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Studies on the Constituents of the Seeds of *Alpinia katsumadai* HAYATA

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Four new diarylheptanoids [(5*R*)-*trans*-1,7-diphenyl-5-hydroxy-6-hepten-3-one (VIIa), (3*S*,5*S*)-*trans*-1,7-diphenyl-3,5-dihydroxy-1-heptene (VIIIa), *trans*-1,7-diphenyl-5-hydroxy-1-heptene (IX) and *trans,trans*-1,7-diphenyl-5-hydroxy-4,6-heptadien-3-one (Xa)] have been isolated from the seeds of *Alpinia katsumadai* HAYATA, together with *trans,trans*-farnesol (I), *trans*-cinnamaldehyde, three flavonoids [alpinetin(II), cardamomin(III) and pinocembrin(IV)], and two known diarylheptanoids [(3*S*,5*R*)-3,5-dihydroxy-1,7-diphenylheptane (V) and *trans,trans*-1,7-diphenyl-4,6-heptadien-3-one (VI)], and their structures were determined on the basis of chemical and spectral evidence. This is the first time that *trans*-cinnamaldehyde, IV, V and VI have been isolated from these seeds.

Keywords——*Alpinia katsumadai*; *Alpinia officinarum*; Zingiberaceae; diarylheptanoid; farnesol; cinnamaldehyde; flavonoid

The seeds of *Alpinia katsumadai* HAYATA (Japanese name: "sōzuku") (Zingiberaceae) are used as an aromatic stomachic. The constituents of the seeds hitherto isolated are 1,8-cineole, α-humulene, *trans,trans*-farnesol(I), linalool, camphor, terpinen-4-ol, carvotanacetone, bornyl acetate, geranyl acetate, methyl cinnamate, nerolidol, alpinetin(II) and cardamomin(III).[1] The present paper describes the isolation and the structural elucidation of further constituents of the seeds of *A. katsumadai*. We isolated four new diarylheptanoids (VIIa, VIIIa, IX and Xa), two known diarylheptanoids (V[2] and VI[3]), *trans, trans*-farnesol,[1a] *trans*-cinnamaldehyde and three known flavonoids(II,[1b] III[1b] and IV[4]). *trans*-Cinnamaldehyde, IV, V and VI have not previously been isolated from these seeds.

Two methods of isolation of the constituents were used, though they gave similar results. Method A was as follows. The seeds were extracted with ethyl ether at room temperature, and the extract was concentrated. The residue was extracted with benzene and acetone, and the fractions were separated by silica gel column chromatography and high pressure liquid chromatography (HPLC). In method B, the seeds were extracted with chloroform under reflux, and the extract was subjected to silica gel colum chromatography and preparative thin layer chromatography (PLC)

Method A gave eight constituents: II, III, IV, V, VI, VIIa, VIIIa and *trans*-cinnamaldehyde. Method B gave nine constituents: I, II, III, IV, VI, VIIa, VIIIa, IX and Xa.

Compound I was obtained as a pale yellow liquid, bp 120—130°C (0.1 mmHg), $C_{15}H_{26}O$ (*m/z* 222, M^+) and was identical with *trans,trans*-farnesol which has already been isolated from the same source,[1a] on the basis of spectral comparisons and elemental analysis.

Compound II was obtained as colorless needles from methanol–chloroform, mp 223—227°C, $C_{16}H_{14}O_4$ (*m/z* 270, M^+), and was identical with alpinetin which has already been isolated from the same source,[1b] on the basis of spectral comparisons and elemental analysis.

Compound III was obtained as orange-yellow needles from methanol-chloroform, mp 205—208°C, $C_{16}H_{14}O_4$ (*m/z* 270, M^+) and was identical with cardamomin, which has already been isolated from the same source,[1b] on the basis of spectral comparisons and elemental analysis.

Compound IV was obtained as colorless needles from hexane–chloroform, mp 205—207°C, $C_{15}H_{12}O_4$ (*m/z* 256, M^+) and was identical with pinocembrin, which has been isolated from

Pinus spp.,[4] on the basis of spectral comparisons and elemental analysis.

Compound V was obtained as colorless needles from hexane, mp 77—79°C, $C_{19}H_{24}O_2$ (isobutane–CIMS, *m/z* 285, $M^+ + 1$), $[\alpha]_D^{18}$ ±0° (*c*=0.2, $CHCl_3$) and was identical with 1,7-diphenyl-3,5-dihydroxyheptane, which has been isolated from *Alnus* spp.[2] and derived from dihydroyashabushiketol(XI),[5] on the basis of spectral comparisons and elemental analysis. Compound V was concluded to have *meso* type configuration from the value of the specific rotation, $[\alpha]_D$, so the structure of V was (3*S*,5*R*)-3,5-dihydroxy-1,7-diphenylheptane.

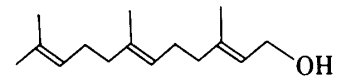
Compound VI was obtained as pale yellow needles from methanol, mp 64—65°C, $C_{19}H_{18}O$ (*m/z* 262 M^+) and was identical with *trans,trans*-1,7-diphenyl-4,6-heptadien-3-one, which has been isolated from *Alnus sieboldiana*,[3] on the basis of spectral comparisons and elemental analysis.

