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STEREOSELECTIVE SYNTHESIS OF (±)-PALITANTIN[1]

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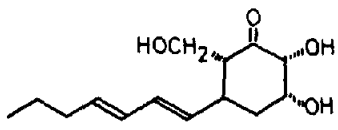
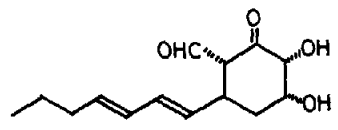
Abstract—Stereoselective synthesis of (±)-palitantin has been completed.

Palitantin (1) was isolated from *Penicillium palitans* Westling by Birkinshaw *et al.*[2] in 1936. Closely related compound, frequentin (2) was also isolated as an antibiotic compound from *Penicillium frequentans* Westling.[3] Though the structural[4] and biosynthetic studies,[5] and the correlation of these compounds were completed,[6] no synthetic method has been reported. We would like to report here the details of the synthesis of (±)-palitantin[7] utilizing efficiently neighboring group effect[8] as a methodology for regioselective reaction.

The Diels–Alder reaction of maleic anhydride and acetoxybutadiene, which was prepared from crotonaldehyde and isopropenyl acetate[9] afforded an adduct 3.[10] Treatment of the adduct with 3% methanolic hydrogen chloride at room temperature to yield quantitatively a dimethyl ester 4. *cis*-Hydroxylation of the ester 4 with osmium tetroxide followed by bisulfite work up gave a triol 5 in 92% yield. The stereochemistry of 5 was confirmed by the fact that the acetate 7 derived from 5 exhibited a signal at δ5.00 (1H, dd, J = 8Hz, 5Hz, –



1



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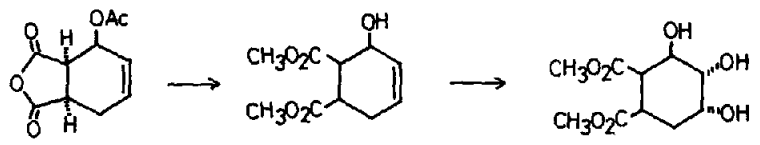
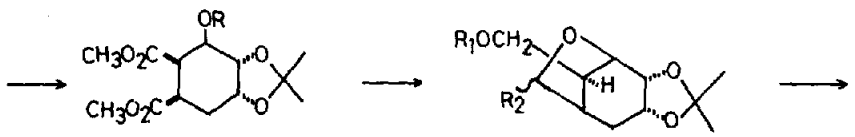
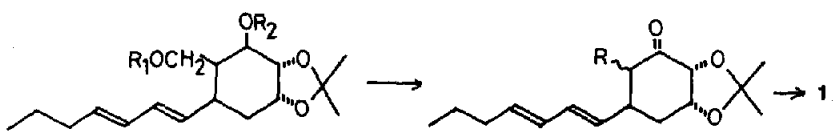


3 4 5



6: R = H
7: R = Ac

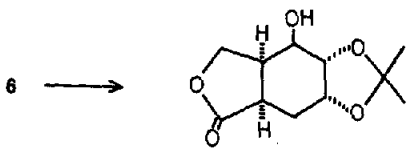
8: R_1 = H, R_2 = ⌣OH
9: R_1 = Ac, R_2 = ⌣OAc
10: R_1 = Ac, R_2 = ····OH



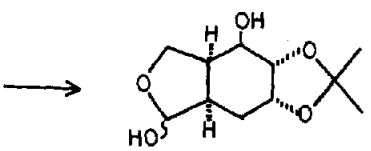
11: R_1, R_2 = Ac
12: R_1 = Ac, R_2 = H
13: R_1, R_2 = H
14: R_1 = C(C_6H_5)$_3$, R_2 = H

15: R = —OC(C_6H_5)$_3$
16: R = ····OC(C_6H_5)$_3$

CHOAc), whose data are compatible to the stable chair conformation arising from the configuration 7. Treatment of the triol **5** with dimethoxypropane and *p*-toluenesulfonic acid in dry acetone afforded an acetonide **6** in 93% yield. Regioselective reduction of the ester **6** was carried out by sodium borohydride utilising neighboring OH group effect to give a lactone **17** in low yield.

