Stereoselective Syntheses of Taiwanin A and Its Isomers Using a Cross-Coupling Reaction

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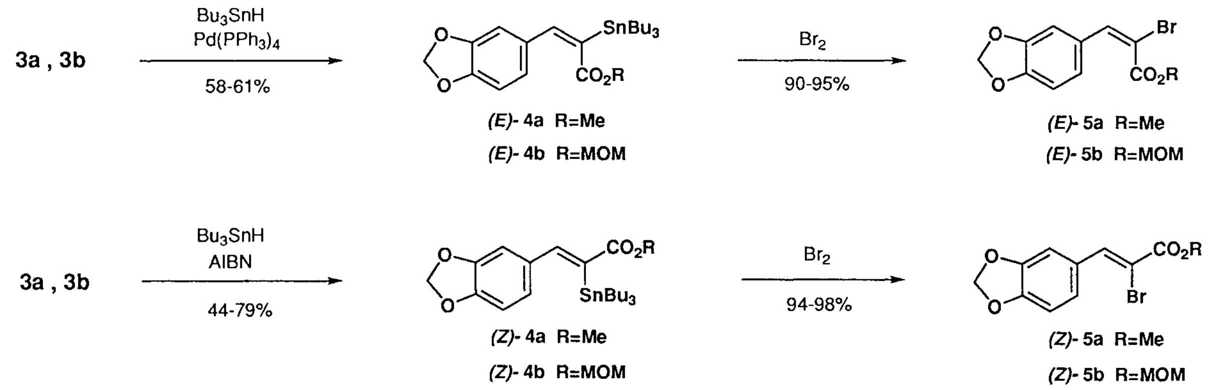
Taiwanin A and its isomers **7** were synthesized by means of the cross-coupling reaction of the vinylstannanes **4** and the vinyl bromides **5**, which were obtained from the propiolic acid esters **3** by stereoselective hydrostannation, as a key step.

Taiwanin A isolated from the *Taiwania Cryptomeriodes* Hayata[1] has attracted considerable interest because of its biological activities such as herbicidal activity.[2] However, the determination of the structure has been confused. At first, Lin et al. assigned it to be an α,β-bis(piperonylidene)-γ-butyrolactone based on spectral data, and assumed it to have a 2*E*,3*Z* configuration.[3] Next, Swoboda et al. proposed that the geometry of the diene should be 2*Z*,3*Z*.[4] These structural determinations were, however, largely based on the speculation that Taiwanin A could not have a 2*E*,3*E* configuration due to the steric interaction between the two aryl groups. On the other hand, Hart et al. suggested that the configuration of the diene was 2*E*,3*E* from the X-ray crystallographic and NMR analyses of (*E*,*E*)-bis(*p*-methoxybenzylidene)succinic anhydride which was synthesized using the Stobbe reaction as a key step.[5]