Compound VIIa was obtained as yellow needles from hexane–benzene, mp 59.5—60.5°C, $C_{19}H_{20}O_2$ (*m/z* 280, M^+), $[\alpha]_D^{23}$ +17.8° (*c*=0.67, EtOH). Acetylation of VIIa gave a monoacetate (VIIb), $C_{21}H_{22}O_3$. Dehydration of VIIa with a trace of sulfuric acid in dioxane gave VI. The infrared (IR) spectrum of VIIa indicated the presence of a saturated ketone (1710 cm^{-1}). The carbon-13 nuclear magnetic resonance (CMR) spectrum of VIIa indicated the presence of three methylenes (δ: 29.47, 45.08 and 49.47), a hydroxylated methine (δ: 68.48), a carbonyl group (δ: 209.68), two unhydrogenated sp^2-carbons (δ: 136.54 and 140.71), and twelve sp^2-carbons bearing a hydrogen. The proton nuclear magnetic resonance (PMR) spectrum of VIIa indicated the presence of two phenyl groups (δ: 6.9—7.4, 10H) and one pair of *trans* olefinic protons (δ: 6.12 and 6.66, *J*=16 Hz). The signal at δ: 6.66 was assigned to 7-H and the signal at δ: 6.12 was assigned to 6-H, because the coupling constants of the former were 16Hz and 2Hz, and the coupling constants of the latter were 16Hz and 6Hz, and the latter proton was coupled with the proton of a hydroxylated methine (δ: 4.60). This methine proton was coupled with the protons at δ: 2.14 (1H, dd, *J*=5 Hz and 16 Hz) and 2.51 (1H, dd, *J*=8 Hz and 16 Hz), and these protons were assigned as methylene protons at the 4-position. The A_2B_2 type protons at δ: 2.34 and 2.79 (*J*=8 Hz) indicated the presence of the structure, ph–CH_2–CH_2–CO. Hydrogenation of VIIa over palladium carbon gave the dihydro derivative, $C_{19}H_{22}O_2$ (*m/z* 282, M^+), $[\alpha]_D^{18}$ +14.56° (*c*=0.52, $CHCl_3$), which was identical with dihydroyashabushiketol (XI). The specific rotation, $[\alpha]_D$, of authentic dihydroyashabushiketol was + 10.81° (*c*=0.07, $CHCl_3$), so the configuration of the 5-position of the dihydro derivative must be the same as in the authentic compound, "*S*",[5] and the configulation of the 5-position of VIIa must be "*R*". Thus, the structure of VIIa was concluded to be (5*R*)-*trans*-1,7-diphenyl-5-hydroxy-6-hepten-3-one.

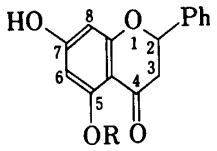
Compound VIIIa was obtained as colorless needles from hexane–benzene, mp 75—77°C, $C_{19}H_{22}O_2$ (*m/z* 282, M^+), $[\alpha]_D^{23}$ +25.19° (*c*=0.63, EtOH). Acetylation of VIIIa gave a diacetate (VIIIb), $C_{23}H_{26}O_4$, and hydrogenation of VIIIa over palladium carbon gave a dihydro derivative, $C_{19}H_{24}O_2$, $[\alpha]_D^{20}$ ±0° (*c*=3.49, MeOH), which was identical with V on the basis of spectral comparisons and *Rf* values on thin layer chromatography (TLC). VIIIa seemed to have no carbonyl group from the IR and CMR spectra. The CMR spectrum of VIIIa indicated the presence of three methylenes (δ: 31.64, 39.55 and 43.24) and two hydroxylated methines (δ: 71.41 and 73.14). The PMR spectrum of VIIIa indicated the presence of two phenyl groups (δ: 7.1—7.5, 10H), a pair of *trans* olefinic protons (δ: 6.22 and 6.59, *J*=16 Hz) and two protons of hydroxylated methines (δ: 3.96 and 4.56). One (δ: 6.22) of olefinic protons was coupled with one (δ: 4.56) of the hydroxylated methine protons. Decoupling experiments showed that the hydroxylated methine protons are neighbors to the protons at δ: 1.6—1.9, not the protons at δ: 2.72. Thus, the structure of VIIIa was concluded to be *trans*-3,5-dihydroxy-1,7-diphenyl-1-heptene. This conclusion was also supported by reduction of VIIa with sodium borohydride to afford the diol derivative VIIIc, which gave the same spectral data as VIIIa. However, the value of specific rotation of VIIIc was different, $[\alpha]_D^{25}$ −13.72 (*c*=3.10, EtOH). The hydrogenation of VIIIc over palladium carbon gave V, $[\alpha]_D^{26}$ ±0 (*c*=2.01, EtOH), *i.e.*, the *meso* type

compound. Hydrogenation of VIIIa and VIIIc gave the same *meso* type compound V, so VIIIa and VIIIc were antipodal. The configuration of VIIIc, derived from VIIa, is "3*R*, 5*R*" and the configuration of VIIIa is "3*S*, 5*S*".