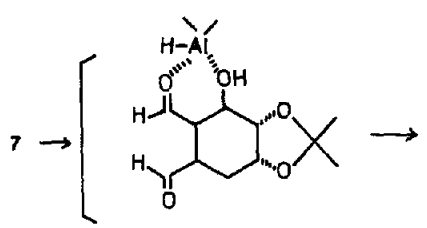


17

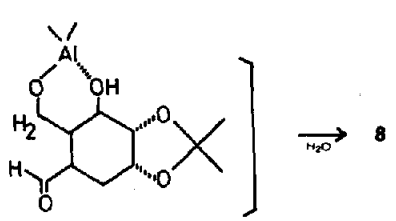


18

The selective formation of the lactone **17** was explained by the chelation of the reagent with nearby OH and ester group. The lactone **17** was easily converted by diisobutylaluminum hydride to a hemiacetal **18** which would serve as a useful intermediate leading to palitantin (**1**). In order to improve the yield of the reduction product **17**, the ester was reduced with diisobutylaluminum hydride. However, in this case, another hemiacetal **8** was directly obtained in 45% yield. Since the PMR spectrum of **8**

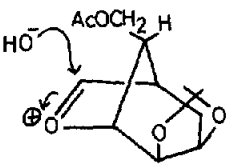


7a

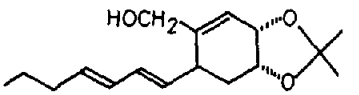


7b

indicates two signals (δ5.54, δ5.67, each 1/2 H) due to the hemiacetal proton, it was deduced that the compound **8** would be a mixture of diastereomeric isomers arising from the hemiacetal moiety. The formation of **8** was rationalised as follows. Reduction of two ester groups would yield a dialdehyde **7a** and subsequent reduction chelated with the reagent gives **7b** which is converted to **8** after hydrolysis. The Wittig reaction of **8** with 2-hexenyltriphenylphosphonium bromide under various



10a



19

conditions gave a dehydrated product **19**. In order to suppress the dehydration, it was intended that by the acetylation of the primary OH group of **8**, the tendency of deprotonation at 8-H would be decreased. Therefore, the hemiacetal **8** were acetylated to a diacetates **9**, and then hydrolysed regio- and stereoselectively to the monoacetate **10**. The stereochemistry of the OH group at the hemiacetal moiety was assigned as α since the signal due to the hemiacetal proton which have 90° of dihedral angle with vicinal 4-H, appeared at δ5.41 as a singlet. Stereoselective formation of **10** would be rationalised by the preferential attack of –OH from less hindered side of the oxonium ion **10a**.

The Wittig reaction of the hemiacetal **10** with (E)-2-hexenyltriphosphonium bromide gave 23.2% of a mixture of two products, diacetate **11** and monoacetate **12** in a ratio of 4:1. Since appreciable amount of **8** was recovered, the formation of the diacetate **11** would be ascribed to intermolecular acyl migration under the reaction conditions.

Treatment of each of **11** and **12** with sodium methoxide yielded the same diol **13** quantitatively. Since in the PMR spectra all three compounds, **11**, **12** and **13** reveal sharp signals, and in the IR spectra typical absorption bands ascribable to *trans* diene system were observed in a range of frequency at 980 ~ 990 cm^{-1}, it is clear that the Wittig reaction proceeded stereoselectively to give only *trans* isomer. The diol **13** was treated with trityl chloride in pyridine to afford a trityl compound **14**, which was quantitatively oxidised with chromium trioxide to a ketone **15**. Epimerisation at C-2 in **15** was carried out with DBU to give a thermodynamically stable isomer **16**, which has an adequate configuration leading to the natural product. Removal of the protective groups, trityl and acetonide groups, proceeded easily with *p*-toluenesulfonic acid in methanol to afford (±)-palitantin (**1**) in 97% yield. Since palitantin was converted to frequentin, present synthesis means in formal sense the synthesis of frequentin.

