CHAPTER II

EXPERIMENTAL

General methods

The NMR spectra were recorded in $CDCl_3$ solution on a Bruker Model ACF 200 spectrometer operated at 200.13 MHz for ^1H and 50.32 MHz for ^{13}C- nuclei. ^1H - NMR and ^{13}C - NMR chemical shifts in $CDCl_3$ are given relative to solvent peak at 7.24 and 77.0 parts per million (ppm.) respectively. The IR absorption spectra were obtained with a Nicolet Impact 410 Fourier Transform Infrared Spectrophotometer using KBr or NaCl cell on neat samples. Mass spectra were determined using a Fisons Instrument Mass spectrometer Model Trio 2000 GC - MS in Electron Impact (EI) mode at 70 ev. Analytical TLC was performed on precoated (0.25mm.) silica gel 60 F-254 plates purchased from Merck and the TLC spots were visualized under vapor iodine. Purification of products was accomplished via Merck silica gel (No. 9385) flash column chromatography. Elemental Analysis were carried out at Chulalongkorn Research Equipment Centre on a Perkin Elmer Elemental Analyzer model 2400 CHNS/O.

All reactions were conducted under dry nitrogen and stirred magnetically. All solvents for the reactions were of reagent grade and were dried and distilled immidiately before use as follows : diethyl ether and tetrahydrofuran (THF) from sodium / benzophenone, dichloromethane from calcium chloride. Other reagents were obtained from Aldrich, Fluka and Merck and were used without further purification, unless otherwise stated. Starting material was geraniol (*trans*-3,7-Dimethyl-2,6-octadien-1-ol) purum ~96% GC which was obtained from Fluka.

Preparation of 3,7-Dimethyl-2,6-octadienyl tetrahydropyranyl ether (2)

To a stirred solution of (1.76 g, 11.43 mmol) of geraniol **(1)** and (1.84 g, 21.87 mmol) of dihydropyran in 25 ml of dichloromethane at room temperature was added (0.22 g, 1.16 mmol) of *p*-toluenesulfonic acid monohydrate, and the mixture was maintained at room temperature for 2 hours. The equilibrium can be shifted toward product by adding excess finely powdered anhydrous K_2CO_3 and stirring the reaction mixture at room temperature. As the acid concentration gradually diminished, the reaction went to completion. After that the solvents were removed in vacuo and the resultant oil was column chromatographed (silica gel, 30%Chloroform-Hexane) to obtain **(2)** (2.62g, 96% yield based on **(1)**) as a colourless oil. (R_f = 0.32; siliga gel / Hexane-Chloroform, 3:2)

ν_{max} (neat) / cm^{-1} 2937(s), 2866(m), 1653(w), 1454(m), 1378(m), 1123(m), 1029(s)

^{1}H - NMR ($CDCl_3$) δ 1.39-1.88 (m, 15H, vinyl-CH_3(×3), CH_2(×3)), 1.95-2.16 (m, 4H, 4-H, 5-H), 3.41-4.25 (m, 4H, 1-H, CH_2-O), 4.56-4.62 (m, 1H, O-CH-O), 4.99-5.12 (m, 1H, 6-H), 5.26-5.39 (m, 1H, 2-H)

^{13}C - NMR ($CDCl_3$) δ 16.4 (CH_3), 17.7 (CH_3), 19.6 (CH_2), 25.5 (CH_2), 25.7 (CH_3), 26.3 (CH_2), 30.7 (CH_2), 39.6 (CH_2), 62.3(CH_2-O),63.6(CH_2-O),97.7(O-CH-O), 120.5 (CH), 124.0 (CH), 131.6 (C), 140.2 (C)

m/z (EI) 136 (12), 85 (100), 69 (53) and 41 (27)

Preparation of 2,6-Dimethyl-8-(2-tetrahydropyranyloxy)-2,6-octadien-1-ol (3)

A mixture of **(2)** (2.56 g, 10.76 mmol), selenium dioxide (0.59 g, 5.32mmol), pyridine (1.80 ml, 22.37 mmol) and ethanol (25 ml) was heated under reflux for 4 hours. Then the solvent was removed in vacuo and the residue extracted with ether. The combined extracts were washed with 5% HCl, 5% $NaHCO_3$, water, brine, dried ($MgSO_4$) and evaporated to give a crude oil. This oil was purified by preparative TLC on silica gel (Hexane-Ether, 3:2, as eluent) to give **(3)** (0.65 g, 48 % yield based on selinium dioxide) as a yellow oil. (R_f = 0.16; siliga gel / Hexane-Ether, 3:2)

ν_{max} (neat) / cm^{-1} 3629-3106(OH)(br), 2942(s), 2866(m), 1658(w), 1454(m), 1383(m), 1119(m), 1024(s)

^1H - NMR ($CDCl_3$) δ 1.29-1.82 (m, 12H, vinyl-CH_3 (×2), CH_2(×3)), 1.88-2.19 (m, 4H, 4-H, 5-H), 2.63 (s, broad, 1H, OH), 3.33-4.18 (m, 6H, 1-H, 8-H, CH_2-O), 4.49-4.56 (m, 1H, O-CH-O), 5.18-5.31 (m, 2H, 3-H, 7-H)

^{13}C - NMR ($CDCl_3$) δ 13.6 (CH_3), 16.3 (CH_3), 19.4 (CH_2), 25.4 (CH_2), 25.7 (CH_2), 30.5 (CH_2), 39.1 (CH_2), 62.1 (CH_2-O), 63.5 (CH_2-O), 68.4 (CH_2-O), 97.6 (O-CH-O), 120.7 (CH), 125.1 (CH), 135.1 (C), 139.8 (C)

m/z (EI) 85 (100), 67(17) and 43 (39)

Preparation of 2,6-Dimethyl-2,6-octadien-1,8-diol (4)

To a stirred solution of **(3)** (0.65 g, 2.56 mmol) in 10 ml of methanol was added *p*-toluenesulfonic acid monohydrate (5.40 mg, 0.03 mmol). The reaction mixture was stirred at 0 °C for 1 hour, and then was stirred at room temperature for 3 hours. The solvent was removed in vacuo and the crude oil was purified by flash chromatography eluting with 40% Ethyl acetate / Hexane to afford **(4)** (0.35 g, 80 % yield based on **(3)**) as a yellow oil. (R_f = 0.15; siliga gel / Ethyl acetate-Hexane, 1:1) (Found : C, 69.50; H, 10.46 $C_{10}H_{18}O_2$ requires C, 70.55; H, 10.66 %)

ν_{max} (neat) / cm^{-1} 3603-3034 (OH)(br), 2915(m), 2864(m), 1658(w), 1441(m), 1380(m), 1000(s)

^1H - NMR ($CDCl_3$) δ 1.55 (s, 3H, vinyl-CH_3), 1.57 (s, 3H, vinyl-CH_3), 1.91-2.16 (m, 4H, 4-H, 5-H), 3.45 (s, broad, 2H, OH (×2)), 3.85 (s, 2H, 1-H), 4.02 (d , 2H, 8-H), 5.27 (t, 2H, 3-H, 7-H)

^{13}C - NMR ($CDCl_3$) δ 13.7 (CH_3), 16.1 (CH_3), 25.4 (CH_2), 39.0 (CH_2), 58.9 (CH_2-O), 68.2 (CH_2-O), 123.9 (CH), 124.9 (CH), 134.9 (C), 138.1 (C)

m/z (EI) 101(22), 83 (57), 70 (100), 55 (76) and 41 (24)

Preparation of Ethyl-2-ethoxycarbonyl-5,9-dimethyldeca-4,8-dienoate (6)

To a solution of geraniol **(1)** (1.32 g, 8.57 mmol) and triphenylphosphine (4.50 g, 17.16 mmol) in dichloromethane was added carbon tetrachloride (2.69 g,

17.47 mmol) and the mixture was stirred at room temperature for 15 minutes. After the mixture was heated at reflux temperature for 4 hours. The solvent was evaporated under reduced pressure and the residue was extracted with n-Hexane to obtain crude geranyl chloride **(5)** as a pale yellow oil which was used without purification for the next reaction.

