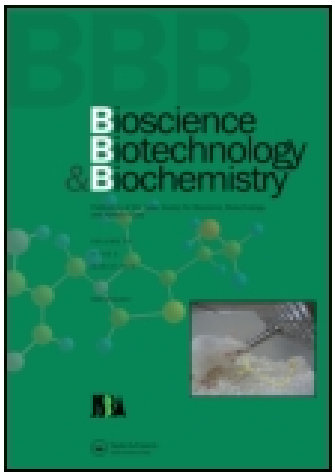


Bioscience, Biotechnology, and Biochemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/tbbb20

Total Synthesis of (+)-Paulownin

Momotoshi Okazaki[a], Fumito Ishibashi[ab], Yoshihiro Shuto[a] & Eiji Taniguchi[ac]
[a] Faculty of Agriculture, Ehime University, Matsuyama 790, Japan
[b] Faculty of Fisheries, Nagasaki University, Nagasaki 852, Japan
[c] Faculty of Agriculture, Kyushu University, Fukuoka 812, Japan
Published online: 12 Jun 2014.

To cite this article: Momotoshi Okazaki, Fumito Ishibashi, Yoshihiro Shuto & Eiji Taniguchi (1997) Total Synthesis of (+)-Paulownin, Bioscience, Biotechnology, and Biochemistry, 61:4, 743-745, DOI: 10.1271/bbb.61.743

To link to this article: http://dx.doi.org/10.1271/bbb.61.743

Biosci. Biotech. Biochem., **61** (4), 743–745, 1997

Note

Total Synthesis of (+)-Paulownin

Momotoshi OKAZAKI, Fumito ISHIBASHI,* Yoshihiro SHUTO, and Eiji TANIGUCHI**

Faculty of Agriculture, Ehime University, Matsuyama 790, Japan
**Faculty of Fisheries, Nagasaki University, Nagasaki 852, Japan*
***Faculty of Agriculture, Kyushu University, Fukuoka 812, Japan*
Received November 5, 1996

(+)-Paulownin, a furofuran lignan from *Paulownia tomentosa*, was stereoselectively synthesized from (*R*)-(+)-3-hydroxybutanolide in 12 steps with a yield of 4.4%.

Key words: stereoselective synthesis; (+)-paulownin; furofuran lignan; (*R*)-(+)-3-hydroxybutanolide

The furofuran lignans are particularly interesting because of their various biological activities,[1] and are good targets for stereocontrolled syntheses.[2] We have recently reported the stereoselective synthesis of (+)-phrymarolin I starting from (+)-malic acid.[3] It was expected that the same strategy would be available to synthesize other lignans having a similar structure. Among them, (+)-paulownin (**1**), which was isolated from *Paulownia tomentosa* (kiri),[4] is a representative furofuran lignan with a tertiary hydroxy function at the C-1 position. The syntheses of paulownin and its C-2 epimer, neopaulownin, have already been achieved as racemates by Kraus and Chen[5] and Mikami *et al.*,[6] respectively. However, a stereoselective synthesis of (+)-paulownin has not yet been reported, so we attempted to stereoselectively prepare the compound from (*R*)-(+)-3-hydroxybutanolide (**2**).[7]

In this experiment, the intermediates up to **9** were prepared according to the same reactions as those used for the synthesis of (+)-phrymarolin I,[3] except for using 3,4-methylenedioxybenzaldehyde for the reaction with the lithium enolate of (*R*)-**2** that had been generated by lithium diisopropylamide (LDA) to prepare **3**. Aldols **3a** and **3b** (63:37 on the basis of NMR data) were obtained in an 80% combined yield and were used in the next reaction as a mixture. After protecting the hydroxy groups of the mixture of **3** with dihydropyran (DHP) and *p*-toluenesulfonic acid (TsOH), the resulting THP–ether was reduced with lithium aluminum hydride and then treated with TsOH in dry methanol to give **4** as the sole product in an 84% yield. When the reaction was done without protection like that reported in the previous paper,[3] **4** was obtained in only an 8% yield. After protecting the primary hydroxy group of **4** with *tert*-butyldiphenylsilyl chloride (TBDPS-Cl), resulting **5** was oxidized to 4-furanone **6** (84% yield). Methylene furan **7** was obtained by the reaction of **6** with Tebbe reagent[8] in a yield of 68%. Oxidation of **7** with a catalytic amount of osmium tetroxide and *N*-methylmorpholine *N*-oxide (NMO) gave **8a** and **8b**, which were separated by silica gel chromatography, in yields of 78% and 13%, respectively. Next, Pfitzner–Moffatt oxidation (DMSO, DCC)[9] of **8a** gave hydroxyaldehyde **9** in a good yield (63% from **7**).