EXPERIMENTAL

All m.ps are uncorected and were determined on a Yanaco Micromelting Point Apparatus MP-3D. The IR spectra were recorded on a Hitachi IR Spectro-photometer Model 285 and PMR spectra on a Hitachi 90 MHz high Resolution Spectrometer Model R-22: the abbreviations *s*, *d*, *t*, *q* and *m* signify singlet, doublet, triplet, quartet and multiplet. Mass spectra were determined on Hitachi RMU-4 Spectrometer.

The starting material, 1-acetoxy-1, 3-butadiene, was prepared from crotonaldehyde and isopropenyl acetate according to known procedure b.p. 48 ~ 52°/32 mmHg.

3-Acetoxy-4-cyclohexen-1,2-dicarboxylic anhydride. This was prepeared from 1-acetoxy-1, 3-butadiene and maleic anhydride by the same procedure previously reported,[10] m.p. 56 ~ 59°.

Dimethyl c-3 - hydroxy - 4 - cyclohexen - r - 1, c - 2 - dicarboxylate (3). A soln of 10 g of the Diels–Alder adduct in 105 ml of methanolic HCl was allowed to stand for 24 hr at room temp. To the mixture was added *ca* 500 ml benzene and the mixture was washed with $NaHCO_3$aq. The organic layer was dried over Na_2SO_4 and evaporated *in vacuo* to give 9.9 g (97%) of oil 4 IR ν_{max}^{KBr}: 3400, 1730 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$: 2.30 ~ 2.45 (2H, m, CH_2), 2.98 ~ 3.14 (2H, m, –CH–), 3.72, 3.74 (each 3H, s, OCH_3), 4.40 (1H, bs, –CHOAc), 5.64 6.02 (2H, m, =CH), MS *m/e*: 214 (M^+). (Found: C, 56.00; H, 6.57. Calc. for $C_{10}H_{14}O_5$; C, 56.07; H, 6.59%).

Dimethyl c-3, t-4, t - 5 - trihydroxy - r - 1, c - 2 - cyclohexanedicarboxylate (5). To a stirred soln of 100 mg (0.47 mmol) of 4 in 1.5 ml THF was added 8.5 mg (0.033 mmol) of osmium tetroxide, and then dropwise a soln of 83 mg (0.27 mmol) barium chlorate in 0.5 ml water for 2.5 hr under ice-cooling. After the addition, the mixture was allowed to stand for 43 hr at room temp under stirring. To the mixture was then added dropwise a soln of 300 mg (2.88 mmol) $NaHSO_3$ in 1 ml water under stirring and ice-cooling, and the mixture was stirred for additional 12 hr at room temp. The mixture was extracted with EtOAc and the extracts were combined and dried over Na_2SO_4, evaporated *in vacuo* to leave 106 mg (91%o) of crystalline 5, which was recrystallised from $CHCl_3$–EtOAc, m.p. 136 ~ 137°, IR ν_{max}^{KBr} 3420 1735 cm^{-1}; PMR $\delta_{TMS}^{C_5D_5N}$ 2.20 ~ 2.90 (2H, m, CH_2), 3.22 ~ 3.61 (2H, m, –CH–), 3.62, 3.71 (each 3H, s, CH_3), 4.48 ~ 4.80 (3H, m, –CHO–). MS *m/e*: 248 (M^+). (Found: C, 48.34; H, 6.52. Calc. for $C_{10}H_{16}O_7$; C, 48.38; H, 6.50%).

Dimethyl c-3, t-4, t-5 - trihydroxy - 4,5 - di - O - isopropylidene - r - 1, c - 2 - cyclohexanedicarboxylate (6). A mixture of 167 mg of 5 in 0.4 ml dry acetone, 0.64 ml dimethoxypropane and 1.85 mg *p*-toluenesulfonic acid was allowed to stand for 3 days at room temp. The mixture was extracted with $CHCl_3$ and the organic layer was washed with $NaHCO_3$aq and then saturated brine, dried over Na_2SO_4, evaporated *in vacuo* to give 181 mg (93%) of an oil 6. IR ν_{max}^{film} 3450, 1720 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 1.35, 1.49 (each 3H, s, CH_3), 2.21 (2H, m, CH_2), 2.89 ~ 3.55 (2H, m, –CH–), 3.75 (6H, s, OCH_3), 4.05 (1H, m, –CHO), 4.25 (1H, t, J = 5Hz, –CHO), 4.45 (1H, q, J = 5Hz, J = 9Hz, –CHO), MS *m/e*: 288 (M^+).