To a mixture of NaH (60% oil suspension; 17.25 mmol, 0.69 g washed with THF) in THF (10 ml), was added diethyl malonate (6.6 ml, 43.47 mmol) in THF (10 ml) at 0 °C under nitrogen. The mixture was stirred at room temperature for 15 minutes. Geranyl chloride **(5)** was then added and the mixture was heated under reflux for 4 hours. The mixture was cooled and extracted with Et_2O. The combined extracts were washed with water and brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was chromatographed on a silica gel column using 1:20 Ethyl acetate/ Hexane as eluent to afford **(6)** (2.06 g, 81 % yield based on **(1)**) as a colourless oil. (R_f = 0.44; siliga gel / Ethyl acetate-Hexane,0.5:4.5) (Found : C, 68.73; H, 9.47 $C_{17}H_{28}O_4$ requires C, 68.89; H, 9.52 %)

ν_{max} (neat) / cm^{-1} 2974(m), 2924(m), 1733(C=O)(s), 1446(m), 1380(m), 1237(m), 1149(m)

^1H - NMR ($CDCl_3$) δ 1.22 (t, 6H, $CO_2CH_2\underline{CH_3}$ (×2)), 1.57 (s, 3H, vinyl-CH_3), 1.61 (s, 3H, vinyl -CH_3), 1.66 (s, 3H, vinyl -CH_3), 1.86-2.10 (m, 4H, 6-H, 7-H), 2.54 (t, 2H, 3-H), 3.31 (t, 1H, 2-H), 4.15 (q, 4H, CO_2CH_2(×2)), 5.02-5.12 (m, 2H, 4-H, 8-H)

^{13}C - NMR ($CDCl_3$) δ 14.2 (CH_3) (×2), 16.0 (CH_3), 17.8 (CH_3), 25.6 (CH_3), 26.7 (CH_2), 27.6 (CH_2), 39.8 (CH_2), 52.1 (CH), 61.2 (CH_2-O)(×2), 119.3 (CH), 124.1 (CH), 131.2 (C), 138.6 (C), 169.4 (C=O) (×2)

m/z (EI) 253(11), 173(33), 153 (47), 69(53) and 41 (100)

Preparation of Methyl-3,3-Di(ethoxycarbonyl)-6,10-dimethylundeca-5,9-dienoate (7)

To a solution of NaH (60% oil suspension; 7.50 mmol, 0.30 g washed with THF) in THF (10 ml), was added **(6)** (1.11 g, 3.75 mmol) in THF (10 ml) at 0 °C under nitrogen. The mixture was stirred at room temperature for 15 minutes.

Methyl bromoacetate (1.14 g, 7.45 mmol) was then added and the mixture was heated under reflux for 4 hours. The mixture was cooled and extracted with diethyl ether. The combined extracts was washed with water and brine, dried ($MgSO_4$), filtered and concentrated under reduce pressure. The resulting residue was purified by flash column chromatography eluting with 1:10 Ethyl acetate / Hexane to give **(7)** (1.08 g, 78 % yield based on **(6)**) as a pale yellow oil. (R_f = 0.48; siliga gel / Ethyl acetate-Hexane, 1: 4) (Found : C, 65.23; H, 8.44 $C_{20}H_{32}O_6$ requires C, 65.19; H, 8.75 %)

ν_{max} (neat) / cm^{-1} 2975(m), 2929(m), 1736 (C=O)(s), 1433(m), 1350(m), 1172(m)

^1H - NMR ($CDCl_3$) δ 1.19 (t, 6H, $CO_2CH_2\underline{CH_3}$ (×2)), 1.57 (s, 3H, vinyl-CH_3), 1.59 (s, 3H, vinyl -CH_3), 1.61 (s, 3H, vinyl -CH_3), 1.81 - 2.02 (m, 4H, 7-H, 8-H), 2.65 (d, 2H, 4-H), 2.84 (s, 2H, 2-H), 3.57 (s, 3H, CO_2CH_3), 4.08 (q, 4H, CO_2CH_2 (×2)), 4.81-5.02 (m, 2H, 5-H, 9-H)

^{13}C - NMR ($CDCl_3$) δ 14.2 (CH_3) (×2), 16.0 (CH_3), 17.9 (CH_3), 25.6 (CH_3), 26.5 (CH_2), 31.7 (CH_2), 36.8 (CH_2), 39.7 (CH_2), 51.2(CH_3-O), 55.7(C), 61.3 (CH_2-O) (×2), 117.7 (CH), 123.9 (CH), 131.4(C), 139.8 (C), 169.9(C=O) (×2), 171.1 (C=O)

m/z (EI) 239 (33), 193 (25), 165 (80), 69 (66) and 41 (100)

Preparation of Methyl-4,4-Di(ethoxycarbonyl)-7,11-dimethyldodeca-6,10-dienoate (8)

By a method similar to that used in the preparation of **(7)**, **(8)** was obtained from NaH (60% oil suspension; 6.50 mmol, 0.26 g washed with THF), **(6)** (0.97 g, 3.28 mmol) and Methyl 3-bromopropionate (1.09 g, 6.53 mmol). Chromatographic purification (silica gel, Ethyl acetate - Haxane, 1:10) of the crude product afforded **(8)** (0.92 g, 73 % yield based on **(6)**) as a pale yellow oil. (R_f = 0.46; siliga gel / Ethyl acetate-Hexane, 1: 4) (Found : C, 65.96; H , 8.88 $C_{21}H_{34}O_6$ requires C, 65.94; H, 8.96 %)

ν_{max} (neat) / cm^{-1} 2980(m), 2924(m), 1730 (C=O)(s), 1444(m), 1362(m), 1177(m)

^{1}H - NMR ($CDCl_3$) δ 1.17 (t, 6H, $CO_2CH_2\underline{CH_3}$ (×2)), 1.52 (s, 3H, vinyl-CH_3), 1.56 (s, 3H, vinyl-CH_3), 1.61 (s, 3H, vinyl -CH_3), 1.85-2.03 (m, 4H, 8-H, 9-H), 2.18 (m, 2H, 3-H), 2.23 (m, 2H, 2-H), 2.55 (d, 2H, 5-H), 3.59 (s, 3H, CO_2CH_3), 4.12 (q, 4H, CO_2CH_2 (×2)), 4.83-5.04 (m, 2H, 6-H, 10-H)

^{13}C - NMR ($CDCl_3$) δ 13.9 (CH_3) (×2), 16.7 (CH_3), 18.0 (CH_3), 25.9 (CH_3), 26.8 (CH_2), 27.9 (CH_2), 29.5 (CH_2), 31.4 (CH_2), 40.1 (CH_2), 51.9 (CH_3-O), 57.2 (C), 61.4 (CH_2-O) (×2), 117.3 (CH), 124.2 (CH), 131.6 (C), 139.7 (C), 171.1 (C=O) (×2), 173.5 (C=O)

m/z (EI) 246 (62), 173 (78), 69 (56) and 41 (100)

Preparation of Methyl -5,5-Di(ethoxycarbonyl)-8,12-dimethyltrideca-7,11-dienoate (9)

The reaction conditions for the preparation of (7) were followed using (6) (0.84 g, 2.84 mmol), NaH (60 % oil suspension; 5.75 mmol, 0.23 g washed with THF) and Methyl 4 - iodobutyrate (1.30 g, 5.70 mmol). The crude product was purified by column chromatography (silica gel, Ethyl acatate - Haxane, 1:10) to give (9) (0.77 g, 68 % yield based on (6)) as a colourless oil. (R_f = 0.45; siliga gel / Ethyl acetate-Hexane, 1 :4) (Found : C, 66.55; H, 8.88 $C_{22}H_{36}O_6$ requires C, 66.64; H, 9.15 %)

ν_{max} (neat) / cm^{-1} 2975(m), 2929(m), 1730 (C=O)(s), 1444(m), 1367(m), 1172(m)

^{1}H - NMR ($CDCl_3$) δ 1.11 (t ,6H ,$CO_2CH_2\underline{CH_3}$ (×2)),1.31-1.40 (m ,2H ,3-H), 1.46 (s, 3H, vinyl-CH_3), 1.49 (s, 3H, vinyl-CH_3), 1.51 (s, 3H, vinyl-CH_3), 1.67-1.78 (m, 2H, 4-H), 1.81-1.98 (m, 4H, 9-H,10-H), 2.14 (t, 2H, 2-H), 2.48 (d, 2H, 6-H), 3.52 (s, 3H, CO_2CH_3), 4.03 (q, 4H, CO_2CH_2 (×2)), 4.78-4.96 (m, 2H, 7-H, 11-H)

^{13}C - NMR ($CDCl_3$) δ 13.9 (CH_3) (×2), 16.0 (CH_3), 17.5 (CH_3), 19.6 (CH_2), 25.4 (CH_3), 26.3 (CH_2), 30.6 (CH_2), 31.4 (CH_2), 33.9 (CH_2), 39.8 (CH_2), 51.2 (CH_3-O), 57.2 (C), 60.9 (CH_2-O) (×2), 117.6 (CH), 123.9 (CH), 131.1 (C), 138.7 (C), 171.1 (C=O) (×2), 173.1 (C=O)

m/z (EI) 69 (62) and 41(100)

Preparation of Methyl-6,6-Di(ethoxycarbonyl)-9,13-dimethyltetradeca-8,12-dienoate (10)