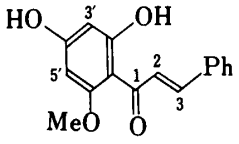
Compound IX was a colorless liquid, $C_{19}H_{22}O$ (*m/z* 226, M^+), $[\alpha]_D^{20}$ ±0° (*c*=0.74, MeOH). No evidence of a carbonyl group could be found in the IR and CMR spectra of IX. The CMR spectrum of IX indicated the presence of four methylenes (δ: 29.26, 32.08, 37.06 and 39.12) and one hydroxylated methine (δ: 70.92). The PMR spectrum of IX indicated the presence of two phenyl groups (δ: 7.22 and 7.28), a pair of *trans* olefinic protons (δ: 6.23 and 6.37, *J*=14 Hz), one proton of a hydroxylated methine (δ: 3.68) and four methylenes [δ: 1.75(5H), 2.29 (2H) and 2.73(2H)]. One (δ: 6.37) of the olefinic protons appeared as a doublet (*J*=14 Hz) and the other (δ: 6.23) was a double triplet (*J*=6 and 14 Hz); the latter signal changed to a doublet on irradiation of the protons at δ: 2.73, and each proton of δ: 2.29 and 2.73 was coupled with the methylene protons (δ: 1.75), not with the methine proton (δ: 3.68). Thus, the structure of IX was concluded to be *trans*-1,7-diphenyl-5-hydroxy-1-heptene. IX seemed to be a racemate.



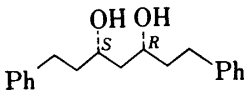
I



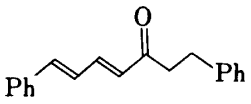
II : R=Me
IV : R=H



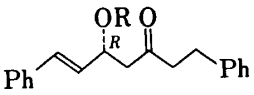
III



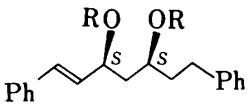
V



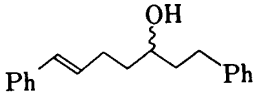
VI



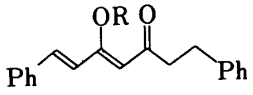
VIIa : R=H
VIIb : R=Ac



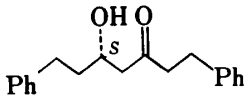
VIIIa : R=H
VIIIb : R=Ac



IX



Xa : R=H
Xb : R=Ac



XI

Chart 1

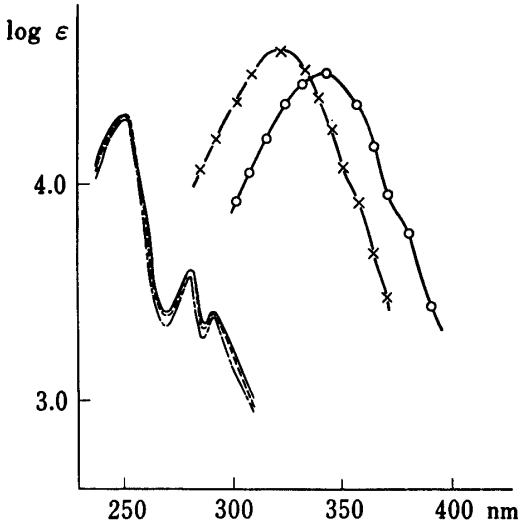


Fig. 1. The UV Spectra of VI, VIIa, VIIIa, IX and Xa in MeOH

×—×—×, VI; ——, VIIa; ·····, VIIIa; – – –, IX; ○—○—○, Xa.

Compound Xa was obtained as orange-yellow needles from hexane, mp 74—75°C, $C_{19}H_{18}O_2$ (*m/z* 278, M^+). Xa was positive to $FeCl_3$ reagent, so it was suggested to be the enol form of a 1,3-diketone. The acetylation of Xa gave a monoacetate (Xb), $C_{21}H_{20}O_3$ (*m/z* 320, M^+). The IR spectrum of Xa indicated the presence of a conjugated ketone (1640 cm^{-1}). The CMR spectrum of Xa indicated the presence of two methylenes (δ: 31.21 and 41.83), a carbonyl group (δ: 199.66), a hydroxylated olefinic carbon(δ: 176.79) and the α-carbon of a β-hydroxy-α, β-unsaturated ketone (δ:

100.72). The PMR spectrum of Xa indicated two phenyl groups[δ: 7.15 (5H) and 7.30(5H)], a pair of *trans* olefinic protons (δ: 6.33 and 7.53, J=16 Hz), two methylenes (δ: 2.65 and 2.94), the α-proton (δ: 5.47, s) and the proton (δ: 15.27, br) of a chelated hydroxy group in a β-hydroxy-α, β-unsaturated kettone moiety. The ultraviolet (UV) spectrum of Xa indicated a δ-phenyldienone structure like that of VI (Fig. 1). Thus, the structure of Xa was concluded to be *trans*, *trans*-1,7-diphenyl-5-hydroxy-4, 6-heptadien-3-one. This compound was also isolated from the *n*-hexane-soluble fraction of *Alpinia officinarum*.

The UV spectra of VI, VIIa, VIIIa, IX and Xa are shown in Fig. 1, and are consistent with the diarylheptanoid structures.

Curcumin was the first isolated diarylheptanoid (from *Curcuma* spp.)[6] Subsequently many diarylheptanoids were isolated from various plants, for example, *Alnus* spp.,[2,3] *Ostrya* spp.,[7] *Centrobium* spp.,[8] *Myrica* spp.,[9] *Acer* spp.,[10] and *Alpinia* spp.[11] We have now added four new diarylheptanoids to this group.