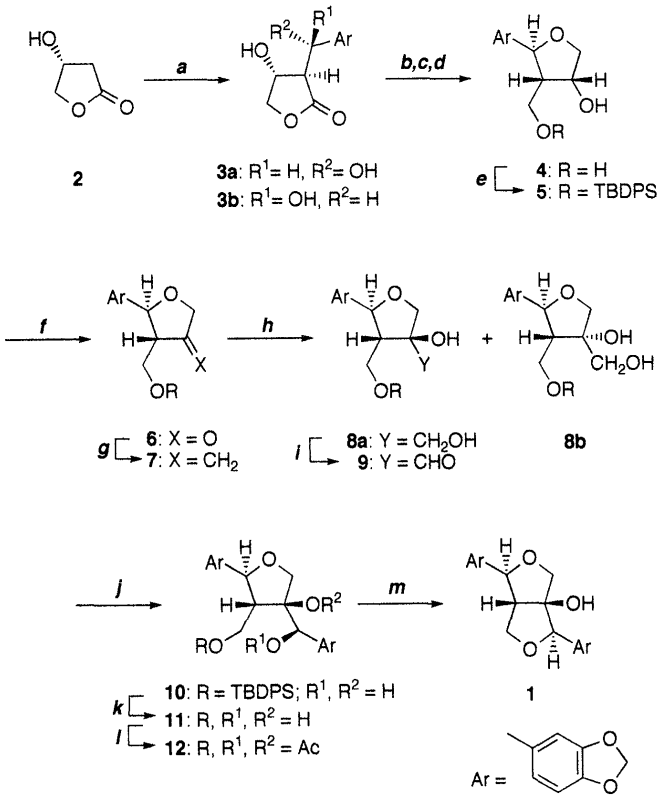
To introduce another aryl substituent, **9** was reacted with 3,4-methylenedioxyphenylmagnesium bromide to give diol **10** in a 28% yield. Removal of the TBDPS group of **10** with tetrabutylammonium fluoride gave triol **11**, whose structure was confirmed by measuring the NMR spectrum after being converted to its triacetate **12**. No other epimer of **12** was found in the spectrum. The hydroxybenzyl position of the product was considered to be of *R*-configuration due to the nucleophilic addition of a phenyl anion from the less-hindered side of cyclic chelation.[10] Finally, triol **11** was subjected to dehydrative cyclization with pyridinium *p*-toluenesulfonate (PPTS)[11] in dichloromethane to afford (+)-paulownin (**1**) in a 74% yield. The value for the optical rotation of **1**, $[\alpha]_D^{25}$ +28.4° (*c* 1.09, $CHCl_3$), is in agreement with that reported for the natural material, $[\alpha]_D^{24}$ +29.0° ($CHCl_3$).[4b]

As a result, (+)-paulownin was stereoselectively synthesized for the first time from (*R*)-(+)-3-hydroxybutanolide in 12 steps with a total yield of 4.4%.

Experimental

All melting point (mp) data are uncorrected. IR spectra were recorded with a Shimadzu IR-420 spectrometer, while the ^{1}H- and ^{13}C-NMR spectra were measured with a JEOL JNM GSX-270 spectrometer at 270 MHz and 68 MHz in $CDCl_3$, respectively. Optical rotation values were measured at 25°C with a Horiba SEPA-200 polarimeter.

(3R,4R)-4-Hydroxy-3-[(1R/S)-1-hydroxy-1-(3,4-methylenedioxyphenyl)-methyl]dihydro-2(3H)-furanone (**3**). A solution of (*R*)-(+)-**2** (2.20 g, 21.6 mmol) in dry THF (15 ml) was added dropwise to a solution of LDA



Scheme Synthesis of (+)-Paulownin (**1**).