By a method similar to that used in the preparation of **(7)**, **(10)** was obtained from NaH (60% oil suspension; 4.50 mmol, 0.18 g washed with THF), **(6)** (0.66 g, 2.23 mmol) and Methyl 5- bromovalerate (0.87 g, 4.46 mmol). Chromatographic purification (silica gel, Ethyl acetate-Hexane, 1:10) of the crude product afforded **(10)** (0.62 g, 67 % yield based on **(6)**) as a pale yellow oil. (R_f = 0.44; siliga gel / Ethyl acetate - Hexane, 1: 4) (Found : C, 67.30; H, 9.74 $C_{23}H_{38}O_6$ requires C, 67.29; H, 9.33 %)

ν_{max} (neat) / cm^{-1} 2955(m), 2929(m), 1736 (C=O)(s), 1439(m), 1372(m), 1178(m)

^{1}H - NMR ($CDCl_3$) δ 1.03-1.25 (m, 8H, $CO_2CH_2\underline{CH_3}$ (×2), 4-H), 1.42 -1.57 (m, 8H, 3-H, vinyl-CH_3 (×2)), 1.64 (s, 3H, vinyl -CH_3), 1.72 -1.88 (m, 2H, 5-H), 1.86-2.06 (m, 4H, 10-H, 11-H), 2.15-2.27 (m, 2H, 2-H), 2.54 (d, 2H, 7-H), 3.58 (3.66) (s, 3H, CO_2CH_3), 3.97-4.16 (m, 4H, CO_2CH_2(×2)), 4.81-5.04 (m, 2H, 8-H, 12-H)

^{13}C - NMR ($CDCl_3$) δ 14.0 (CH_3) (×2), 16.0 (CH_3), 17.6 (CH_3), 23.6 (CH_2), 25.1 (CH_2), 25.6 (CH_3), 26.5 (CH_2), 31.0 (CH_2), 31.8 (CH_2), 33.7(34.0) (CH_2), 39.8 (CH_2), 51.3 (52.2) (CH_3-O), 57.5 (C), 60.1 (61.0) (CH_2-O) (×2), 117.6 (CH), 124.0 (CH), 131.3 (C), 138.9 (C), 171.4 (172.0) (C=O) (×2), 173.3(173.7) (C=O)

m/z (EI) 69 (73) and 41 (100)

Preparation of Methyl-7,7-Di(ethoxycarbonyl)-10,14-dimethylpentadeca-9,13-dienoate (11)

The reaction conditions for the preparation of **(7)** were followed using **(6)** (0.58 g, 1.96 mmol), NaH (60% oil suspension; 4.00 mmol, 0.16 g washed with THF) and Methyl 6 - bromocaproate (0.82 g, 3.92 mmol). The crude product was purified by column chromatography (silica gel, Ethyl acetate - Hexane, 1:10) to give **(11)** (0.52 g, 63 % yield based on **(6)**) as a colourless oil. (R_f = 0.46; siliga gel / Ethyl acetate-Hexane, 1: 4) (Found : C, 67.84; H, 9.35 $C_{24}H_{40}O_6$ requires C, 67.90; H, 9.50 %)

ν_{max} (neat) / cm^{-1} 2934(m), 2863(m), 1736 (C=O)(s), 1439(m), 1372(m), 1178(m)

^1H - NMR ($CDCl_3$) δ 1.01-1.39 (m, 10H, $CO_2CH_2\underline{CH_3}$ (×2), 4-H, 5-H), 1.47-1.58 (m, 8H, 3-H, vinyl-CH_3 (×2)), 1.62 (s, 3H, vinyl-CH_3), 1.73-1.84 (m, 2H, 6-H), 1.84-2.09 (m, 4H, 11-H, 12-H), 2.18-2.27 (m, 2H, 2-H), 2.58 (d, 2H, 8-H), 3.59 (3.67) (s,3H,CO_2CH_3), 3.99-4.18 (m, 4H, CO_2CH_2(×2)), 4.82-5.07 (m, 2H, 9-H, 13-H)

^{13}C - NMR ($CDCl_3$) δ 14.1 (CH_3) (×2), 16.1 (CH_3), 17.6 (CH_3), 23.7 (CH_2), 24.7 (CH_2), 25.6 (CH_3), 26.5 (CH_2), 29.3 (CH_2), 30.9 (CH_2), 31.9 (CH_2), 33.9(34.2) (CH_2), 39.9 (CH_2), 51.4 (52.2) (CH_3-O), 57.5 (C), 60.1 (61.0) (CH_2-O) (×2), 117.7 (CH), 124.0 (CH), 131.4 (C), 138.8 (C), 171.6 (172.1) (C=O) (×2), 173.6 (174.0) (C=O)

m/z (EI) 379 (11), 69 (66) and 41 (100)

Preparation of 3,3-Di(hydroxymethyl)-6,10-dimethylundeca-5,9-dien-1-ol (12)

To a suspension of $LiAlH_4$ (0.05 g, 1.32 mmol) in tetrahydrofuran (10 ml) at 0 °C, was added a solution of (7) (0.29 g, 0.79 mmol) in tetrahydrofuran (10ml) portionwise. After being stirred for overnight at room temperature, Et_2O and water were added to the reaction mixture . The resulting mixture was extracted with Et_2O. The combined extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography eluting with 50 % Ethyl acetate-Hexane to give **(12)** (0.15 g, 75 % yield based on (7)) as a colourless oil. (R_f = 0.06; siliga gel / Ethyl acetate-Hexane, 1:1) (Found : C, 70.03; H, 11.24 $C_{15}H_{28}O_3$ requires C , 70.27; H, 11.01 %)

ν_{max} (neat) / cm^{-1} 3616-3050(OH)(br), 2966(s), 2925(s), 1439(m), 1374(m), 1040(s)

^1H - NMR ($CDCl_3$) δ 1.55 (s, 6H, vinyl-CH_3 (×2)), 1.58-1.68 (m, 5H, 2-H, vinyl-CH_3), 1.92 (d,2H, 4-H), 1.96-2.08 (m, 4H, 7-H, 8-H), 3.50 (s,4H, CH_2-O (×2)), 3.68 (t, 2H, 1-H), 3.76-4.09 (s, broad, 3H, OH (×3)), 4.93-5.17 (m, 2H, 5-H, 9-H)

^{13}C - NMR ($CDCl_3$) δ 16.1 (CH_3), 17.7 (CH_3), 25.7 (CH_3), 26.5 (CH_2), 31.2 (CH_2), 35.2 (CH_2), 40.1(CH_2), 42.5 (C), 58.4 (CH_2-O), 67.6 (CH_2-O) (×2), 118.9(CH), 124.1 (CH), 131.6 (C), 138.1 (C)

m/z (EI) 69 (64) and 41 (100)

Preparation of 4,4-Di(hydroxymethyl)-7,11-dimethyldodeca-6,10-dien-1-ol (13)

The reaction conditions for the preparation of **(12)** were followed using **(8)** (0.50 g, 1.31 mmol) and $LiAlH_4$ (0.08 g, 2.11 mmol). The residue was purified by flash chromatography eluting with 50 % Ethyl acetate / Hexane to give **(13)** (0.26g, 74 % yield based on **(8)**) as a colourless oil. (R_f = 0.06; siliga gel / Ethyl acetate - Hexane, 1:1) (Found : C, 71.26; H, 11.21 $C_{16}H_{30}O_3$ requires C, 71.07; H, 11.18 %)

ν_{max} (neat) / cm^{-1} 3616-3041(OH)(br), 2931(s), 2872(s), 1445(m), 1380(m), 1051(s)

^1H - NMR ($CDCl_3$) δ 1.30-1.49 (m, 4H, 2-H, 3-H), 1.55 (s, 6H, vinyl-CH_3 (×2)), 1.63 (s, 3H, vinyl -CH_3), 1.82 (d, 2H, 5-H), 1.89-2.15 (m, 4H, 8-H, 9-H), 3.33-3.67 (m, 6H, 1-H, CH_2-O (×2)), 3.89-4.25 (s, broad, 3H, OH (×3)), 4.92-5.14 (m, 2H, 6-H, 10-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.7 (CH_3), 25.7 (CH_3), 25.8 (CH_2), 26.6 (CH_2) (×2), 29.6 (CH_2), 40.0 (CH_2), 42.0 (C), 62.9 (CH_2-O), 67.9 (CH_2-O) (×2), 118.8 (CH), 124.2 (CH), 131.5 (C), 137.6 (C)

m/z (EI) 69 (49) and 41 (100)

Preparation of 5,5-Di(hydroxymethyl)-8,12-dimethyltrideca-7,11-dien-1-ol (14)

By a method similar to that used in the preparation of **(12)**, **(14)** was obtained from $LiAlH_4$ (0.11 g, 2.90 mmol) and **(9)** (0.73 g, 1.84 mmol). The residue was purified by flash column chromatography eluting with 50 % Ethyl acetate / Haxene to give **(14)** (0.38 g, 73 % yield based on **(9)**) as a colourless oil. (R_f = 0.07; siliga gel / Ethyl acetate - Hexane, 1:1) (Found : C, 71.93; H, 11.69 $C_{17}H_{32}O_3$ requires C, 71.79; H, 11.34 %)