Dimethyl c-3 - acetoxy - t-4, t-5 - dihydroxy - t-4, t-5 - di - O - isopropylidene - r - 1, c - 2 - dicarboxylate (7). A soln of 97 mg of 6 and 0.4 ml Ac_2O in 0.8 ml pyridine was allowed to stand for 12 hr. The mixture was poured onto ice-water, and the mixture was extracted with benzene. The combined extracts were washed with brine and dried over Na_2SO_4 evaporated *in vacuo* to yield 110 mg (99%) of 7, IR ν_{max}^{film} 1740 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 1.36, 1.49 (each 3H, s, CH_3), 2.07 (3H, s, $COCH_3$), 2.35 (2H, m, CH_2), 3.08 (1H, m, –CH–), 3.42 (1H, dd, J = 4.5Hz, J = 5Hz, –CH–), 3.68 (6H, s, OCH_3), 4.45 (2H, m, –CHO), 5.00 (1H, dd, J = 5Hz, J = 8Hz, –CHOAc).

8-Hydroxymethyl-5, 6-di-O-isopropylidene-3, 5, 6-trihydroxy - 2 - oxabicyclo [3, 2, 1] *heptanes* (8). To a stirred soln of 236 mg (0.82 mmol) of 6 in 3.2 ml dry toluene was added dropwise 3.2 ml (5.6 mmol) of a 1.76 M soln of diisobutylaluminum hydride in hexane at –60°. After keeping for 3 hr at the temp, to the mixture was added EtOAc and water, and the mixture was filtered through Highflosupercell, which was then washed with EtOAc. The combined filtrates were separated, and the organic layer was dried over Na_2SO_4, evaporated *in vacuo* to give a residue, which was chromatographed on a silica gel column using $CHCl_3$–EtOAc (1:1) as eluent to afford 86 mg (45%) of 8, mp 112 ~ 114°, recrystallised from toluene, IR ν_{max}^{film} 3400 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 1.32, 1.42 (each 3H, s, CH_3), 1.70 ~ 2.20 (2H, m, CH_2), 2.30 ~ 2.86 (2H, m, –CH–), 3.65 (1H, m, –CHO–), 3.90 ~ 4.51 (4H, m, –CHO, $–CH_2O$), 5.54 (½H, s, OCHO), 5.67 (½H, d, J = 5.5Hz, OCHO), MS *m/e*: 230 (M^+). (Found: C, 56.44; H, 7.77. Calc. for $C_{11}H_{18}O_6$; C, 57.38; H, 7.88%).

5, 6 - Di - O - isopropylidene - 3 - acetoxy - 8 - hydroxymethyl - 2 - oxabicyclo [3, 2, 1] *heptanes* (9). A soln of 577 mg (2.51 mmol) of 8 and 1.5 ml Ac_2O in 3 ml pyridine was allowed to stand for 12 hr at room temp. The mixture was poured onto ice, and extracted with benzene. The extracts were dried over Na_2SO_4 and concentrated *in vacuo* to yield 750 mg (95%) of 9, IR ν_{max}^{film} 1740 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 1.34, 1.46 (each 3H, s, CH_3), 2.04, 2.08, 2.09 (6H, s, $COCH_3$), 5.21 (1H, m, –CHO–), 6.19 (½H, s, –CHOAc), 6.35 (½H, d, J = 6Hz, –CHOAc), MS *m/e*: 314 (M^+).