Reagents and conditions: a) LDA, piperonal, −78°C (80%); b) DHP, TsOH; (c) $LiAlH_4$, −10°C; d) TsOH, 50°C (84%, 3 steps); e) TBDPS-Cl, Et_3N, DMAP (89%); f) $(COCl)_2$, DMSO, Et_3N, −78°C (95%); g) Tebbe reagent, −78°C to 25°C (68%); h) OsO_4, NMO, 5°C (76%); i) DCC, DMSO, TFA (83%); j) 3,4-methylenedioxyphenylmagnesium bromide; k) TBAF (26% from **9**); l) Ac_2O, pyr, DMAP (72%); m) PPTS, reflux (69%).

[prepared from 1.6 N *n*-BuLi in *n*-hexane (29.7 ml, 47.5 mmol) and diisopropylamine (6.66 ml, 47.5 mmol)] in THF (100 ml) at −78°C under N_2. After 2 h, piperonal (3.23 g, 21.6 mmol) in THF (20 ml) was added dropwise to the reaction mixture. After stirring for 3 h at −78°C, the mixture was worked up with 1 N HCl and extracted with EtOAc. The organic layer was successively washed with satd. aq. $NaHCO_3$ and brine. After drying (Na_2SO_4) and concentration, the residue was chromatographed on silica gel (*n*-hexane/EtOAc, 1:1 to 1:3), providing 2.72 g of **3a** as white crystals and 1.60 g of **3b** as a colorless oil. The total yield was 4.32 g (80%). **3a** (*erythro*): mp 112–114°C; ^{1}H-NMR δ: 6.97–6.76 (m, 3H), 5.94 (s, 2H), 5.15 (dd, 1H, J=3.7, 0.7 Hz), 4.94 (d, 1H, J=4.3 Hz), 4.53 (m, 1H), 4.42 (d, 1H, J=0.7 Hz), 4.38 (dd, 1H, J=9.5, 4.2 Hz), 4.03 (dd, 1H, J=9.5, 2.0 Hz), 2.66 (m, 1H); ^{13}C-NMR δ: 178.02, 149.11, 148.14, 138.31, 120.26, 109.13, 107.69, 102.44, 76.97, 72.45, 68.82, 58.47; IR ν_{max} ($CHCl_3$) cm^{-1}: 3495, 3047, 1773, 1744, 1491, 1256, 1196, 1046, 940; $[\alpha]_D^{25}$ +13.8° (*c* 0.54, EtOH). *Anal.* Found: C, 57.29; H, 4.81%. Calcd. for $C_{12}H_{12}O_6$: C, 57.14; H, 4.77%. **3b** (*threo*): ^{1}H-NMR δ: 6.94–6.79 (m, 3H), 5.98 (s, 2H), 4.90 (d, 1H, J=7.6 Hz), 4.40 (m, 1H), 4.25 (dd, 1H, J=9.5, 7.0 Hz), 3.97 (dd, 1H, J=9.5, 6.1 Hz), 3.79 (br, 1H), 2.87 (dd, 1H, J=7.6, 6.7 Hz), 2.09 (br, 1H)); ^{13}C-NMR δ: 176.28, 148.31, 147.95, 133.36, 119.81, 108.46, 106.79, 101.36, 72.76, 72.21, 68.98, 55.16; IR ν_{max} ($CHCl_3$) cm^{-1}: 3483, 3040, 1759, 1721, 1500, 1256, 1208, 1031, 962; $[\alpha]_D^{25}$ +87.3° (*c* 0.81, EtOH). *Anal.* Found: C, 56.96; H, 4.91%. Calcd. for $C_{12}H_{12}O_6$: C, 57.14; H, 4.77%.