ν_{max} (neat) / cm^{-1} 3615-3078(OH)(br), 2929(s), 2866(s), 1444(m), 1378(m), 1050(s)

^1H - NMR ($CDCl_3$) δ 1.15-1.39 (m, 4H, 2-H, 3-H), 1.42-1.53 (m, 2H, 4-H), 1.58 (s, 6H, vinyl-CH_3 (×2)), 1.63 (s, 3H, vinyl-CH_3), 1.87 (d, 2H, 6-H), 1.90-2.15 (m, 4H, 9-H, 10-H), 3.46 (s, 4H, CH_2-O (×2)), 3.52-4.77 (m, 5H, 1-H, OH (×3)), 4.93-5.18 (m, 2H, 7-H, 11-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.7 (CH_3), 18.8 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 29.5 (CH_2), 29.9 (CH_2), 32.9 (CH_2), 40.1 (CH_2), 42.3 (C), 61.9 (CH_2-O), 67.7 (CH_2-O) (×2), 119.1 (CH), 124.2 (CH), 131.5 (C), 137.6 (C)

m/z (EI) 81 (60), 69 (68) and 41 (100)

Preparation of 6,6-Di(hydroxymethyl)-9,13-dimethyltetradeca-8,12-dien-1-ol (15)

The reaction conditions for the preparation of (12) were followed using (10) (0.62 g, 1.51 mmol) and $LiAlH_4$ (0.09 g, 2.37 mmol). The residue was purified by flash chromatography eluting with 50 % Ethyl acetate / Hexane to give (15) (0.32 g, 71 % yield based on (10)) as a colourless oil. (R_f = 0.08; siliga gel / Ethyl acetate-Hexane, 1: 1) (Found : C, 72.79; H, 11.38 $C_{18}H_{34}O_3$ requires C, 72.44; H, 11.48 %)

ν_{max} (neat) / cm^{-1} 3636-3052(OH)(br), 2929(s), 2858(s), 1444(m), 1372(m), 1050(s)

^1H - NMR ($CDCl_3$) δ 1.15-1.34 (m, 6H, 2-H, 3-H, 4-H), 1.43-1.60 (m, 8H, vinyl-CH_3 (×2), 5-H), 1.64 (s, 3H, vinyl-CH_3), 1.88 (d, 2H, 7-H), 1.95 - 2.09 (m, 4H , 10-H, 11-H), 2.95 (s, broad, 1H, OH), 3.47 (s, 4H, CH_2-O (×2)), 3.51-3.64 (m, 4H, 1-H, OH (×2)), 4.97-5.15 (m, 2H, 8-H, 12-H)

^{13}C - NMR ($CDCl_3$) δ 16.1 (CH_3), 17.7 (CH_3), 22.5 (CH_2), 25.7 (CH_3), 26.6 (CH_2) (×2), 29.5 (CH_2), 30.7 (CH_2), 32.3 (CH_2), 40.1 (CH_2), 42.2 (C), 62.5 (CH_2-O), 68.2 (CH_2-O)(×2), 119.2 (CH), 124.2 (CH), 131.5 (C), 137.5 (C)

m/z (EI) 81 (60), 69 (76) and 41 (100)

Preparation of 7,7-Di(hydroxymethyl)-10,14-dimethylpentadeca-9,13-dien-1-ol (16)

By a method similar to that used in the preparation of **(12)**, **(16)** was obtained from $LiAlH_4$ (0.06 g, 1.58 mmol) and **(11)** (0.45 g, 1.06 mmol). The residue was purified by flash column chromatography eluting with 50 % Ethyl acetate / Hexane to give **(16)** (0.23 g, 70 % based on **(11)**) as a colourless oil. (R_f = 0.10; siliga gel / Ethyl acetate - Hexane, 1:1) (Found : C, 73.21; H, 11.74 $C_{19}H_{36}O_3$ requires C, 73.03; H, 11.61 %)

ν_{max} (neat) / cm^{-1} 3590-3078(OH)(br), 2929(s), 2858(s), 1449(m), 1378(m), 1040(s)

^1H - NMR ($CDCl_3$) δ 1.13-1.39 (m, 8H, 2-H, 3-H, 4-H, 5-H), 1.40-1.58 (m, 8H, vinyl-CH_3 (×2), 6-H), 1.63 (s, 3H, vinyl-CH_3), 1.88 (d, 2H, 8-H), 1.91 - 2.09 (m, 4H, 11-H, 12-H), 3.16 (s, broad, 1H, OH), 3.44 (s, 4H, CH_2-O (×2)), 3.49-3.68 (m, 4H , 1-H, OH (×2)), 4.95-5.17 (m, 2H, 9-H, 13-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.7 (CH_3), 22.8 (CH_2), 25.6 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 29.3 (CH_2), 30.2 (CH_2), 30.6 (CH_2), 32.5 (CH_2), 40.1(CH_2), 42.1 (C), 62.5 (CH_2-O), 68.1 (CH_2-O) (×2), 119.3 (CH), 124.2 (CH), 131.4 (C), 137.4 (C)

m/z (EI) 81 (59), 69 (79) and 41 (100)

Preparation of 2-Hydroxymethyl-5,9-dimethyldeca-4,8-dien-1-ol (17)

By a method similar to that used in the preparation of **(12)**, **(17)** was obtained from $LiAlH_4$ (0.10 g, 2.64 mmol) and **(6)** (0.53 g, 1.79 mmol). The residue was purified by flash chromatograph y eluting with 40% Ethyl acetate / Hexane to give **(17)** (0.28 g, 74 % yield based on **(6)**) as a colourless oil. (R_f = 0.23; siliga gel / Ethyl acetate- Hexane, 1:1) (Found : C, 73.23; H, 11.48 $C_{13}H_{24}O_3$ requires C, 73.54; H, 11.39 %)

ν_{max} (neat) / cm^{-1} 3683-3058(OH)(br), 2924(s), 2847(s), 1441(m), 1375(m), 1033(s)

^1H - NMR ($CDCl_3$) δ 1.52 (s, 6H, vinyl-CH_3 (×2)), 1.61 (s, 3H, vinyl- CH_3), 1.65-1.79 (m, 1H, 2-H), 1.80-2.09 (m, 6H, 3-H, 6-H, 7-H), 3.42-3.58 (m, 2H, 1-H),

3.58-3.70 (m, 2H, CH_2-O), 3.89 (s, 2H, OH (× 2)), 4.92-5.13 (m, 2H, 4-H, 8-H)

^{13}C - NMR ($CDCl_3$) δ 15.9 (CH_3), 17.6 (CH_3), 25.6 (CH_3), 26.4 (CH_2), 26.6 (CH_2), 39.7 (CH_2), 42.8 (CH), 65.0 (CH_2-O) (×2), 121.8 (CH), 124.2 (CH), 131.3 (C), 136.7 (C)

m/z (EI) 123 (11), 81 (51), 69 (71) and 41 (100)

Preparation of Methyl-2-methoxycarbonyl-5,9-dimethyldeca-4,8-dienoate (18)

To a solution of geraniol **(1)** (0.83 g, 5.39 mmol) and triphenylphosphine (2.83 g, 10.79 mmol) in dichloromethane was added carbon tetrachloride (1.74 g, 11.30 mmol) and the mixture was stirred at room temperature for 15 minutes. After that, the mixture was heated at reflux temperature for 4 hours. The solvent was evaporated under reduced pressure and the residue was extracted with n-Hexane to obtained crude geranyl chloride **(5)** as a pale yellow oil which was used without purification for the next reaction.

To a mixture of NaH (60 % oil suspension; 10.75 mmol, 0.43g washed with THF) in THF (10 ml), was added dimethyl malonate (3.10 ml, 27.12 mmol) in THF (10 ml) at 0 °C under nitrogen. The mixture was stirred at room temperature for 15 minutes. Geranyl chloride **(5)** was then added and the mixture heated under reflux for 4 hours. The mixture was cooled and extracted with diethyl ether. The combined extracts were washed with water and brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was chromatographed on a silica gel column using 1:20 Ethyl acetate / Hexane as eluent to afford **(18)** (1.34 g, 93 % yield based on **(1)**) as a colourless oil. (R_f = 0.46; siliga gel / Ethyl acetate- Hexane, 1:4) (Found : C, 67.22; H, 8.88 $C_{15}H_{24}O_4$ requires C, 67.14; H, 9.01 %)

ν_{max} (neat) / cm^{-1} 2955(m), 2919(m), 1741 (C=O)(s), 1434(m), 1342(m), 1239(m), 1152(m)