Experimental

All melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO IRA-2 or JASCO A-302 grating infrared spectrophotometer, and UV spectra were recorded on a Hitachi model 200-10 or Shimadzu UV-210 spectrometer. Optical rotations were determined on a JASCO DIP-4 or JASCO DIP-180 automatic polarimater. PMR spectra were recorded on a Hitachi R-24B (60 MHz), JEOL JNM-FX 90Q FT (90 MHz), JEOL PS-100 (100 MHz), Varian XL-200 (200 MHz) or JEOL FX-200 (200 MHz) NMR spectrometer with tetramethylsilane (TMS) as an internal standard (δ value) (s, singlet; d, doublet; t, triplet; q, quartet; br, broad). CMR spectra were recorded on a JEOL JNM-FX 90Q FT (90 MHz) or JEOL FX-100 (100 MHz) NMR spectrometer with TMS as an internal standard (δ value). Mass spectra (MS) were recorded on a JEOL JMS-D100, JEOL JMS-01SG-2, Hitachi M-80 or Hitachi RMU-7L mass spectrometer. TLC was carried out on Kiesel gel 60 GF_{254} (Merck) or precoated Kiesel gel 60 F_{254} (Merck), and PLC was carried out using Kiesel gel 60 PF_{254} (Merck). Column chromatography was carried out on Kiesel gel type 60 (Merck). HPLC was carried out on the CIG column system ($22\phi \times 300$ mm, Kusano Scientific Co., Tokyo) with Iatrobeads (60 μ spherical silica gel beads, Iatron Co., Tokyo).

Isolation of Constituents——Method A: The crushed seeds (1 kg) of *Alpinia katsumadai* (commercial product) were extracted three times with Et_2O at room temperature. Removal of the Et_2O *in vacuo* afforded 26 g of extract, which was extracted with benzene to give the benzene extract (18g) and an insoluble solid (8g). The benzene–insoluble part was extracted with acetone. Concentration of the acetone extract gave cardamomin (III) (3g). Recrystallization of the poorly acetone-soluble part from acetone gave alpinetin (II) (3g). The benzene extract was chromatographed on a silica gel column with a hexane–AcOEt gradient system as the developer. The eluates with hexane–AcOEt (9: 1) were subjected to HPLC (hexane: AcOEt: MeCN=45: 4: 1) to give VI (0.24 g) and *trans*-cinnamaldehyde (0.12 g). The eluate with hexane: AcOEt (4: 1) was subjected to HPLC (hexane: AcOEt: MeCN=20: 3: 2), and extracted with $CHCl_3$. The $CHCl_3$ extract was purified by HPLC (hexane: AcOEt: MeCN=20: 3: 2) to give IV (0.26 g) and VIIa (0.91 g). The eluate with hexane: AcOEt (2: 1) was subjected to HPLC (hexane: AcOEt=2: 1) and HPLC (benzene: iso-PrOH=19: 1), followed by Sephadex (LH-20) column chromatography (MeOH) to give V (20 mg) and VIIIa (1.56 g).

Method B: The crushed seeds (3 kg) of *A. katsumadai*, (commercial product) were extracted with $CHCl_3$ under reflux three times. The $CHCl_3$ extract was concentrated under reduced pressure. The residual extract (250 g) was chromatographed on a silica gel column with a benzene–AcOEt gradient system as the developer. The resultant eluates were recombined on the basis of their TLC pattern to give eleven fractions, Fr. 1—11. Fr. 4 (16 g) was recrystallized from hexane–benzene to give VI (10 g). Fr. 5 (28 g) was chromatographed repeatedly on a silica gel column with a hexane–benzene gradient system as the developer, and was subjected to PLC with benzene: hexane (1: 1) to give Xa (0.1 g). Fr. 6 (35 g) was recrystallized from benzene–$CHCl_3$ to give cardamomin (III) (5 g), and the mother liquor was column-chromatographed repeatedly with a hexane–AcOEt gradient system to give *trans*,*trans*-farnesol (I) (5 g) and pinocembrin (IV) (1 g). Fr. 8 (20 g) was also chromatographed on a silica gel column with a $CHCl_3$–MeOH gradient system and subjected to PLC ($CHCl_3$: MeOH=20: 1) to give I (0.5 g), VI (0.8 g), VIIa (4.2 g), IX (0.2 g) and III (2 g). Fr. 10 (8.5 g) was chromatographed on a silica gel column with a $CHCl_3$–MeOH gradient system to give VIIIa (2 g). Fr. 11 (15 g) was recrystallized from MeOH–$CHCl_3$ to give alpinetin (II) (10 g).

Compound I (*trans*,*trans*-Farnesol)——Pale yellow liquid, bp 120—130°C (0.1 mmHg). IR (liquid film) cm^{-1}: 3400, 1670, 1448, 1380, 1110, 950, 838. MS *m/z* (relative intensity %): 222 (M^+, 1.3), 161 (3), 136 (7), 121 (7), 109 (8), 107 (9), 95 (9), 93 (19), 81 (26), 69 (100), 68 (12), 67 (12). PMR ($CDCl_3$) δ: 1.0—1.3

(2H, m), 1.58 (6H, s), 1.65 (6H, s), 1.9—2.3 (6H, m), 4.04 (2H, d, J=7 Hz), 5.05 (2H, m), 5.37 (1H, t, J=7 Hz). *Anal.* Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.71; H, 11.57. This was identical with *trans,trans*-farnesol on the basis of bp, IR, MS and PMR comparisons.

Compound II (Alpinetin)——Colorless needles from $CHCl_3$–MeOH, mp 223—227°C [lit. 225°C (MeOH)].[1b] IR (KBr) cm^{-1}: 3520, 3200, 3075, 1636, 1610, 1580, 1474, 1315, 1274, 1210, 1110, 840, 770, 700. UV λ_{max}^{MeOH} nm (log ε): 225 (sh), 285 (4.44). PMR (methanol-d_4) δ: 2.70 (1H, dd, J=4, 16 Hz at C-3), 2.98 (1H, dd, J=12, 16 Hz, at C-3), 3.68 (3H, s, OCH_3), 5.32 (1H, dd, J=4, 12 Hz, at C-2), 6.20 (2H, m, at C-6, 8), 7.0—7.5 (5H, m). MS m/z (rel. int. %): 270 (M^+, 48), 193 (22), 167 (16), 166 (100), 138 (31). *Anal.* Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.05; H, 5.26. This was identical with an authentic sample on the basis of mp, IR, MS, UV and PMR comparisons.

