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to afford **24** (0.59 g) in 70% yield. IR (Neat) : 3440 cm^{-1} (OH); PMR ($CDCl_3$) : δ 0.90 (dist.t, 3H, CH_3), 1.15-1.80 (m, 14H, 7 x CH_2), 2.00 (br.s, 1H, OH, exchanges with D_2O), 4.10 (m, 1H, $C\underline{H}OH$), 5.10-6.30 (m, 3H, olefinic); Analysis calculated for $C_{11}H_{22}O$: C, 77.65; H, 12.94; Found : C, 77.4; H, 12.9%.

3-Benzoyloxy-1-undecene (25)

The compound **24** (0.667 g, 3.92 m.mol) in pyridine (5 ml) was cooled to 0°, benzoylchloride (0.83 g, 6 m.mol) was added and stirred for 6 hr at room temperature. The reaction was quenched with ice and extracted with benzene. The combined organic extractions were washed with successively with cold 5% aqueous HCl, 5% aqueous $NaHCO_3$, brine and dried (Na_2SO_4). Concentration of the solution afforded **25** (0.93 g) in 87% yield. IR (Neat) : 1720 cm^{-1}, br (C=O); PMR ($CDCl_3$) : δ 0.90 (dist.t, 3H, CH_3), 1.15-1.80 (m, 14H, 7 x CH_2), 5.00-6.30 (m, 4H, olefinic, $C\underline{H}OBz$), 7.25-7.55 (m, 3H, Ar-H), 7.95-8.20 (m, 2H, Ar-H); Mass : 274 (M^+); Analysis calculated for $C_{18}H_{26}O_2$: C, 78.83; H, 9.49; Found : C, 78.62; H, 9.42%.

2-Benzoyloxy-1-decanal (26)

Catalytic amount of OsO_4 was added to a mixture of compound **25** (0.525 g, 1.9 m.mol) in THF-water mixture (14 ml, 10:4). After 15 min, $NaHCO_3$ (0.320 g, 3.8 m.mol) was added and cooled to 0°, $NaIO_4$ (1.01 g, 4.7 m.mol) was added in portions and stirred for 3 hr at room temperature. The reaction mixture was filtered, THF was removed and extracted with dichloromethane. The combined organic layer was washed with water, aqueous $NaHCO_3$, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to afford **26** (0.4 g) in 75% yield. IR (Neat) : 1720 cm^{-1}, br.(C=O), PMR ($CDCl_3$) : δ 0.90 (dist.t, 3H, CH_3), 1.15-1.80 (m, 14H, 7 x CH_2), 5.15 (t, 1H, $C\underline{H}OBz$), 7.25-7.60 (m, 3H, Ar-H), 7.95-8.20 (m, 2H, Ar-H), 9.60 (s, 1H, CHO); Mass : 276 (M^+); Analysis calculated for $C_{17}H_{24}O_3$: C, 73.91; H, 8.69; Found : C, 74.0; H, 8.41%.

8-Carboxyl-1-octanetriphenylphosphonium iodide (27)

A mixture of 8-bromo-1-octanoic acid[3c] (4.46 g, 0.02 mol) and sodium iodide (6.0 g, 0.04 mol) in acetonitrile (50 ml) was refluxed for 6 hr. Acetonitrile was removed, water added and extracted with benzene. The combined benzene layer was washed with hypo solution, water, dried (Na_2SO_4) and concentrated to give 8-iodo-1-octanoic acid (5.2 g) in almost quantitative yield.

A mixture of 8-iodo-1-octanoic acid (5.2 g, 0.02 mol) and triphenylphosphine (5.24 g, 0.02 mol) in benzene was refluxed for 12 hr under nitrogen atmosphere. The benzene was removed and product was repeatedly washed with dry pet. ether to give colourless glassy material (9.47 g) in almost quantitative yield.

Methyl-10-benzoyloxy-8E-octadecenoate (28)

To the suspension of Wittig salt **27** (1.064 g, 2 m.mol) in THF (10 ml) and HMPA (5 ml) was added n-butyl lithium (0.256 g, 2 m.mol) dropwise at -78° under nitrogen atmosphere. After 20 min, the aldehyde **26** (0.278 g, 1 m.mol) was added at -78°C and the reaction mixture was allowed to come to room temperature and stirred for further 6 hr. The reaction was quenched with ammonium chloride, acidified with dil. HCl and extracted with chloroform. The combined chloroform extractions were washed with water, dried (Na_2SO_4) and concentrated. The crude acid was treated with etherial diazomethane at 0° to get the corresponding methyl ester. The ester was isomerised with $I_2/h\nu$ in benzene. The reaction mixture was further diluted with benzene, washed with hypo solution, water, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to afford **28** (0.232 g) in 55% overall yield. IR (Neat) : 1720 (C=O), 960 cm^{-1}d (trans double bond); PMR ($CDCl_3$) :δ 0.85 (dist.t, 3H, CH_3), 1.10-1.85 (m, 22H, 11 x CH_2), 2.00-2.40 (m, 4H, $CH{=}CHC\underline{H}_2$, $C\underline{H}_2CO_2Me$), 3.65 (s, 3H, OCH_3), 5.25-6.00 (m, 3H, olefinic, $C\underline{H}OBz$), 7.30-7.60 (m, 3H, Ar-H), 7.95-8.15 (m, 2H, Ar-H); Mass : 416 (M^+); Analysis calculated for $C_{26}H_{40}O_4$: C, 75.00; H, 9.61; Found: C, 75.15; H, 9.55%.

10-Hydroxy-8E-octadecenoic acid (4)

A mixture of ester **28** (0.100 g, 0.24 m.mol) and K_2CO_3 (0.34 g, 0.8 m.mol) in aqueous methanol (10 ml, 8:2) was stirred at room temperature for 12 hr. It was diluted with water, carefully acidified with dilute HCl and extracted with ether. The etherial layer was washed with water, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to afford **4** (0.053 g) in 75% yield. IR (Neat) : 3450 (OH, COOH), 1700 cm^{-1} (C=O); PMR ($CDCl_3$) : δ 0.90 (dist.t, 3H, CH_3), 1.20-1.80 (m, 22H, 11 x CH_2), 2.10-2.40 (m, 4H, $CH{=}CHC\underline{H}_2$, $C\underline{H}_2CO_2H$), 4.15 (m, 1H, $C\underline{H}OH$), 5.10-5.50 (m, 2H, olefinic); Mass : 298 (M^+); Analysis calculated for $C_{18}H_{34}O_3$: C, 72.48; H, 11.41; Found : C, 72.25; H, 11.15%.

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