^{1}H - NMR ($CDCl_3$) δ 1.55 (s, 3H, vinyl-CH_3), 1.59 (s, 3H, vinyl-CH_3), 1.63 (s, 3H, vinyl-CH_3), 1.85-2.08 (m, 4H, 6-H, 7-H), 2.57 (t, 2H, 3-H), 3.33 (t, 1H, 2-H), 3.68 (s, 6H, CH_3-O (× 2)), 4.96-5.12 (m, 2H, 4-H, 8-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.6 (CH_3), 25.6 (CH_3), 26.5 (CH_2), 27.5 (CH_2), 39.6 (CH_2), 51.9 (CH), 52.4 (CH_3-O) (×2), 119.4 (CH), 123.9 (CH), 131.4 (C), 138.7 (C), 169.6 (C=O) (×2)

m/z (EI) 237 (10), 136 (58), 69 (74) and 41 (100)

Preparation of Methyl-3,3-Di(methoxycarbonyl)-6,10-dimethylundeca-5,9-dienoate (19)

To a solution of NaH (60% oil suspension; 7.00 mmol, 0.28 g washed with THF) in THF (10ml), was added **(18)** (0.94 g, 3.51 mmol) in THF (10ml) at 0°C under nitrogen. The mixture was stirred at room temperature for 15 minutes. Methyl bromoacetate (1.07 g, 6.99 mmol) was then added and the mixture heated under reflux for 4 hours. The mixture was cooled and extracted with diethyl ether. The combined extracts was washed with water and brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography eluting with 1:10 Ethyl acetate / Hexane to give **(19)** (0.98 g, 82 %yield based on **(18)**) as a colourless oil. (R_f = 0.43; siliga gel / Ethyl acetate - Hexane, 1 : 4) (Found : C, 63.56; H, 8.09 $C_{18}H_{28}O_6$ requires C, 63.51; H, 8.29 %)

ν_{max} (neat) / cm^{-1} 2950(m), 2919(m), 1736 (C=O)(s), 1439(m), 1357(m), 1291(m), 1173(m)

^{1}H - NMR ($CDCl_3$) δ 1.52 (s, 3H, vinyl-CH_3), 1.55 (s, 3H, vinyl-CH_3), 1.59-1.70 (m, 3H, vinyl-CH_3), 1.88-2.10 (m, 4H, 7-H, 8-H), 2.71 (d, 2H, 4-H), 2.91 (s, 2H, 2-H), 3.62 (s, 3H, CH_3-O), 3.70 (s, 6H, CH_3-O (× 2)), 4.81-5.06 (m, 2H, 5-H, 9-H)

^{13}C - NMR ($CDCl_3$) δ 15.9 (CH_3), 17.6 (CH_3), 25.6 (CH_3), 26.4 (CH_2), 31.9 (CH_2), 36.9 (CH_2), 39.9 (CH_2), 51.7 (CH_3-O), 52.7 (CH_3-O) (×2), 55.6 (C), 117.4 (CH), 123.9 (CH), 131.6 (C), 140.2 (C), 170.7 (C=O) (×2), 171.1 (C=O)

m/z (EI) 265 (12), 211 (58), 69 (45) and 41 (68)

Preparation of Methyl-4,4-Di(methoxycarbonyl)-7,11-dimethyldodeca-6,10-dienoate (20)

By a method similar to that used in the preparation of **(19)**, **(20)** was obtained from NaH (60 % oil suspension; 6.00 mmol, 0.24 g washed with THF), **(18)** (0.80g, 2.99mmol) and Methyl 3-bromopropionate (1.00g, 5.99mmol). Chromatographic purification (silica gel, Ethyl acetate - Hexane, 1:10) of the crude product afforded **(20)** (0.82 g, 78 % yield based on **(18)**) as a colourles oil. (R_f = 0.39 ; siliga gel / Ethyl acetate - Hexane , 1: 4) (Found : C , 64.43 ; H , 8 .57 $C_{19}H_{30}O_6$ requires C, 64.39; H, 8.53 %)

ν_{max} (neat) / cm^{-1} 2950(m), 2919(m), 1731 (C=O)(s), 1439(m), 1378(m), 1219(m), 1173(m)

^{1}H - NMR ($CDCl_3$) δ 1.56 (s, 3H, vinyl-CH_3), 1.58 (s, 3H, vinyl-CH_3), 1.65 (s, 3H, vinyl-CH_3), 1.91-2.06 (m, 4H, 8-H, 9-H), 2.11-2.35 (m, 4H, 2-H, 3-H), 2.59 (d, 2H, 5-H), 3.64 (s, 3H, CH_3-O), 3.68 (s, 6H, CH_3-O (× 2)), 4.88 - 5.08 (m, 2H , 6-H, 10-H)

^{13}C - NMR ($CDCl_3$) δ 16.1 (CH_3), 17.7 (CH_3), 25.6 (CH_3), 26.5 (CH_2), 27.7 (CH_2), 29.4 (CH_2), 31.8 (CH_2), 39.9 (CH_2), 51.7 (CH_3-O), 52.4 (CH_3-O) (×2), 57.0 (C), 117.2 (CH), 123.9 (CH), 131.6 (C), 139.6 (C), 171.5 (C=O) (×2), 173.2(C=O)

m/z (EI) 69 (64) and 41 (90)

Preparation of Methyl-5,5-Di(methoxycarbonyl)-8,12-dimethyltrideca-7,11-dienoate (21)

The reaction conditions for the preparation of **(19)** were followed using **(18)** (2.29 g, 8.54 mmol), NaH (60 % oil suspension; 17.00 mmol, 0.68 g washed with THF) and Methyl 4-iodobutyrate (3.90, 17.11 mmol). The crude product was purified by column chromatography (silica gel, Ethyl acetate - Hexane, 1:10) to give **(21)** (2.31 g, 74 % yield based on **(18)**) as a pale yellow oil. (R_f = 0.35; siliga gel/Ethyl acetate -Hexane, 1:4) (Found : C, 65.29; H, 8.67 $C_{20}H_{32}O_6$ requires C, 65.19; H, 8.75 %)

ν_{max} (neat) / cm^{-1} 2950(m), 2919(m), 1731 (C=O)(s), 1434(m), 1214(m), 1173(m)

^1H - NMR ($CDCl_3$) δ 1.32-1.48 (m, 2H, 3-H), 1.49 (s, 3H, vinyl- CH_3), 1.50 (s, 3H, vinyl-CH_3), 1.57 (s, 3H, vinyl-CH_3), 1.68-1.84 (m, 2H, 4-H), 1.88-2.03 (m, 4H, 9-H, 10-H), 2.20 (t, 2H, 2-H), 2.53 (d, 2H, 6-H), 3.55 (s, 3H, CH_3-O) , 3.60 (s, 6H, CH_3-O (× 2)), 4.79-5.01 (m, 2H, 7-H, 11-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.6 (CH_3), 19.7 (CH_2), 25.5 (CH_3), 26.4 (CH_2), 30.9 (CH_2), 31.6(CH_2), 34.0 (CH_2), 39.8 (CH_2), 51.4 (CH_3-O), 52.2 (CH_3-O) (×2), 57.5 (C), 117.4 (CH), 123.9 (CH), 131.3 (C), 139.1 (C), 171.7 (C=O) (×2), 173.2 (C=O)

m/z (EI) 232 (87), 69 (73) and 41 (100)

Preparation of Methyl-6,6-Di(methoxycarbonyl)-9,13-dimethyltetradeca-8,12-dienoate (22)

By a method similar to that used in the preparation of **(19)**, **(22)** was obtained from NaH (60 % oil suspension; 11.75 mmol, 0.47g washed with THF), **(18)** (1.58g, 5.90mmol) and Methyl 5-bromovalerate (2.30g, 11.79 mmol). Chromatographic purification (silica gel, Ethyl acetate - Hexane, 1:10) of the crude product afforded **(22)** (1.58 g, 70 % yield based on **(18)**) as a colourless oil. (R_f = 0.33; siliga gel / Ethyl acetate- Hexane, 1:4) (Found : C, 66.10; H , 8.84 $C_{21}H_{34}O_6$ requires C, 65.94; H, 8.96 %)

ν_{max} (neat) / cm^{-1} 2950(m), 2924(m), 1731 (C=O)(s), 1434(m), 1214(m), 1168(m)

^1H - NMR ($CDCl_3$) δ 1.07-1.26 (m, 2H, 4-H), 1.57 (s, 6H, vinyl-CH_3 (×2)), 1.60-1.66 (m,5H,vinyl-CH_3,3-H), 1.75-1.88 (m,2H,5-H), 1.91-2.10 (m,4H,10-H,11-H), 2.28 (t, 2H, 2-H), 2.58 (d, 2H, 7-H), 3.63 (s, 3H, CH_3-O), 3.67 (s, 6H, CH_3-O (× 2)), 4.85-5.09 (m, 2H, 8-H, 12-H)

^{13}C - NMR ($CDCl_3$) δ 16.1 (CH_3), 17.7 (CH_3), 23.7 (CH_2), 25.1 (CH_2), 25.7 (CH_3), 26.5 (CH_2), 31.0 (CH_2), 31.9 (CH_2), 33.7 (CH_2), 39.9 (CH_2), 51.5 (CH_3-O),