Rel-(8S, 3R, 5R, 6S) - 8 - acetoxymethyl - 5, 6 - di - O - isopropylidene - 3, 5, 6 - trihydroxy - 2 - oxabicyclo [3.2.1] *heptane* (10). To a mixture of 1.136 g (3.62 mmol) of 9, 50 ml acetone and 50 ml water was gently introduced 20 ml gaseous HCl which was absorbed into a syringe from conc HCl bottle. After 12 hr, the mixture was extracted with EtOAc, and the extracts were washed with a $NaHCO_3$aq and with brine, dried over Na_2SO_4 and evaporated *in vacuo*. Purification of the residue by column chromatography on silica gel with $CHCl_3$–EtOAc (1:1) afforded 602 mg (65%) of 10, which was recrystallised from ether, m.p. 115 ~ 116°, ν_{max}^{KBr} 3400, 1745 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 1.31, 1.47 (each 3H, s, CH_3), 1.50 ~ 2.00 (2H, m, CH_2), 2.07 (3H, s, OCH_3), 2.45 ~ 2.99 (2H, m, –CH–), 3.62 (1H, dd, J = 3.5Hz, J = 8Hz, –CHO–), 4.05 ~ 4.59 (3H, m, –CHO–), 5.24 (1H, dt, J = 1.5Hz, J = 3.5Hz, –CHO–), 5.41 (1H, s, –CHO–). (Found: C, 57.24; H, 7.45. Calc. for $C_{13}H_{20}O_5$; C, 57.34; H, 7.40%).

c - 3 - Acetoxy - c - 2 - acetoxymethyl - t - , t - 5 - dihydroxy - 4, 5 - di - O - isopropylidene - r - 1 - [(1E, 3E) - 1, 3 - heptadienyl] cyclohexane (11) *and c - 2 - acetoxymethyl - t - 5, t - 6 - dihydroxy - 5, 6 - di - O - isopropylidene - c - 3 - [(1E, 3E) - 1, 3 - heptadienyl] - r - 1 - cyclohexanol* (12). To a stirred suspension of 2.156 g (5.07 mmol) E-2-hexenyltriphosphonium bromide in 3.9 ml dry THF was added rapidly 2.23 ml (5.22 mmol) 2.34 M n-BuLi soln under ice-cooling. After 30 min, 655 mg (2.39 mmol) of 10 in 0.78 ml dry THF was added. The mixture was stirred for 2 hr at 5 ~ 10°, and additional 8.5 hr at room temp. To the mixture was added benzene, and the mixture was washed with aqueous ammonium chloride, and evaporated *in vacuo*. The residue was extracted with ether and the combined extracts were dried over Na_2SO_4 and evaporated *in vacuo* to give a residue. Purification of the residue by column chromatography over silica gel with benzene–EtOAc (1:1) afforded 178 mg (19.5%) of 11, IR ν_{max}^{film} 1745, 985 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 0.90 (3H, t, J = 7Hz, $–CH_3$), 1.36, 1.51 (each 3H, s, CH_3), 2.02, 2.12 (each 3H, s, $COCH_3$), 1.15 ~ 2.25 (6H, m, $–CH_2–$) 2.29 ~ 2.56 (1H, m, –CH–), 2.60 ~ 3.00 (1H, m, –CH–), 4.10 (2H, d, J = 5.5Hz, $–CH_2O–$), 4.16 (1H, t, J = 6Hz, –CHO–), 4.32 ~ 4.53 (1H, m, –CHO–), 5.08 (1H, dd, J = 4.5Hz, J = 6Hz, –CHOAc), 5.28 ~ 6.39 (4H, m, =CH), MS *m/e*: 380 (M^+). Further elution with $CHCl_3$–MeOH (93:7) yielded 41 mg (5%) of 12, IR ν_{max}^{film} 3460, 1740, 990 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 0.92 (3H, t, J = 7Hz, CH_3), 1.36, 1.51 (each 3H, s, CH_3), 2.03 (3H, s, $COCH_3$), 1.12 ~ 2.11 (6H, m, $–CH_2–$), 2.12 ~ 2.40 (1H, m, –CH–), 2.45 ~ 2.90 (1H, m, –CH–), 3.89 (1H, dd, J = 4Hz, J = 6.5Hz, –CHO–), 4.20 (2H, m, $–CH_2–$), 4.31 ~ 4.50 (1H, m, –CHO), 5.40 ~ 6.21 (4H, m, =CH), MS *m/e*: 338 (M^+).