Compound III (Cardamomin)——Orange-yellow needles from $CHCl_3$–MeOH, mp 205—208°C [lit. 207°C (Et_2O)].[1b] IR (KBr) cm^{-1}: 3150, 1622, 1543, 1485, 1340, 1322, 1257, 1244, 1210, 1170, 1115, 972, 828, 792, 769, 702. UV λ_{max}^{MeOH} nm (log ε): 235 (sh), 342 (4.42). MS m/z (rel. int. %): 270 (M^+, 52), 269 (48), 242 (13), 193 (100), 178 (10), 167 (47), 166 (19), 152 (18), 138 (21), 131 (13), 124 (20), 115 (12), 103 (43), 102 (17), 91 (15), 77 (55), 69 (46). PMR (acetone-d_6) δ: 3.97 (3H, s, OCH_3), 5.99 (1H, d, J=2 Hz, at C-3′), 6.08 (1H, d, J=2 Hz, at C-5′), 7.3—7.5 (3H, m), 7.6—7.8 (2H, m), 7.71 (1H, d, J=15 Hz, at C-2), 8.01 (1H, d, J=15 Hz, at C-3), 9.33 (1H, br, OH), 14.11 (1H, br, OH). *Anal.* Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.38; H, 5.41. This was identical with an authentic sample on the basis of mp, IR, UV, MS and PMR comparisons.

Compound IV (Pinocembrin)——Colorless needles from hexane–$CHCl_3$, mp 205—207°C [lit. mp 203—204°C (EtOH)].[4] IR (KBr) cm^{-1}: 3050, 1625, 1597, 1580, 1483, 1300, 1170, 1090, 825, 770. UV λ_{max}^{MeOH} nm (log ε): 289 (4.59). MS m/z (rel. int. %): 256 (M^+, 93) 255 (54), 238 (8), 179 (93), 153 (38), 152 (100), 124 (47), 111 (11), 104 (26), 103 (22), 96 (18), 91 (13), 77 (23), 69 (31). PMR (methanol-d_4) δ: 2.73 (1H, dd, J=4, 18 Hz, at C-3), 2.98 (1H, dd, J=12, 18 Hz at C-3), 5.30 (1H, dd, J=4, 12 Hz, at C-2), 5.90 (2H, s, at C-6, 8), 7.30 (5H, br), 12.00 (1H, br, OH). *Anal.* Calcd for $C_{15}H_{12}O_4$: C, 70.30; H, 4.72. Found: C, 70.31; H, 4.74. This was identical with an authentic sample on the basis of mp, IR, UV, MS and PMR comparisons.

Compound V[(3*S*, 5*R*)-3,5-Dihydroxy-1,7-diphenylheptane]——Colorless needles from hexane, mp 77—79°C (lit. liquid).[5] $[\alpha]_D^{18}$ ±0° (c=0.2, $CHCl_3$), *meso* type. IR (KBr) cm^{-1}: 3350, 3030, 1600, 1495, 1453, 1106, 1056, 1041, 846, 755, 710. UV λ_{max}^{MeOH} nm (log ε): 247 (2.65), 252 (2.70), 258 (2.75), 262 (2.77), 264 (2.70), 268 (2.74). Isobutane-CIMS m/z (rel. int. %): 285 (M^++1, 53), 267 (57), 249 (100), 205 (26), 170 (53), 117 (59), 91 (69). MS m/z (rel. int. %): 266 (M^+-H_2O, 1.6), 248 (4), 144 (19), 134 (16), 117 (22), 105 (15), 104 (12), 92 (29), 91 (100). PMR ($CDCl_3$) δ: 1.5—2.0 (6H, m, at C-2, 4, 6), 2.73 (4H, m, at C-1, 7), 3.89 (2H, m, at C-3, 5), 7.1—7.4 (10H, m, arom. protons). CMR ($CDCl_3$) δ: 31.86 (t), 39.88 (t), 43.07 (t), 72.28 (d), 126.03 (d), 128.57 (d), 142.11 (s). *Anal.* Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.66. Found: C, 80.36; H, 8.66. This was identical with an authentic sample on the basis of IR, MS and PMR comparisons.

Compound VI(*trans,trans*-1,7-Diphenyl-4,6-heptadien-3-one)——Yellow needles from MeOH, mp 64—65°C [lit. mp 61.0—62.5 (EtOH)].[3] IR (KBr) cm^{-1}: 1675, 1655, 1620, 1600, 1585, 1498, 1453, 1415, 1365, 1286, 1173, 1190, 996. UV λ_{max}^{MeOH} nm (log ε): 233 (3.90), 322 (4.54). MS m/z (rel. int. %): 262 (M^+, 49), 171 (46), 158 (20), 157 (100), 130 (36), 129 (58), 128 (83), 127 (36), 115 (23), 105 (16), 91 (41), 77 (37). PMR ($CDCl_3$) δ: 2.90 (4H, br, at C-1, 2), 6.20 (1H, d, J=15 Hz, at C-4), 6.6—7.0 (2H, m, at C-5, 6), 7.0—7.5 (11H, m, at C-7, arom. prot.). CMR ($CDCl_3$) δ: 30.12 (t), 42.21 (t), 126.03 (d), 126.62 (d), 127.16 (d), 128.30 (d), 128.73 (d), 129.06 (d), 129.44 (d), 135.99 (s), 141.20 (d and s), 142.44 (d), 198.89 (s). *Anal.* Calcd for $C_{19}H_{18}O$: C, 86.98; H, 6.91. Found: C, 87.10; H, 6.71. This was identical with an authentic sample on the basis of mp, IR, MS and PMR comparisons.