52.3 (CH_3-O) (×2), 57.6 (C), 117.6 (CH), 124.0 (CH), 131.5 (C), 139.2 (C), 172.0 (C=O) (×2), 173.8 (C=O)

m/z (EI) 246 (71), 193 (58), 69 (72) and 41 (100)

Preparation of Methyl-7,7-Di(methoxycarbonyl)-10,14-dimethylpentadeca-9,13-dienoate (23)

The reaction conditions for the preparation of **(19)** were followed using **(18)** (1.75 g, 6.53 mmol), NaH (60% oil suspension; 13.00 mmol, 0.52 g, washed with THF) and Methyl 6-bromocaproate (2.74 g, 13.11 mmol). The crude product was purified by column chromatography (silica gel, Ethyl acetate-Hexane, 1:10) to give **(23)** (1.75 g, 68 % yield based on **(18)**) as a pale yellow oil. (R_f = 0.34; siliga gel / Ethyl acetate- Hexane, 1:4) (Found : C, 66.78; H, 8.93 $C_{22}H_{36}O_6$ requires C, 66.64; H, 9.15 %)

ν_{max} (neat) / cm^{-1} 2950(m), 2929(m), 1731 (C=O)(s), 1434(m), 1209(m), 1173(m)

^{1}H - NMR ($CDCl_3$) δ 1.08 -1.40 (m, 4H, 4-H, 5-H), 1.57 (s, 6H,vinyl- CH_3 (×2)), 1.65 (s, 5H, vinyl-CH_3, 3-H), 1.78-1.86 (m, 2H, 6-H), 1.94-2.10 (m, 4H, 11-H, 12-H), 2.26 (t, 2H, 2-H), 2.58 (d, 2H, 8-H), 3.63 (s, 3H, CH_3-O), 3.67 (s, 6H, CH_3-O (× 2)), 4.88 - 5.10 (m, 2H, 9-H, 13-H)

^{13}C - NMR ($CDCl_3$) δ 16.1 (CH_3), 17.7 (CH_3), 23.8 (CH_2), 24.7 (CH_2), 25.6 (CH_3), 26.5 (CH_2), 29.3 (CH_2), 31.1 (CH_2), 32.1 (CH_2), 33.9 (CH_2), 39.9 (CH_2), 51.4 (CH_3-O), 52.2 (CH_3-O)(×2), 57.7 (C), 117.7 (CH), 124.0 (CH), 131.4 (C) , 139.1 (C), 172.0 (C=O) (×2), 174.0 (C=O)

m/z (EI) 69 (72) and 41 (100)

Preparation of Methyl-3-methoxycarbonyl-6,10-dimethylundeca-5,9-dienoate (24)

A mixture of **(19)** (1.73 g, 5.09 mmol), sodium chloride (0.60 g, 10.26 mmol), water (0.30 g, 16.67 mmol) and DMSO (25 ml) was refluxed for 2 hours. After cooling to room temperature, the mixture was diluted with water and

extracted with diethyl ether. The combined extracts were washed with water, dried ($MgSO_4$), filtered and evaporated to remove the ether. The remaining oil was chromatographed on a silica gel column using 1:25 Ethyl acetate / Hexane as eluent to afford **(24)** (1.07 g, 74 % yield based on **(19)**) as a pale yellow oil. (R_f = 0.30; siliga gel / Ethyl acetate-Hexane, 0.5:4.5) (Found : C, 68.21; H, 9.18 $C_{16}H_{26}O_4$ requires C, 68.06; H, 9.28 %)

ν_{max} (neat) / cm^{-1} 2960(m), 2858(m), 1741 (C=O)(s), 1439(m), 1372(m), 1168(m)

^1H - NMR ($CDCl_3$) δ 1.55 (s, 6H, vinyl-CH_3(×2)), 1.63 (s, 3H, vinyl-CH_3), 1.85-2.12 (m, 4H, 7-H, 8-H), 2.15-2.46 (m, 3H, 3-H, 4-H), 2.50-2.91 (m, 2H, 2-H), 3.63 (s, 3H, CH_3-O), 3.65 (s, 3H, CH_3-O), 5.02 (t, 2H, 5-H, 9-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.6 (CH_3), 25.6 (CH_3), 26.5 (CH_2), 30.0 (CH_2), 34.8 (CH_2), 39.7 (CH_2), 41.4 (CH), 51.6 (CH_3-O), 51.8 (CH_3-O), 120.0 (CH), 124.0 (CH), 131.5 (C), 138.4 (C), 172.6 (C=O), 175.0 (C=O)

m/z (EI) 207 (20), 153 (28), 69 (53) and 41 (78)

Preparation of Methyl-4-methoxycarbonyl-7,11-dimethyldodeca-6,10-dienoate (25)

By a method similar to that used in the preparation of **(24)**, **(25)** was obtained from **(20)** (0.41 g, 1.16 mmol), sodium chloride (0.14 g, 2.39 mmol), water (0.07 g, 3.89 mmol) and DMSO (6 ml). Chromatographic purification (silica gel,Ethyl acetate - Hexane, 1:25) of the crude product afforded **(25)** (0.26 g, 76 % yield based on **(20)**) as a colourless oil. (R_f = 0.33; siliga gel / Ethyl acetate - Hexane, 0.5: 4.5) (Found : C, 68.96; H, 9.47 $C_{17}H_{28}O_4$ requires C, 68.89; H, 9.52 %)

ν_{max} (neat) / cm^{-1} 2955(m), 2858(m), 1736 (C=O)(s), 1444(m), 1370(m), 1163(m)

^1H - NMR ($CDCl_3$) δ 1.56 (s, 6H , vinyl-CH_3 (×2)), 1.64 (s, 3H, vinyl-CH_3), 1.78-1.92 (m, 1H, 4-H), 1.94-2.12 (m, 4H, 8-H, 9-H), 2.14-2.50 (m, 6H, 2-H, 3-H , 5-H), 3.63 (s, 6H, CH_3-O (×2)), 5.03 (t, 2H, 6-H, 10-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.6 (CH_3), 25.6 (CH_3), 26.5 (CH_2), 26.6 (CH_2), 30.6 (CH_2), 31.8 (CH_2), 39.7 (CH_2), 45.0 (CH), 51.5 (CH_3-O), 51.6 (CH_3-O), 120.5 (CH), 124.1 (CH), 131.4 (C), 137.7 (C), 173.4 (C=O), 175.6 (C=O)

m/z (EI) 233 (32), 167 (37), 135 (80), 107 (87), 69 (55) and 41 (100)

Preparation of Methyl-5-methoxycarbonyl-8,12-dimethyltrideca-7,11-dienoate (26)

A mixture of **(21)** (1.29 g, 3.51 mmol), sodium chloride (0.41 g, 7.01 mmol), water (0.19 g, 10.56 mmol) and DMSO (17 ml) was refluxed for 4 hours . After cooling to room temperature, the mixture was quenched with water and extracted with diethyl ether. The combined extracts were washed with water, dried with ($MgSO_4$), filtered and evaporated to remove the ether. The remaining oil was chromatographed on a silica gel column using 1:25 Ethyl acetate / Hexane as eluent to afford **(26)** (0.77 g, 71 % yield based on **(21)**) as a pale yellow oil. (R_f = 0.33; siliga gel / Ethyl acetate-Hexane, 0.5: 4.5) (Found : C, 69.80; H, 9.77 $C_{18}H_{30}O_4$ requires C, 69.64; H, 9.74 %)

ν_{max} (neat) / cm^{-1} 2955(m), 2863(m), 1736 (C=O)(s), 1434(m), 1368(m), 1163(m)

^1H - NMR ($CDCl_3$) δ 1.40-1.60 (m, 8H, 3-H, vinyl-CH_3 (×2)), 1.61-1.67 (m, 5H, 4-H, vinyl -CH_3), 1.83 - 2.10 (m, 4H, 9-H, 10-H), 2.12-2.46 (m, 5H,2-H,5-H, 6-H), 3.64 (s, 6H, CH_3-O (×2)), 4.95-5.11 (m, 2H, 7-H, 11-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.7 (CH_3), 22.8 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 30.7 (CH_2), 31.1 (CH_2), 33.9 (CH_2), 39.7 (CH_2), 45.6 (CH), 51.4 (CH_3-O), 51.5 (CH_3-O), 120.8 (CH), 124.1 (CH), 131.4 (C), 137.5 (C), 173.8 (C=O), 176.1 (C=O)

m/z (EI) 69 (65) and 41 (100)

Preparation of Methyl-6-methoxycarbonyl-9,13-dimethyltetradeca-8,12-dienoate (27)