t - 5, t - 6 - Dihydroxy - 5, 6 - di - O - isopropylidene - c - 1 - [(1E, 3E) - 1, 3 - heptadinyl] - c - 2 - hydroxymethyl - r - 1 - cyclohexanol (13) *from* 11. A soln of 48 mg (0.89 mmol) NaOMe and 154 mg (0.405 mmol) of 11 was allowed to stand for 12 hr under stirring at room temp. To the mixture was added 10 ml water and the mixture was extracted with EtOAc. The combined extracts were dried over $NaSO_4$ and evaporated *in vacuo* to give 120 mg (quantitative) of 13, which was recrystallised from n-hexane to give a pure sam-

ple, mp 85.4~86.7°, IR ν_{max}^{KBr} 3460, 1620, 980 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 0.90 (3H, t, J = 6Hz, CH_3), 1.37, 1.51 (each 3H, s, CH_3), 1.15~2.40 (6H, m, $-CH_2-$), 2.45~2.90 (1H, m, $-\dot{C}H-$), 3.67~3.85 (2H, m, $-CH_2O-$), 3.97 (1H, dd, J = 4.5Hz, J = 7Hz, $-\dot{C}HO$), 4.18 (1H, q, J = 7Hz, J = 5Hz, $-\dot{C}HO-$), 4.30~4.50 (1H, m, $-\dot{C}HO-$), 5.22~6.29 (4H, m, $\rangle=\langle^{H}$). (Found: C, 68.86; H, 9.70. Calc. for $C_{17}H_{28}O_4$, C, 68.89; H, 9.52%). *From* **12**. A soln of 6 mg of sodium methoxide and 40 mg of **12** in 0.7 ml of dry methanol was treated by the same way and yielded 35 mg (quantitative) of **13**, which was identical with the previous sample **13** derived from **11**.

t - 5, *t* - 6 - *Dihydroxy* - 5, 6 - *di* - *O* - *isopropylidene* - *c* - 3 - [(1*E*, 3*E*) - 1, 3 - *heptadienyl*] - *c* - 2 - *trityloxymethyl* - *r* - 1 - *cyclohexanol* (**14**). A soln of 159 mg of **13** and 181 mg trityl chloride in 0.6 ml dry pyridine was allowed to stand for 2 days at room temp. The mixture was poured into benzene and the organic layer was washed with water and dried over Na_2SO_4, and evaporated *in vacuo* to give a residue, which was chromatographed on a silica gel eluting with benzene-EtOAc (9:1) to afford 196 mg (68%) of **14**. IR ν_{max}^{film} 3470, 3050, 1600, 990 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 0.91 (3H, t, J = 6.5Hz, CH_3), 1.35, 1.51 (each 3H, s, CH_3), 2.12~2.35 (1H, m, $-\dot{C}H-$), 2.45~2.82 (1H, m, $-\dot{C}H-$), 3.28 (2H, ddd, J = 10Hz, J = 7Hz, J = 5.5Hz, $-CH_2O-$), 3.82 (1H, dd, J = 7Hz, J = 4Hz, $-CH_2O-$), 3.98 (1H, dd, J = 7Hz, J = 5Hz, $-\dot{C}HO-$), 4.22~4.43 (1H, m, $-\dot{C}HO-$), 5.23~6.22 (4H, m, $\rangle=\langle^{H}$), 7.05~7.79 (15H, m, ArH). MS *m/e*: 538 (M^+).