(2S,3R,4R)-4-Hydroxy-3-hydroxymethyl-2-(3,4-methylenedioxyphenyl)-tetrahydrofuran (**4**). The hydroxy groups in the mixture of **3a** and **3b** (2.45 g, 9.72 mmol) were protected with DHP (1.95 ml, 21.4 mmol) according to the general method. Without purification, the THP–ether (4.15 g) in dry THF (10 ml) was added to a slurry of LAH (0.55 g, 14.6 mmol) in dry THF (40 ml) at −10°C under N_2. After stirring for 1 h, the reaction mixture was carefully quenched with 2 N HCl (15 ml) and extracted with EtOAc. The organic layer was successively washed with satd. aq. $NaHCO_3$ and brine. The solvent was removed, and the oily residue was dried as an azeotrope with toluene. The crude product (4.14 g) in dry MeOH (50 ml) was warmed with a catalytic amount of TsOH (*ca.* 10 mg) at 50°C for 12 h. After removing the solvent, the residue was diluted with EtOAc and successively washed with satd. aq. $NaHCO_3$ and brine. The organic layer was dried (Na_2SO_4) and concentrated. The residue was recrystallized from benzene to give 1.94 g (84%) of **4** as white crystals, mp 111–112°C; ^{1}H-NMR δ: 6.87–6.74 (m, 3H), 5.96 (s, 2H), 4.72 (d, 1H, J=10.1 Hz), 4.60 (m, 1H), 4.32 (d, 1H, J=2.0 Hz), 4.22 (dd, 1H, J=9.4, 4.3 Hz), 3.85–3.77 (m, 2H), 3.70 (dd, 1H, J=9.4, 2.1 Hz), 3.67 (d, 1H, J=1.2 Hz), 2.06 (m, 1H); ^{13}C-NMR δ: 149.12, 148.15, 136.63, 120.52, 108.25, 107.00, 101.63, 81.26, 74.71, 72.51, 57.23, 46.77; IR ν_{max} ($CHCl_3$) cm^{-1}: 3310, 1458, 1431, 1196, 1055, 983; $[\alpha]_D^{25}$ +49.3° (*c* 1.60, EtOH). *Anal.* Found: C, 60.31; H, 5.93%. Calcd. for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92%.

(2S,3R,4R)-3-[(tert-Butyldiphenylsilyl)oxy]methyl-4-hydroxy-2-(3,4-methylenedioxyphenyl)tetrahydrofuran (**5**). A mixture of **4** (1.53 g, 6.54 mmol), TBDPS-Cl (1.92 ml, 7.39 mmol), Et_3N (1.16 ml, 8.35 mmol) and a catalytic amount of DMAP in dry CH_2Cl_2 (20 ml) was allowed to stand at room temperature for 30 h. The mixture was successively washed with 10% aq. NH_4Cl and brine, before the organic layer was dried (Na_2SO_4) and concentrated. The residue was chromatographed on silica gel (*n*-hexane/EtOAc, 3:1 to 2:1) to give 2.73 g of **5** (89%) as a colorless oil. ^{1}H-NMR δ: 7.72–7.33 (m, 10H), 6.66–6.48 (m, 3H), 5.89 (s, 2H), 4.73 (d, 1H, J=10.1 Hz), 4.63 (m, 1H), 4.22 (dd, 1H, J=9.8, 4.3 Hz), 3.93–3.82 (m, 3H), 3.21 (br, 1H), 2.08 (m, 1H), 1.07 (s, 9H); ^{13}C-NMR δ: 147.77, 147.09, 135.59, 135.48, 134.76, 130.08, 129.97, 129.85, 127.90, 127.84, 127.63, 127.55, 119.82, 107.93, 106.43, 100.90, 80.37, 75.71, 73.99, 60.54, 53.76, 26.83, 19.05; IR ν_{max} ($CHCl_3$) cm^{-1}: 3980, 2953, 1736, 1467, 1432, 1203, 1043, 705. *Anal.* Found: C, 70.00; H, 6.77%. Calcd. for $C_{28}H_{32}O_5Si$: C, 70.56; H, 6.77%.