A mixture of **(22)** (1.05 g, 2.75 mmol), sodium chloride (0.32 g, 5.47 mmol), water (0.15 g, 8.33 mmol) and DMSO (13 ml) was refluxed for 6 hours. After cooling to room temperature, the mixture was quenched with water and extracted with diethyl ether. The combined extracts were washed with water, dried ($MgSO_4$), filtered and evaporated to remove the ether. The remaining oil was chromatographed on a silica gel column using 1:25 Ethyl acetate / Hexane as eluent to afford **(27)** (0.65 g, 73 % yield based on **(22)**) as a colourless oil. (R_f = 0.41; siliga gel /Ethyl acetate-Hexane, 0.5: 4.5) (Found : C, 70.34; H, 10.03 $C_{19}H_{32}O_4$ requires C , 70.34; H, 9.94 %)

ν_{max} (neat) / cm^{-1} 2950(m), 2858(m), 1736 (C=O)(s), 1439(m), 1380(m), 1157(m)

^1H - NMR ($CDCl_3$) δ 1.17-1.38 (m, 2H, 4-H), 1.40-1.58 (s, 8H, vinyl-CH_3 (×2), 3-H), 1.60-1.69 (s, 5H, vinyl-CH_3, 5-H), 1.86-2.09 (m, 4H, 10-H, 11-H), 2.11-2.40 (m, 5H, 2-H, 6-H,7-H), 3.61 (s, 3H, CH_3-O), 3.62 (s, 3H, CH_3-O), 4.94-5.09 (m, 2H, 8-H, 12-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.6 (CH_3), 24.8 (CH_2), 25.6 (CH_3), 26.6 (CH_2), 26.9 (CH_2), 30.7 (CH_2), 31.3 (CH_2), 33.8 (CH_2), 39.7 (CH_2), 45.7 (CH), 51.3 (CH_3-O), 51.4 (CH_3-O), 121.0 (CH), 124.1 (CH), 131.3 (C), 137.3 (C), 173.9 (C=O), 176.3 (C=O)

m/z (EI) 69 (68) and 41 (100)

Preparation of Methyl-7-methoxycarbonyl-10,14-dimethylpentadeca-9,13-dienoate (28)

The reaction conditions for the preparation of **(27)** were followed using **(23)** (1.28 g, 3.23 mmol), sodium chloride (0.38 g, 6.50 mmol), water (0.18 g, 10.00 mmol) and DMSO(16 ml). The crude product was purified by column chromatography (silica gel, Ethyl acetate- Hexane, 1:25) to give **(28)** (0.79 g, 72 % yield based on **(23)**) as a pale yellow oil. (R_f = 0.41; siliga gel / Ethyl acetate -

Hexane, 0.5:4.5) (Found : C, 71.18; H, 10.11 $C_{20}H_{34}O_4$ requires C, 70.97; H, 10.12 %)

ν_{max} (neat) / cm^{-1} 2929(m), 2858(m), 1736 (C=O)(s), 1434(m), 1374(m), 1163(m)

^1H - NMR ($CDCl_3$) δ 1.17-1.32 (m, 4H, 4-H, 5-H), 1.40-1.59 (m, 8H, vinyl-CH_3 (×2), 3-H), 1.61-1.70 (m, 5H, vinyl-CH_3, 6-H), 1.86-2.08 (m, 4H, 11-H, 12-H), 2.11-2.40 (m, 5H, 2-H, 7-H, 8-H), 3.62 (s, 3H, CH_3-O), 3.63 (s, 3H, CH_3-O) , 4.96-5.10 (m, 2H, 9-H, 13-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.6 (CH_3), 24.7 (CH_2), 25.6 (CH_3), 26.6 (CH_2), 27.1 (CH_2), 29.0 (CH_2), 30.8 (CH_2), 31.5 (CH_2), 33.9 (CH_2), 39.7(CH_2) , 45.8 (CH), 51.3 (CH_3-O), 51.4 (CH_3-O), 121.1 (CH), 124.1 (CH), 131.3 (C), 137.2 (C), 174.1 (C=O), 176.4 (C=O)

m/z (EI) 291 (11), 69 (72) and 41 (100)

Preparation of 3-Hydroxymethyl-6,10-dimethylundeca-5,9-dien-1-ol (29)

To a suspension of $LiAlH_4$ (0.06 g, 1.58 mmol) in THF (10ml) at 0°C, was added a solution of **(24)** (0.29 g, 1.03 mmol) in THF (10 ml) portionwise. After being stirred for overnight at room temperature, Et_2O and water were added to the reaction mixture. The resulting mixture was extracted with Et_2O. The combined extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography eluting with 40 % Ethyl acetate /Hexane to give **(29)** (0.20 g, 86 % yield based on **(24)**) as a colourless oil. (R_f = 0.22; siliga gel / Ethyl acetate-Hexane, 1:1) (Found : C, 74.41; H, 11.81 $C_{14}H_{26}O_2$ requires C, 74.29; H, 11.58 %)

ν_{max} (neat) / cm^{-1} 3625-3058 (OH)(br), 2917(s), 2875(s), 1447(m), 1374(m), 1048(m)

^1H - NMR ($CDCl_3$) δ 1.56 (s, 6H, vinyl-CH_3 (×2)), 1.64 (s, 5H, vinyl-CH_3, 2-H), 1.82-2.10 (m, 7H, 3-H, 4-H, 7-H, 8-H), 3.36-3.79 (m, 4H, 1-H, CH_2-O), 3.91 (s, broad, 2H, OH (×2)), 5.00-5.15 (m, 2H, 5-H, 9-H)

^{13}C - NMR ($CDCl_3$) δ 16.1 (CH_3), 17.7 (CH_3), 25.7 (CH_3), 26.6 (CH_2), 30.4 (CH_2), 35.6 (CH_2), 39.8 (CH_2), 40.3 (CH), 61.1 (CH_2-O), 66.2 (CH_2-O), 122.3 (CH), 124.2 (CH), 131.4 (C), 136.6 (C)

m/z (EI) 69 (85) and 41 (100)

Preparation of 4-Hydroxymethyl-7,11-dimethyldodeca-6,10-dien-1-ol (30)

By a method similar to that used in the preparation of **(29)**, **(30)** was obtained from $LiAlH_4$ (0.13 g, 3.43 mmol) and **(25)** (0.66 g, 2.23 mmol). The residue was purified by flash column chromatography eluting with 40 % Ethyl acetate/ Hexane to give **(30)** (0.45 g, 84 % yield based on **(25)**) as a colourless oil. (R_f = 0.20; siliga gel / Ethyl acetate - Hexane, 1:1) (Found : C, 75.09; H, 11.68 $C_{15}H_{28}O_2$ requires C, 74.95; H, 11.74 %)

ν_{max} (neat) / cm^{-1} 3591-3066 (OH)(br), 2923(s), 2876(s), 1449(m), 1374(m), 1057(m)

^1H - NMR ($CDCl_3$) δ 1.16-2.59 (m, 10H, vinyl-CH_3 (×2), 2-H, 3-H), 1.63 (s , 3H, vinyl-CH_3), 1.80-2.11 (m,7H, 4-H, 5-H, 8-H, 9-H), 3.10-3.65 (m,6H, 1-H, CH_2-O , OH (×2)), 4.94-5.16 (m, 2H, 6-H, 10-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.6 (CH_3), 25.7 (CH_3), 26.6 (CH_2), 26.8 (CH_2), 29.6 (CH_2) (×2), 39.8 (CH_2), 40.8 (CH), 62.7 (CH_2-O), 65.0 (CH_2-O), 122.4 (CH), 124.2 (CH), 131.4 (C), 136.3 (C)

m/z (EI) 179 (10), 69 (73) and 41 (100)

Preparation of 5-Hydroxymethyl-8,12-dimethyltrideca-7,11-dien-1-ol (31)

The reaction conditions for the preparation of **(29)** were followed using **(26)** (0.73 g, 2.35 mmol) and $LiAlH_4$ (0.14 g, 3.69 mmol). The residue was purified by flash column chromatography eluting with 40 % Ethyl acetate / Hexane to give **(31)** (0.49 g, 82 % yield based on **(26)**) as a colourless oil. (R_f = 0.23; siliga gel / Ethyl acetate - Hexane,1:1) (Found : C, 75.60; H, 11.94 $C_{16}H_{30}O_2$ requires C, 75.54; H, 11.89 %)

ν_{max} (neat) / cm^{-1} 3633-3067 (OH)(br), 2927(s), 2857(s), 1445(m), 1378(m), 1048(m)

^1H - NMR ($CDCl_3$) δ 1.11-1.41 (m, 4H, 2-H,3-H),1.42-1.59 (m, 8H, vinyl-CH_3 (×2), 4-H), 1.65 (s, 3H, vinyl-CH_3), 1.88 - 2.10 (m, 9H, OH (×2), 5-H, 6-H, 9-H, 10-H), 3.49 (d, 2H,CH_2-O), 3.60 (t, 2H,1-H), 4.94-5.19 (m, 2H, 7-H,11-H)