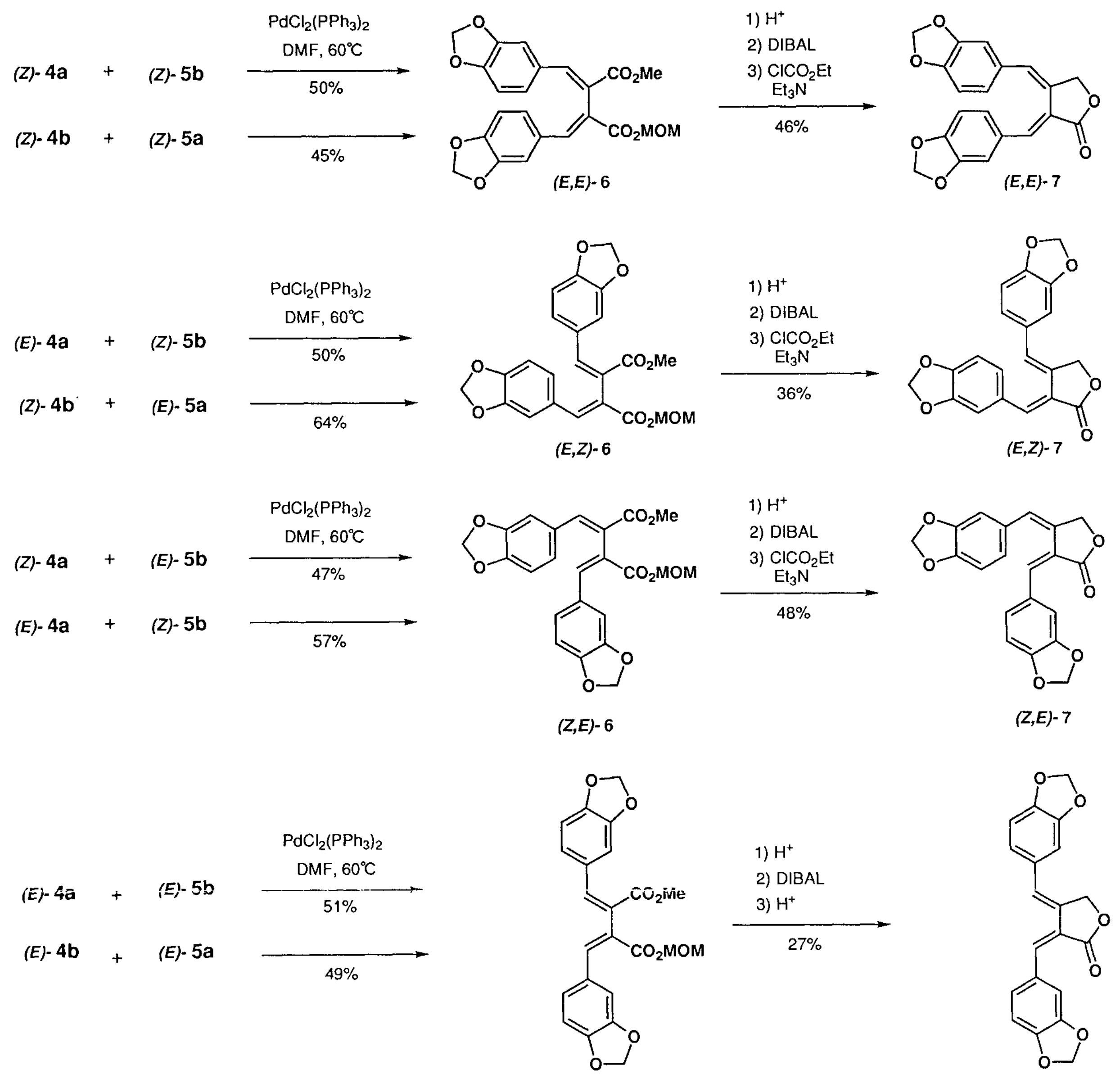
In the course of our synthetic study for exploring biologically active compounds having a diene structure, we planned to synthesize all isomers of Taiwanin A leading to the clear determination of its stereochemistry. The only method so far for the construction of this type of the diene system has been based on the Stobbe reaction.[6] Here, we wish to report a comprehensive synthetic method of Taiwanin A and its isomers **7** by means of the cross-coupling reaction of the vinylstannanes **4** and the vinyl bromides **5**, derived from the piperonylpropiolic acid esters **3**, in the presence of a Pd catalyst.[7]

The piperonylpropiolic acid methyl ester **3a** and methoxymethyl (MOM) ester **3b** were obtained from the piperonal **1** via the dibromolefin **2** in good yields[8] (Scheme 1). Hydrostannation of **3** in the presence of $Pd(PPh_3)_4$[9] proceeded stereoselectively to afford the *syn*-adducts (*E*)-**4** in good yields.[10] On the other hand, hydrostannation of **3** in the presence of 2,2′-azobisisobutyronitrile[11] (AIBN) proceeded stereoselectively to afford the *anti*-adducts (*Z*)-**4** in good yields. Treatment of the vinylstannanes (*E*)-**4** with bromine gave the vinyl bromides (*E*)-**5**,[12] with retention of the configuration, in high yields. Similarly, (*Z*)-**5** was obtained from the (*Z*)-vinylstannanes **4** in high yields.

The cross-coupling reaction of the vinylstannane (*Z*)-**4a** and the vinyl bromide (*Z*)-**5b** thus obtained proceeded smoothly in the presence of $PdCl_2(PPh_3)_2$ in DMF at 60 °C[13] to provide the bis(piperonylidene)succinic acid ester (*E*,*E*)-**6** in 50% yield without any change of the configuration (Scheme 2). In this reaction, the formation of the homo-coupling product was observed, albeit in a low yield. Similarly, appropriate combination of the vinylstannanes **4** and the vinyl bromides **5** gave the corresponding bis(piperonylidene)succinic acid esters **6** in moderate yields. Removal of the MOM group of the diester (*E*,*E*)-**6** by acid hydrolysis gave the half-ester in



Scheme 1



Scheme 2

a quantitative yield. Selective reduction of the methyl ester group with diisobutylaluminum hydride and subsequent cyclization via the mixed anhydride provided the lactone (*E,E*)-**7** in 46% yield. All the other diesters **6** were also transformed into the corresponding lactones **7** in good yields.[14]

The chemical shifts of the two vinyl protons of all the isomers thus obtained are shown in Table 1. The chemical shifts of (*E,E*)-**7** which are clearly distinguishable from those of the other isomers are completely in accord with those of natural Taiwanin A.[3] Furthermore, the structure of (*E,E*)-**7** was confirmed by X-ray analysis (Figure 1). Thus, we have verified beyond doubt that Taiwanin A possesses 2*E*,3*E* configuration.