(4R,5S)-4-[(tert-Butyldiphenylsilyl)oxy]methyl-5-(3,4-methylenedioxyphenyl)dihydro-3(2H)-furanone (**6**). To a solution of DMSO (0.96 ml, 13.5 mmol) in dry CH_2Cl_2 (20 ml) was added dropwise oxalyl chloride (0.59 ml, 6.74 mmol) in CH_2Cl_2 (6 ml) at −78°C under N_2. The reaction mixture was stirred for 10 min before additing **5** (2.57 g, 5.39 mmol) in CH_2Cl_2 (10 ml). After 1 h, Et_3N (2.63 ml, 18.9 mmol) was added, and the mixture was allowed to warm to 0°C. After stirring for 30 min, the mixture was quenched with 10% aq. NH_4Cl and extracted with CH_2Cl_2. The organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The residue was recrystallized from *n*-hexane/EtOAc (9:1) to give 2.42 g of **6** (95%) as white crystals, mp 99–100°C; ^{1}H-NMR δ: 7.72–7.35 (m, 10H), 6.83–6.73 (m, 3H), 5.93 (s, 2H), 5.26 (d, 1H, J=9.8 Hz), 4.33 (d, 1H, J=6.8 Hz), 4.16 (dd, 1H, J=10.7, 3.4 Hz), 3.98 (d, 1H, J=6.8 Hz), 3.64 (dd, 1H, J=10.7, 2.9 Hz), 2.34 (m, 1H), 1.04 (s, 9H); ^{13}C-NMR δ: 213.96, 147.73, 147.09, 135.63, 135.57, 134.77, 129.86, 129.58, 128.00, 127.81, 127.75, 127.66, 120.14, 108.19, 106.59, 101.12, 81.20, 72.40, 58.85, 57.16, 26.76, 19.24; IR ν_{max} ($CHCl_3$) cm^{-1}: 2848, 1773, 1256, 1118, 1050, 765; $[\alpha]_D^{25}$ +7.8° (*c* 0.90, $CHCl_3$). *Anal.* Found: C, 70.56; H, 6.45%. Calcd. for $C_{28}H_{30}O_5Si$: C, 70.86; H, 6.37%.

(2S,3R)-3-[(tert-Butyldiphenylsilyl)oxy]methyl-4-methylene-2-(3,4-methylenedioxyphenyl)tetrahydrofuran (**7**). Tebbe reagent (0.5 M in PhMe, 10.40 ml, 5.20 mmol, Aldrich Chem. Co.) was added dropwise to a stirred solution of **6** (2.35 g, 4.95 mmol) in dry THF (150 ml) at −75°C under N_2. After stirring for 4 h at room temperature, Et_2O (150 ml) was added to the mixture, and then 1 N NaOH was added until no more gas evolved. The organic phase was dried (Na_2SO_4) and concentrated. Flash chromatography of the residue on silica gel (*n*-hexane/EtOAc, 9:1 to 4:1) provided 1.59 g of **7** (68%) as a colorless oil. ^{1}H-NMR δ: 7.71–7.34 (m, 10H), 6.89–6.69 (m, 3H), 5.92 (s, 2H), 4.99 (d, 1H, J=2.0 Hz), 4.94 (d, 1H, J=2.0 Hz), 4.88 (d, 1H, J=6.7 Hz), 4.55 (d, 1H, J=13.4 Hz), 4.39 (dd, 1H, J=12.1, 2.0 Hz), 3.79–3.63 (m, 2H), 2.75 (m, 1H), 1.06 (s, 9H); ^{13}C-NMR δ: 148.75, 147.74, 146.95, 135.67, 135.61, 135.57, 135.50, 133.41, 133.27, 129.69, 127.66, 127.64, 119.89, 107.99, 106.80, 100.10, 83.60, 71.46, 64.04, 54.05, 26.79, 19.22; IR ν_{max} ($CHCl_3$) cm^{-1}: 2986, 2518, 1491, 1250, 1105, 1046; $[\alpha]_D^{25}$ +1.0° (*c* 1.27, EtOH). *Anal.* Found: C, 73.32; H, 6.96%. Calcd. for $C_{29}H_{32}O_4Si$: C, 73.69; H, 6.82%.