Compound VIIa [(5*R*)-*trans*-1,7-Diphenyl-5-hydroxy-6-hepten-3-one]——Yellow needles from hexane–benzene, mp 59.5—60.5°C. $[\alpha]_D^{28}$ +17.8° (c=0.67, EtOH). IR (KBr) cm^{-1}: 3275, 1710, 1603, 1496, 1418, 1381, 1349, 1145, 1110, 1050, 1020, 980, 757, 705. UV λ_{max}^{MeOH} nm (log ε): 251 (4.31), 283 (3.61), 292 (3.43). MS m/z (rel. int. %): 280 (M^+, 4.5), 262 (8), 175 (10), 171 (8), 148 (31), 133 (34), 132 (29), 131 (48), 130 (17), 115 (13), 105 (76), 104 (35), 103 (34), 91 (100), 77 (40). PMR (C_6D_6) δ: 2.14 (1H, dd, J=5, 16 Hz at $C\text{-}4_{eq}$), 2.34 (2H, t, J=8 Hz, at C-2), 2.51 (1H, dd, J=8, 16 Hz, at $C\text{-}4_{ax}$), 2.79 (2H, t, J=8 Hz, at C-1), 3.27 (1H, br, OH), 4.69 (1H, m, at C-5), 6.12 (1H, dd, J=6, 16 Hz, at C-6), 6.66 (1H, dd, J=2, 16 Hz, at C-7), 6.9—7.4 (10H, arom. prot.). CMR ($CDCl_3$) δ: 29.47 (t), 45.08 (t), 49.47 (t), 68.48 (d), 126.13 (d), 126.51 (d), 127.70 (d), 128.24 (d), 128.52 (d), 130.30 (d), 130.47 (d), 136.54 (s), 140.71 (s), 209.68 (s). *Anal.* Calcd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19. Found: C, 81.75; H, 7.27.

Acetylation of VIIa——VIIa (120 mg) was dissolved in pyridine (0.5 ml) and Ac_2O (0.2 ml), and the solution was stirred at room temperature overnight, then diluted with ice-water and extracted with $CHCl_3$. The extract was washed with water, dried over Na_2SO_4 and concentrated to give a pale yellow liquid, 120 mg, which was purified by PLC (hexane: AcOEt=3: 1, Rf=0.6) to give pure liquid monoacetate (VIIb), 40 mg. IR (liq. film) cm^{-1}: 1740, 1720, 1607, 1500, 1460, 1380, 1248, 1030, 975, 704. MS m/z (rel. int. %) ($C_{21}H_{22}O_3$= 322), 322 (M^+, 54), 279 (22), 262 (35), 171 (35), 157 (69), 133 (32), 131 (74), 130 (46), 129 (57), 128 (63), 115 (27), 105 (62), 103 (25), 91 (100). PMR ($CDCl_3$) δ: 2.02 (3H, s, $COCH_3$), 2.81 (6H, m, at C-4, 1, 2), 5.82 (1H, dt, J=6, 7 Hz, at C-5), 6.14 (1H, dd, J=7, 16 Hz, at C-6), 6.60 (1H, d, J=16 Hz, at C-7), 7.0—7.3 (10H, m, arom. prot.) CMR ($CDCl_3$) δ: 21.02 (q), 29.53 (t), 44.86 (t), 47.52 (t), 70.44 (d), 126.13 (d), 126.35 (d), 126.62

(d), 128.08 (d), 128.24 (d), 128.52 (d), 132.85 (d), 136.05 (s), 140.81 (s), 169.75 (s), 205.72 (s).

Dehydration of VIIa to VI——Three drops of 50% H_2SO_4 aq were added to a solution of VIIa (140 mg) in dioxane (8 ml), and the mixture was refluxed for 30 min, then diluted with water and extracted to give a pale yellow liquid, which was purified by PLC (hexane: AcOEt=3: 1, Rf=0.5). The purified product was recrystallized from MeOH to give yellow needles, 50 mg, mp 64—65°C. It was identical with VI on the basis of mp, IR, MS, PMR, CMR and TLC comparisons.