This synthetic process will give a general method for stereoselective syntheses of all isomers of the α,β-dibenzylidene-γ-butyrolactones which are also important intermediates[6] for the syntheses of natural products such as lignans.

Table 1. Chemical Shifts of Vinyl Protons of Taiwanin A[3] and Compounds **7**

Compound	^{1}H NMR (DMSO-d_6) δ
Taiwanin A	6.68, 7.47
(*E*, *E*)-**7**	6.68, 7.47
(*E*, *Z*)-**7**	7.33, 7.35
(*Z*, *E*)-**7**	6.48, 7.46
(*Z*, *Z*)-**7**	7.05, 7.59

Mps were measured using a Yamato MP-21 melting-point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1640 infrared spectrophotometer. NMR spectra were recorded on a Bruker AC-200 spectrometer with Me_4Si as an internal standard. Mass spectra were recorded on a Hitachi M-2000A spectrometer at 70 eV. Column chromatography was carried out on silica gel (Kieselgel 60, 70–230 mesh, E. Merck).

Table 2. Compounds **5** Prepared

Product[a]	Yield[b] (%)	mp (°C)	IR (film or KBr) ν (cm^{-1})	^{1}H NMR (CDCl$_3$) δ, J (Hz)	MS m/z (%)
(*E*)-**5a**	90	oil	1725, 1595, 1500, 1490, 1450, 1240	3.80 (s, 3H, CO_2CH_3), 5.98 (s, 2H, OCH_2O), 6.78 (s, 2H, Ar), 6.85 (s, 1H, Ar), 7.25 (s, 1H, vinyl)	286 (48), 284 (M$^+$, 49), 205 (100)
(*E*)-**5b**	95	oil	1730, 1600, 1500, 1490, 1450, 1260, 1240	3.43 (s, 3H, $OCH_2OC\underline{H}_3$), 5.33 (s, 2H, $OC\underline{H}_2OCH_3$), 5.98 (s, 2H, OCH_2O), 6.77 (d, 1H, J = 8.0, Ar), 6.84 (dd, 1H, J = 8.0, 1.7, Ar), 6.91 (d, 1H, J = 1.7, Ar), 7.28 (s, 1H, vinyl)	316 (25), 314 (M$^+$, 27), 45 (100)
(*Z*)-**5a**	94	106–107	1710, 1590, 1505, 1450, 1265, 1230	3.89 (s, 3H, CO_2CH_3), 6.04 (s, 2H, OCH_2O), 6.86 (d, 1H, J = 8.2, Ar), 7.30 (dd, 1H, J = 8.2, 1.8, Ar), 7.65 (d, 1H, J = 1.8, Ar), 8.14 (s, 1H, vinyl)	286 (79), 284 (M$^+$, 80), 205 (100)
(*Z*)-**5b**	98	82–83	1690, 1610, 1595, 1500, 1455, 1265, 1230	3.55 (s, 3H, $OCH_2OC\underline{H}_3$), 5.43 (s, 2H, $OC\underline{H}_2OCH_3$), 6.04 (s, 2H, OCH_2O), 6.87 (d, 1H, J = 8.1, Ar), 7.32 (dd, 1H, J = 8.1, 1.8, Ar), 7.67 (d, 1H, J = 1.8, Ar), 8.19 (s, 1H, vinyl)	316 (27), 314 (M$^+$, 28), 45 (100)

[a] Satisfactory microanalyses obtained: C ± 0.23, H ± 0.05.

[b] Yield of pure isolated product.