(2S,3R,4RS)-3-[(tert-Butyldiphenylsilyl)oxy]methyl-4-hydroxy-4-hydroxymethyl-2-(3,4-methylenedioxyphenyl)tetrahydrofuran (**8a** and **8b**). To a solution of **7** (1.31 g, 2.75 mmol) in a mixture of acetone (30 ml) and H_2O (9 ml) was added NMO (0.48 g, 4.13 mmol) and 1% aq. OsO_4 (1 ml), and then the mixture was vigorously stirred overnight at 5°C under N_2. After additing 5% aq. $NaHSO_3$ (4 ml), the mixture was concentrated. The oily residue was taken up in EtOAc, washed with brine, dried (Na_2SO_4) and concentrated. The residue was chromatographed on silica gel (benzene/EtOAc, 2:1 to 1:1) to give 1.05 g of **8a** (76%) as a colorless oil and 0.19 g of **8b** (13%) as a colorless oil. **8a**: ^{1}H-NMR δ: 7.65–7.30 (m, 10H), 6.77–6.51 (m, 3H), 5.93 (dd, 2H, J=3.4, 1.5 Hz), 4.40 (d, 1H, J=7.9 Hz), 4.00 (dd, 1H, J=11.8, 1.6 Hz), 4.00 (d, 1H, J=9.7 Hz), 3.74–3.71 (m, 2H), 3.72 (d, 1H, J=9.7 Hz), 3.69 (dd, 1H, J=11.8, 0.8 Hz), 3.34 (br, 1H), 3.01 (br, 1H), 2.34 (m, 1H), 1.06 (s, 9H); ^{13}C-NMR δ: 147.79, 147.11, 135.54, 135.46, 135.35, 130.14, 130.09, 127.94, 127.87, 119.64, 107.87, 106.63, 100.94, 82.67, 82.09, 75.90, 64.06, 61.60, 59.53, 26.79, 19.01; IR ν_{max} ($CHCl_3$) cm^{-1}: 3568, 3453, 1739, 1495, 1256, 1119, 1047; $[\alpha]_D^{25}$ +10.4° (*c* 0.93, EtOH). *Anal.* Found: C, 68.96; H, 6.69%. Calcd. for $C_{29}H_{34}O_6Si$: C, 68.75; H, 6.76%. **8b**: ^{1}H-NMR δ: 7.65–7.30 (m, 10H), 6.33–6.41 (m, 3H), 5.92 (dd, 2H, J=1.8, 1.2 Hz), 4.57 (d, 1H, J=9.8 Hz), 4.07 (d, 1H, J=10.1 Hz), 3.89 (dd, 1H, J=6.4, 2.0 Hz), 3.86 (dd, 1H, J=9.0, 2.0 Hz), 3.77 (br, 1H), 3.77 (d, 1H, J=10.1 Hz), 3.70 (dd, 1H, J=9.0, 2.6 Hz), 3.65 (dd, 1H, J=6.4, 3.1 Hz), 3.40 (br, 1H), 1.95 (m, 1H) 1.05 (s, 9H); ^{13}C-NMR δ: 147.75, 147.23, 135.53, 135.47, 135.34, 130.16, 130.11, 127.95, 127.85, 119.87, 107.93, 106.37, 100.94, 81.76, 81.30, 76.58, 67.20, 59.79, 57.01, 26.70, 18.92; IR ν_{max} ($CHCl_3$) cm^{-1}: 3572, 3453, 1762, 1502, 1261, 1119; $[\alpha]_D^{25}$ +31.8° (*c* 0.37, EtOH). *Anal.* Found: C, 69.15; H, 6.58%. Calcd. for $C_{29}H_{34}O_6Si$: C, 68.75; H, 6.76%.