Hydrogenation of VIIa to Dihydroyashabushiketol (XI)——A solution of VIIa (100 mg) in MeOH (50 ml) was stirred with 5% Pd-C (30 mg) for 4 h at room temperature under an H_2 atmosphere, then the catalyst was removed by filtration and the filtrate was concentrated *in vacuo*. The residual solid was recrystallized from hexane to give colorless needles (XI), 50 mg, mp 52—53°C. $[\alpha]_D^{18}$ +14.56 (c=0.52, $CHCl_3$). IR (KBr) cm^{-1}: 3325, 1710, 1602, 1496, 1453, 1379, 1100, 1081, 754, 700. MS m/z (rel. int. %): 282 (M^+, 3), 264 (16), 159 (11), 148 (12), 134 (10), 133 (17), 105 (50), 104 (18), 103 (11), 92 (23), 91 (100), 79 (15), 78 (21), 77 (23). PMR ($CDCl_3$) δ: 1.73 (2H, m, at C-6), 2.54 (2H, d, J=6 Hz, at C-4), 2.6—2.9 (6H, m, at C-1, 2, 7), 4.03 (1H, quintet, J=6 Hz, at C-5), 7.0—7.3 (10H, m, arom. prot.). CMR ($CDCl_3$) δ: 29.47 (t), 31.70 (t), 38.09 (t), 44.92 (t), 49.36 (t), 66.91 (d), 125.81 (d), 126.13 (d), 128.19 (d), 128.35 (d), 128.46 (d), 140.65 (s), 141.74 (s), 210.60 (s). *Anal.* Calcd for $C_{19}H_{22}O_2$: C, 80.81; H, 7.85. Found: C, 80.75; H, 7.90. XI was identical with dihydroyashabushiketol[5] on the basis of mp, IR, PMR, TLC and $[\alpha]_D$ comparisons with an authentic sample. $[\alpha]_D^{18}$ of the authentic sample was +10.81° (c=0.07, $CHCl_3$) in our laboratory.

Compound VIIIa[(3*S*,5*S*)-*trans*-3,5-Dihydroxy-1,7-diphenyl-1-heptene]——Colorless needles from hexane–benzene, mp 75—77°C. $[\alpha]_D^{23}$ +25.19° (c=0.63, EtOH). IR (KBr) cm^{-1}: 3500, 1600, 1495, 1451, 1368, 1073, 1005, 754, 695. UV λ_{max}^{MeOH} nm (log ε): 252 (4.30), 283 (3.56), 292 (3.42). MS m/z (rel. int. %): 282 (M^+, 3), 264 (80), 246 (8), 173 (10), 159 (35), 133 (100), 104 (94), 91 (42). PMR ($CDCl_3$, 200 MHz) δ: 1.6—1.9 (4H, m, at C-4, 6), 2.72 (2H, m, at C-7), 3.12 (2H, br, OH), 3.96 (1H, quintet, J=6 Hz, at C-5), 4.54 (1H, q, J=6 Hz, at C-3), 6.22 (1H, dd, J=6, 16 Hz, at C-2), 6.59 (1H, d, J=16 Hz, at C-1), 7.1—7.5 (10H, m, arom. prot.). CMR ($CDCl_3$) δ: 31.64 (t), 39.55 (t), 43.24 (t), 71.41 (d), 73.14 (d), 125.75 (d), 126.46 (d), 127.59 (d), 128.35 (d), 128.52 (d), 129.93 (d), 131.88 (d), 136.59 (s), 141.90 (s). *Anal.* Calcd for $C_{19}H_{22}O_2$: C, 80.81; H, 7.85. Found: C, 80.53; H, 7.86.

Acetylation of VIIIa——A solution of VIIIa (170 mg) in Ac_2O (0.5 ml) and pyridine (1 ml) was allowed to stand at room temperature for 5 h. The reaction mixture was treated in the previously described manner to give a crude pale yellow liquid, 180 mg. The crude acetate was purified by PLC (hexane: AcOEt=3: 1, Rf=0.6) to give a colorless liquid diacetate (VIIIb), 80 mg. $[\alpha]_D^{20}$ −19.8° (c=5.14, MeOH). IR (liq. film) cm^{-1}: 1745, 1608, 1502, 1460, 1382, 1250, 1035, 976, 763, 707. MS m/z (rel. int. %) ($C_{23}H_{26}O_4$=366): 366 (M^+, 0.5), 159 (42), 155 (42), 146 (30), 142 (40), 133 (45), 131 (61), 130 (23), 129 (25), 117 (30), 115 (24), 105 (26), 104 (36), 91 (100). PMR ($CDCl_3$) δ: 1.6—2.3 (4H, m, at C-4, 6), 1.95 (3H, s, $COCH_3$), 1.98 (3H, s, $COCH_3$), 2.65 (2H, dd, J=8, 16 Hz, at C-7), 5.05 (1H, m, at C-5), 5.45 (1H, q, J=6 Hz, at C-3), 6.02 (1H, dd, J=6, 16 Hz, at C-2), 6.52 (1H, d, J=16 Hz, at C-1), 7.0—7.3 (10H, m, arom. prot.). CMR ($CDCl_3$) δ: 21.02 (q), 21.13 (q), 31.53 (t), 35.92 (t), 39.01 (t), 70.49 (t), 71.74 (d), 125.97 (d), 126.62 (d), 126.94 (d), 127.98 (d), 128.30 (d), 128.41 (d), 128.57 (d), 132.80 (d), 136.21 (s), 141.20 (s), 169.80 (s), 170.28 (s).

Hydrogenation of VIIIa to V——A solution of VIIIa (250 mg) in MeOH (50 ml) was stirred with 5% Pd-C (50 mg) for 3 h at room temperature under an H_2 atmosphere, then the mixture was treated in the manner described previously, and the product was purified by PLC (benzene: AcOEt=1.2: 1, Rf=0.6). It was recrystallized from hexane to give colorless needles, 120 mg, mp 79°C. $[\alpha]_D^{20}$ ±0° (c=3.49, MeOH). It was shown to be identical with V by mp, IR, MS, PMR and TLC comparisons.