^{13}C - NMR ($CDCl_3$) δ 16.1 (CH_3), 17.7 (CH_3), 23.0 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 29.7 (CH_2), 30.5 (CH_2), 32.9 (CH_2), 39.8 (CH_2), 41.2 (CH), 62.6 (CH_2-O), 65.5 (CH_2-O), 122.5(CH), 124.2 (CH), 131.4 (C), 136.4 (C)

m/z (EI) 193(14), 69 (80) and 41 (100)

Preparation of 6-Hydroxymethyl-9,13-dimethyltetradeca-8,12-dien-1-ol (32)

By a method similar to that used in the preparation of **(29)**, **(32)** was obtained from $LiAlH_4$ (0.11 g, 2.90 mmol) and **(27)** (0.58 g, 1.79 mmol). The residue was purified by flash column chromatography eluting with 40% Ethyl acetate / Hexane to give **(32)** (0.40 g, 83 % yield based on **(27)**) as a colourless oil. (R_f = 0.25; siliga gel / Ethyl acetate - Hexane, 1:1) (Found : C, 76.13; H, 12.07 $C_{17}H_{32}O_2$ requires C, 76.07; H, 12.02 %)

ν_{max} (neat) / cm^{-1} 3616-3064 (OH)(br), 2927(s), 2857(s), 1454(m), 1374(m), 1043(m)

^1H - NMR ($CDCl_3$) δ 1.10-1.38 (m, 6H, 2-H, 3-H,4-H),1.39-1.58 (m,8H, vinyl-CH_3 (×2), 5-H), 1.63 (s, 3H, vinyl-CH_3),1.85-2.13 (m, 7H, 6-H,7-H, 10-H, 11-H) , 2.31 (s, 2H, OH (×2)), 3.45 (d, 2H, CH_2-O), 3.57(t, 2H,1-H), 4.92-5.15 (m, 2H, 8-H, 12-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.7 (CH_3), 25.7 (CH_3), 26.0 (CH_2), 26.6 (CH_2), 26.7 (CH_2), 29.6 (CH_2), 30.7 (CH_2), 32.6 (CH_2), 39.8 (CH_2), 41.1(CH), 62.7 (CH_2-O), 65.6 (CH_2-O), 122.6 (CH), 124.2 (CH), 131.4 (C), 136.3 (C)

m/z (EI) 207 (21), 69 (82) and 41 (100)

Preparation of 7-Hydromethyl-10,14-dimethylpentadeca-9,13-dien-1-ol (33)

The reaction conditions for the preparation of **(29)** were followed using **(28)** (0.70 g, 2.07 mmol) and $LiAlH_4$ (0.12 g, 3.16 mmol). The residue was purified by

flash column chromatography eluting with 40 % Ethyl acetate / Hexane to give **(33)** (0.48 g, 82 % yield based on **(28)**) as a colourless oil. (R_f = 0.28; siliga gel / Ethyl acetate- Hexane, 1:1) (Found : C, 76.65; H, 11.99 $C_{18}H_{34}O_2$ requires C, 76.54; H, 12.13 %)

ν_{max} (neat) / cm^{-1} 3593-3065 (OH)(br), 2927(s), 2852(s), 1445(m), 1374(m), 1057(m)

^1H - NMR ($CDCl_3$) δ 1.11-1.38 (m, 8H, 2-H, 3-H, 4-H, 5-H), 1.39-1.59 (m, 8H, vinyl-CH_3 (×2), 6-H), 1.63 (s, 3H,vinyl-CH_3), 1.81-2.10 (m, 7H, 7-H, 8-H,11-H, 12-H), 2.17 (s, 2H, OH (×2)), 3.45 (d, 2H, CH_2-O), 3.56 (t, 2H, 1-H), 4.97-5.18 (m, 2H, 9-H, 13-H)

^{13}C - NMR ($CDCl_3$) δ 16.0 (CH_3), 17.6 (CH_3), 25.7 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 26.9 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 30.7 (CH_2), 32.7 (CH_2), 39.8 (CH_2), 41.2 (CH), 62.8 (CH_2-O), 65.6 (CH_2-O), 122.6 (CH), 124.2 (CH), 131.4 (C), 136.2 (C)

m/z (EI) 221 (15), 69 (84) and 41 (100)

Assay Method for Inhibition of adenosine 3′, 5′ - cyclic monophosphate phosphodiesterase (PDE).

Samples were tested for inhibition of cAMP phosphodiesterase activity in duplicate by following experimental of Nattaya Chairungsrilerd and co-workers. [21]

Bioassay. Phosphodiesterase activity was determined from the amount of inorganic phosphate liberated from the reaction of adenosine 5′-monophosphate and 5′ nucleotidase. It was determined by the malachite green method which is highly sensitive to inorganic phosphate. Phosphodiesterase assay solutions were as follows. (a). The enzyme solution contains phosphodiesterase (0.3 units / ml.), 5′-nucleotidase (13.4 units/ml.), $MgCl_2$ (50 mM.) and Tris-HCl (500 mM.). (b). The reaction mixture A contains malachite green (1.68 mM.), polyvinyl alcohol(23.2 g/l) and ammonium molybdate in 6N HCl (57.2 g / l). Sample was dissolved in 1.5 % dimethyl sulphoxide. The reaction was started by the addition of cyclic AMP (10 mM, 100μl.) to the enzyme solution (400 μl.) at 30°C. After that, sample solution (500 μl.), the reagent mixture A (1.0 ml.) and 25 % sodium citrate (200 μl.) were

added to above solution successsively every 5 min. The absorbancc of the coloured complex was measured at 630 nm. using a UV spectrophometer. A mixed reagent blank was used as reference, obtained by this procedure using potassium dihydrogen phosphate solutions of known concentrations, was used to determine the amount of phosphorus present in the assay. (Table 1, Figure 3) In the control experiment, dimethyl sulphoxide was added instead of the solution of sample to minimize the effect of the solvent. Biological activity of samples was compared with caffeine (reference compound for phosphodiesterase assay). All reagents were prepared freshly and distilled water was used in making these reagents.

Table 1 : Concentration and Absorbance of standard phosphate solution (NaH_2PO_4 aqueous solution).

Concentration of Phosphate (μM.)	Absorbance at 630 nm.
0.0	0.00
10.0	0.28
20.0	0.55
30.0	0.82
40.0	1.00

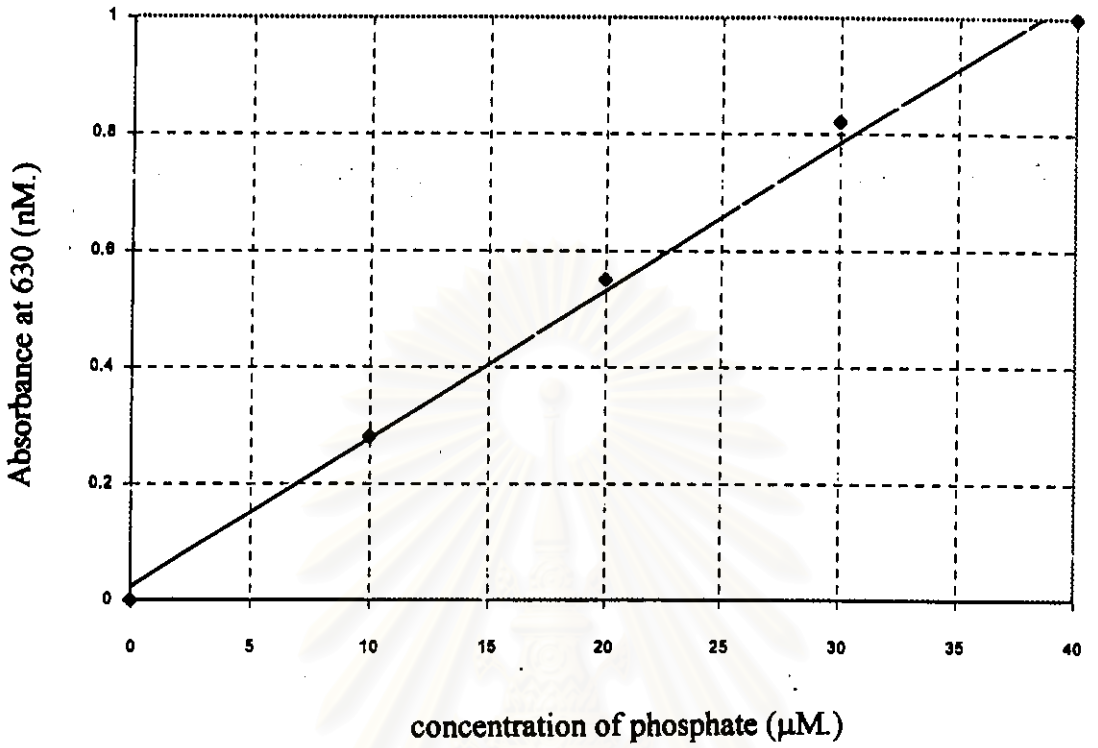

Figure 3 : Standard curve of standard phosphate solution