(2S,3R,4S)-3-[(tert-Butyldiphenylsilyl)oxy]methyl-4-formyl-4-hydroxy-2-(3,4-methylenedioxyphenyl)tetrahydrofuran (**9**). To a solution of **8a** (0.65 g, 1.28 mmol) in dry DMSO (2 ml) and dry benzene (2 ml) were added trifluoroacetic acid (74 µl, 0.96 mmol), pyridine (0.21 ml, 2.50 mmol) and DCC (0.79 g, 3.84 mmol) at 0°C. After stirring for 20 h at room temperature, the reaction mixture was filtered and diluted with 1 N HCl (10 ml), before being extracted with Et_2O. The organic phase was successively washed with satd. aq. $NaHCO_3$ and brine, before the dried (Na_2SO_4) organic layer was concentrated. The residue was chromatographed on silica gel (*n*-hexane/EtOAc, 3:1) to afford 0.54 g of **9** (83%) as a colorless oil. ^{1}H-NMR δ: 10.13 (s, 1H), 7.63–7.27 (m, 10H), 6.74–6.58 (m, 3H), 5.91 (s, 2H), 5.02 (d, 1H, J=9.3 Hz), 4.19 (d, 1H, J=9.5 Hz), 4.05 (d, 1H, J=9.5 Hz), 3.97 (br, 1H), 3.79 (dd, 1H, J=10.4, 3.2 Hz), 3.54 (dd, 1H, J=10.4, 4.5 Hz), 2.44 (m, 1H), 1.07 (s, 9H); ^{13}C-NMR δ: 200.05, 147.97, 147.37, 135.72, 135.58, 134.26, 130.10, 129.96, 127.89, 127.81, 119.78, 107.98, 106.32, 101.03, 85.11, 81.22, 72.98, 61.91, 57.94, 26.83, 19.07; IR ν_{max} ($CHCl_3$) cm^{-1}: 3517, 2940, 1731, 1496, 1256, 1120, 1047, 709. *Anal.* Found: C, 68.49; H, 6.45%. Calcd. for $C_{29}H_{32}O_6Si$: C, 69.02;

H, 6.39%.

(2S,3R,4S)-4-Hydroxy-3-hydroxymethyl-4-[(1R)-1-hydroxy-1-(3,4-methylenedioxyphenyl)methyl]-2-(3,4-methylenedioxyphenyl)tetrahydrofuran (**11**). To a solution of **9** (0.48 g, 0.95 mmol) in dry THF (5 ml) was added 3,4-methylenedioxyphenylmagnesium bromide [prepared from Mg (0.3 g, 12.34 mmol) and 4-bromo-1,2-methylenedioxybenzene (0.35 ml, 2.91 mmol)] in dry THF (10 ml) at −5°C under N_2. After stirring for 6 h at room temperature, AcOH was added, and the mixture was quenched with 1 N HCl and then extracted with Et_2O. The organic phase was successively washed with satd. aq. $NaHCO_3$, and brine. The dried (Na_2SO_4) organic layer was concentrated, and the residue was filtered through a short silica gel column, eluting with *n*-hexane/EtOAc (2 : 1) to give **10** as a colorless oil.

Crude **10** (0.21 g) in THF (5 ml) was treated with tetrabutylammonium fluoride (0.5 ml of 1.0 M in THF, 0.50 mmol) at 0°C. After stirring for 2 h at room temperature, the reaction mixture was diluted with H_2O (10 ml) and extracted with EtOAc. The organic layer was successively washed with 1 N HCl, satd. aq. $NaHCO_3$ and brine. The dried (Na_2SO_4) organic layer was concentrated, and the residue was chromatographed on silica gel (*n*-hexane/EtOAc, 1 : 2) to afford 87 mg of **11** (26%) from **9** as a colorless oil. The structure of **11** was confirmed after conversion to its triacetate **12**.

(2S,3R,4S)-4-Acetoxy-3-acetoxymethyl-4-[(1R)-1-acetoxy-1-(3,4-methylenedioxyphenyl)methyl]-2-(3,4-methylenedioxyphenyl)tetrahydrofuran (**12**). A mixture of **11** (60 mg, 0.154 mmol) and a catalytic amount of DMAP in Ac_2O (0.5 ml) and pyridine (0.5 ml) was allowed to stand at room temperature for 24 h. The reaction mixture was concentrated and purified by flash column chromatography (*n*-hexane/EtOAc, 2 : 1) to afford 57 mg of **12** (72%) as a colorless oil. ^{1}H-NMR δ: 6.92–6.74 (m, 6H), 6.02 (s, 1H), 5.98 (s, 2H), 5.95 (s, 2H), 4.74 (d, 1H, J=8.7 Hz), 4.43 (dd, 1H, J=10.1, 5.3 Hz), 4.25 (dd, 1H, J=10.1, 4.1 Hz), 4.11 (d, 1H, J=10.6 Hz), 3.88 (d, 1H, J=10.6 Hz), 3.19 (m, 1H), 2.09 (s, 3H), 2.05 (s, 3H), 2.00 (s, 3H); ^{13}C-NMR δ: 170.61, 170.00, 169.89, 148.07, 148.03, 147.65, 147.58, 120.32, 120.26, 108.38, 108.12, 107.99, 107.86, 107.82, 101.83, 101.07, 83.99, 76.13, 75.42, 63.79, 61.36, 21.26, 20.94, 20.67; IR ν_{max} ($CHCl_3$) cm^{-1}: 3004, 1743, 1495, 1269, 1200, 1047, 778. *Anal.* Found: C, 60.70; H, 5.09%. Calcd. for $C_{26}H_{26}O_{11}$: C, 60.49; H, 5.13%.