Reduction of VIIa to VIIIc——A solution of VIIa (240 mg) in MeOH (8 ml) was stirred with $NaBH_4$ (80 mg) for 3 h at room temperature. The reaction mixture was diluted with water and extracted with $CHCl_3$. The extract was washed with water, dried over Na_2SO_4, and concentrated to give a colorless solid, which was recrystallized from hexane–benzene to give colorless needles (VIIIc), 150 mg, mp 75—77°C. $[\alpha]_D^{25}$ −13.72° (c=3.10, EtOH). It was identical with VIIIa on the basis of mp, TLC, IR, PMR and CMR comparisons, but the value of the specific rotation was different. VIIIc is the antipode of VIIIa.

Hydrogenation of VIIIc to V——A solution of VIIIc (79 mg) in MeOH (10 ml) was stirred with 5% Pd-C (20 mg) for 3 h at room temperature under an H_2 atmosphere, then treated in the previously described manner. The product was recrystallized from hexane to give colorless needles, 45 mg. mp 79°C. $[\alpha]_D^{26}$ +0° (c=2.01, EtOH). It was identical with V on the basis of mp, IR, PMR, CMR and TLC comparisons.

Compound IX (*trans*-1,7-Diphenyl-5-hydroxy-1-heptene)——Colorless liquid, $[\alpha]_D^{20}$ ±0° (c=0.74, MeOH), IR (liq. film) cm^{-1}: 3370, 2930, 1600, 1494, 1452, 966, 748, 700. UV λ_{max}^{MeOH} nm (log ε): 252 (4.20), 283 (3.49), 292 (3.33). Hi-MS m/z (rel. int. %): 266.165 (M^+, Calcd for $C_{19}H_{22}O$: 266.167). MS m/z (rel. int. %): 266 (M^+, 2.6), 157 (11), 144 (44), 143 (15), 131 (12), 129 (28), 117 (37), 91 (100). PMR ($CDCl_3$) δ: 1.75 (4H, m, at C-4, 6), 2.29 (2H, m, at C-7), 2.73 (2H, dt, J=6, 7 Hz, at C-3), 3.68 (1H, quintet, J=6 Hz, at C-5), 6.23 (1H, dt, J=6, 14 Hz, at C-2), 6.37 (1H, d, J=14 Hz, at C-1), 7.22 (5H, m, arom. prot.), 7.28 (5H, m, arom. prot.). CMR ($CDCl_3$) δ: 29.26 (t), 32.08 (t), 37.06 (t), 39.12 (t), 70.92 (d), 125.86 (d), 125.97 (d), 126.94 (d), 128.41 (d), 130.36 (d), 137.67 (s), 142.06 (s).

Compound Xa (*trans*,*trans*-1,7-Diphenyl-5-hydroxy-4,6-heptadien-3-one)——Orange-yellow needles from hexane, mp 74—75°C. Xa was positive to $FeCl_3$ reagent. IR (KBr) cm^{-1}: 1640, 1600, 1590, 1428,

1130, 974, 892, 750, 699. UV λ_{max}^{MeOH} nm (log ε): 341 (4.50), 358 (sh), 377 (sh). MS *m/z* (rel. int. %): 278 (M^+, 49), 187 (27), 173 (60), 146 (36), 145 (34), 131 (100), 105 (17), 104 (18), 103 (47), 91 (53). PMR ($CDCl_3$) δ: 2.62 (2H, m, at C-2), 2.93 (2H, m, at C-1), 5.47 (1H, s, at C-4), 6.33 (1H, d, $J=16$ Hz, at C-6), 7.15 (5H, br, arom. prot.), 7.30 (5H, m, arom. prot.), 7.53 (1H, d, $J=16$ Hz, at C-7), 15.27 (1H, br, OH). CMR ($CDCl_3$) δ: 31.21 (t), 41.83 (t), 100.72 (d), 122.83 (d), 126.19 (d), 127.87 (d), 128.24 (d), 128.46 (d), 128.84 (d), 129.82 (d), 135.07 (s), 139.68 (d), 140.81 (s), 176.79 (s), 199.66 (s). *Anal.* Calcd for $C_{19}H_{18}O_2$: C, 81.98; H, 6.52. Found: C, 82.00; H, 6.59.

Acetylation of Xa——A solution of Xa (40 mg) in Ac_2O (0.5 ml) and pyridine (0.5 ml) were acetylated in the previously described manner. The acetylated product was purified by PLC ($CHCl_3$, $Rf=0.4$) to give a liquid monoacetate (Xb), 25 mg. MS *m/z* (rel. int. %) ($C_{21}H_{20}O_3=320$): 320 (M^+, 6), 277 (40), 185 (48), 173 (100), 155 (21), 146 (37), 145 (45), 131 (88), 105 (33), 103 (47), 91 (75), 77 (42). PMR ($CDCl_3$) δ: 2.40 (3H, s, $COCH_3$), 2.85 (4H, m, at C-1, 2), 6.08 (1H, s, at C-4), 6.62 (1H, d, $J=16$ Hz, at C-6), 7.07 (1H, d, $J=16$ Hz, at C-7), 7.0—7.5 (10H, m, arom. prot.).

***trans*-Cinnamaldehyde**——Yellow liquid. IR (liq. film) cm^{-1}: 1680 (C=O). UV λ_{max}^{MeOH} nm (log ε): 281 (4.30). PMR ($CDCl_3$) δ: 6.71 (1H, dd, $J=8$, 16 Hz, at C-2), 7.3—7.7 (6H, overlap. m, arom. prot. and C-3), 9.70 (1H, d, $J=8$ Hz, at C-1). MS *m/z* (rel. int. %): 132 (M^+, 80), 131 (100), 103 (40).

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