t, 5, *t* - 6 - *Dihydroxy* - 5, 6 - *di* - *O* - *isopropylidene* - *c* - 3 - [(1*E*, 3*E*) - 1, 3 - *heptadienyl*] - *r* - 2 - *trityloxymethyl* - 1 - *cyclohexanone* (**15**). To a stirred soln of 0.22 ml pyridine in 3.3 ml dry CH_2Cl_2 was added 137 mg (1.37 mmol) CrO_3 at room temp. After 15 min, 107 mg (0.199 mmol) of **14** was added. The mixture was stirred for an additional 30 min and the resultant ppts were filtered off through a column of a small amount of silicic acid, and the column was washed with CH_2Cl_2. The combined filtrates were evaporated *in vacuo* to give 102 mg (quantitative) of **15**, IR ν_{max}^{film} 3050, 1600, 985 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 0.90 (3H, t, J = 6.5Hz, CH_3), 1.36, 1.45 (each 3H, s, CH_3), 1.89~2.22 (4H, m, $-CH_2-$), 2.74~3.11 (2H, m, $-\dot{C}H-$), 3.35 (2H, ddd, J = 9Hz, J = 6Hz, J = 6Hz, $-CH_2O-$), 4.30 (1H, d, J = 5.5Hz, $-\dot{C}HO-$), 4.40~4.65 (1H, m, $-\dot{C}HO$), 5.50~6.23 (4H, m, $\rangle=\langle^{H}$), 7.15~7.78 (15H, m, ArH). MS *m/e*: 536 (M^+).

c - 5, *c* - 6 - *Dihydroxy* - 5, 6 - *di* - *O* - *isopropylidene* - *c* - 3 - [(1*E*, 3*E*) - 1, 3 - *heptadienyl*] - *r* - 2 - *trityloxymethyl* - 1 - *cyclohexanone* (**16**). A soln of 101 mg (0.188 mmol) of **15** and 4 drops 1, 5-diazabicyclo[5, 4, 0] undecene-5 in 20 ml dry benzene was allowed to stand for 5 hr at 25°. The reaction was quenched by the addition of NH_4Claq and the mixture was extracted with benzene. The combined extracts were dried over Na_2SO_4 and evaporated *in vacuo* to give a residue. The residue was chromatographed on a silica gel column with benzene-EtOAc (9:1) to afford 73 mg (72%) of **16**, IR ν_{max}^{film} 1725, 980 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 0.91 (3H, t, J = 6.5Hz, CH_3), 1.45, 1.50 (each 3H, s, CH_3), 1.90~2.98 (6H, m, $-CH_2-$, $-\dot{C}H-$), 3.38 (2H, ddd, J = 9Hz, J = 5.5Hz, J = 3.5Hz, $-\dot{C}H_2O-$), 4.31 (1H, d, J = 7Hz, $-\dot{C}HO-$), 4.47~4.71 (1H, m, $-\dot{C}HO-$), 4.99~6.09 (4H, m, $\rangle=\langle^{H}$), 6.95~7.81 (15H, m, ArH).

(±)-*Palitantin* (**1**). A soln of 13 mg (0.024 mmol) of **16** and 7.8 mg (0.041 mmol) *p*-toluenesulfonic acid in 2.6 ml dry MeOH was allowed to stand for 5 hr under stirring at 25°. To the mixture was added water and the mixture was extracted three times with EtOAc. The combined extracts were dried over Na_2SO_4 and evaporated *in vacuo* to leave a residue, which was chromatographed on a silica gel column eluting with $CHCl_3$–EtOAc–MeOH (4:4:1) to yield 6 mg (97%) (±)-palitantin, recyrystallised from water to give pure sample, mp 139~141°; IR ν_{max}^{KBr} 3440, 1725, 980 cm^{-1}, PMR $\delta_{TMS}^{CDCl_3}$ 0.91 (3H, t, J = 6.5Hz, CH_3), 1.15~1.56 (2H, m, $-CH_2-$), 1.59~3.10 (6H, m, $-CH_2-$, $-\dot{C}H-$), 3.80 (2H, d, J = 5Hz, $-CH_2O-$), 4.20~4.31 (1H, m, $-\dot{C}HO-$), 4.32~4.50 (1H, m, $-CHO-$), 5.10 6.30 (4H, m, $\rangle=\langle^{H}$), MS *m/e*: 254 (M^+). (Found: C, 66.02; H, 8.62. Calc. for $C_{14}H_{22}O_4$, C, 66.11; H, 8.72%).

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