(1S,2R,5R,6S)-1-Hydroxy-2,6-bis(3,4-methylenedioxyphenyl)-3,7-dioxabicyclo[3.3.0]octane (paulownin, **1**). A mixture of **11** (43 mg, 0.111 mmol) and a catalytic amount of PPTS (*ca.* 10 mg) in CH_2Cl_2 (7 ml) was refluxed for 12 h. The reaction mixture was concentrated and purified by flash column chromatography (benzene/EtOAc, 9 : 1) to afford 28 mg of **1** (69%). ^{1}H-NMR δ: 6.97–6.77 (m, 6H), 5.99 (s, 2H), 5.96 (s, 2H), 4.84 (d, 1H, J=4.9 Hz), 4.82 (s, 1H), 4.52 (dd, 1H, J=9.2, 8.3 Hz), 4.05 (d, 1H, J=9.4 Hz), 3.91 (d, 1H, J=9.4 Hz), 3.84 (dd, 1H, J=9.2, 5.9 Hz), 3.05 (m, 1H), 2.18 (br, 1H); $[\alpha]_D^{25}$ +28.4° (*c* 1.09, $CHCl_3$), {natural **1**, $[\alpha]_D^{25}$ +29.0° ($CHCl_3$)}.[4b]

References

1) W. D. MacRae and G. H. N. Towers, *Phytochemistry*, **23**, 1207–1220 (1984).
2) T. Ogiku, S. Yoshida, H. Ohmizu, and T. Iwasaki, *J. Org. Chem.*, **60**, 1148–1153 (1995); H. Suginome, K. Orito, K. Yorita, M. Ishikawa, N. Shimoyama, and T. Sasaki, *J. Org. Chem.*, **60**, 3052–3064 (1995); T. Wirth, K. J. Kulicke, and G. Fragale, *J. Org. Chem.*, **61**, 2686–2689 (1996) and references cited therein.
3) M. Okazaki, F. Ishibashi, Y. Shuto, and E. Taniguchi, *Biosci. Biotech. Biochem.*, **61**, 660–663 (1997).
4) a) K. Takahashi, Y. Tanaka, K. Kobayashi, and T. Nakagawa, *Yakugaku Zasshi* (in Japanese), **83**, 1101–1105 (1963); b) K. Takahashi and T. Nakagawa, *Chem. Pharm. Bull.*, **14**, 641–647 (1966).
5) G. A. Kraus and L. Chen, *J. Am. Chem. Soc.*, **112**, 3464–3466 (1990).
6) K. Mikami, H. Matsueda, and T. Nakai, *Synlett*, **1993**, 235–236.
7) S. Saito, T. Hasegawa, M. Inaba, R. Nishida, T. Fujii, S. Nomizu, and T. Moriwake, *Chem. Lett.*, **1984**, 1389–1392.
8) F. N. Tebbe, G. W. Parshall, and G. S. Reddy, *J. Am. Chem. Soc.*, **100**, 3611–3613 (1978); D. L. J. Clive, P. L. Wickens, and L. Wikens, *J. Org. Chem.*, **60**, 5532–5536 (1995).
9) K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **87**, 5661–5670 (1965); K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **87**, 5670–5678 (1965).
10) C. Kibayashi, *J. Synthetic Org. Chem., Jpn.*, **53**, 700–711 (1995).
11) S. Takano, T. Ohkawa, S. Tamori, S. Satoh, and K. Ogasawara, *J. Chem. Soc., Chem. Commun.*, **1988**, 189–191.