Table 3. Compounds **6** Prepared

Product[a]	Yield[b,c] (%)	mp (°C)	IR (film or KBr) ν (cm^{-1})	^{1}H NMR (CDCl$_3$) δ, J (Hz)	MS m/z (%)
(*E*, *E*)-**6**	50, 45	126–127	1715, 1595, 1500, 1490, 1450, 1230	3.31 (s, 3H, $OCH_2OC\underline{H}_3$), 3.72 (s, 3H, CO_2CH_3), 5.28 (ABq, 2H, J = 5.9, ΔAB = 7.9, $OC\underline{H}_2OCH_3$), 5.94 (s, 4H, OCH_2O), 6.74 (m, 2H, Ar), 7.05 (m, 4H, Ar), 7.84 (s, 1H, vinyl), 7.87 (s, 1H, vinyl)	440 (M$^+$, 13), 408 (24), 149 (100)
(*E*, *Z*)-**6**	52, 64	oil	1715, 1600, 1500, 1490, 1450, 1235	3.48 (s, 3H, $OCH_2OC\underline{H}_3$), 3.72 (s, 3H, CO_2CH_3), 5.35 (s, 2H, $OC\underline{H}_2OCH_3$), 5.95 (s, 2H, OCH_2O), 5.98 (s, 2H, OCH_2O), 6.73 (s, 1H, vinyl), 6.77 (d, 2H, J = 8.0, Ar), 6.83 (dd, 1H, J = 8.0, 1.6, Ar), 6.98 (d, 1H, J = 1.6, Ar), 7.08 (dd, 1H, J = 8.0, 1.6, Ar), 7.14 (d, 1H, J = 1.6, Ar), 7.78 (s, 1H, vinyl)	440 (M$^+$, 10), 408 (17), 149 (100)
(*Z*, *E*)-**6**	47, 57	104–105	1715, 1600, 1500, 1490, 1450, 1240	3.35 (s, 3H, $OCH_2OC\underline{H}_3$), 3.80 (s, 3H, CO_2CH_3), 5.21 (s, 2H, $OC\underline{H}_2OCH_3$), 5.94 (s, 2H, OCH_2O), 5.97 (s, 2H, OCH_2O), 6.74 (s, 1H, vinyl), 6.77 (d, 2H, J = 8.0, Ar), 6.86 (dd, 1H, J = 8.0, 1.6, Ar), 7.03 (d, 1H, J = 1.6, Ar), 7.07 (dd, 1H, J = 8.0, 1.6, Ar), 7.13 (d, 1H, J = 1.6, Ar), 7.75 (s, 1H, vinyl)	440 (M$^+$, 6), 408 (16), 149 (100)
(*Z*, *Z*)-**6**	51, 49	143–144	1730, 1715, 1620, 1595, 1495, 1455, 1270	3.37 (s, 3H, $OCH_2OC\underline{H}_3$), 3.78 (s, 3H, CO_2CH_3), 5.33 (s, 2H, $OC\underline{H}_2OCH_3$), 5.97 (s, 2H, OCH_2O), 5.98 (s, 2H, OCH_2O), 6.75 (s, 1H, vinyl), 6.77 (s, 1H, vinyl), 6.78 (d, 2H, J = 8.0, Ar), 6.84 (dd, 1H, J = 8.0, 1.6, Ar), 6.84 (d, 1H, J = 1.6, Ar), 6.89 (dd, 1H, J = 8.0, 1.6, Ar), 6.91 (d, 1H, J = 1.6, Ar)	440 (M$^+$, 6), 408 (14), 149 (100)

[a] Satisfactory microanalyses obtained: C ± 0.26, H ± 0.02.

[b] Yield of pure isolated product.

[c] See Scheme 2

Table 4. Compounds **7** Prepared

Product[a]	Yield[b] (%)	mp (°C)	IR (KBr) ν (cm^{-1})	^{1}H NMR (DMSO-d_6) δ, J (Hz)	MS m/z (%)
(*E*, *E*)-**7**	46	202–203	1755, 1590, 1500, 1490, 1445, 1245	5.04 (d, 2H, J = 1.6, CH_2), 5.84 (s, 2H, OCH_2O), 5.90 (s, 2H, OCH_2O), 6.16 (d, 1H, J = 1.5, Ar), 6.36 (d, 1H, J = 1.5, Ar), 6.38 (dd, 1H, J = 8.0, 1.5, Ar), 6.55 (d, 1H, J = 8.0, Ar), 6.63 (d, 1H, J = 8.0, Ar), 6.68 (s, 1H, vinyl), 6.76 (dd, 1H, J = 8.0, 1.5, Ar), 7.47 (s, 1H, vinyl)	350 (M$^+$, 100)
(*E*, *Z*)-**7**	36	175–176	1765, 1590, 1505, 1490, 1445, 1270	5.21 (d, 2H, J = 2.0, CH_2), 6.06 (s, 2H, OCH_2O), 6.10 (s, 2H, OCH_2O), 6.74 (dd, 1H, J = 8.1, 1.5, Ar), 6.85 (d, 1H, J = 1.5, Ar), 6.96 (d, 1H, J = 8.1, Ar), 7.03 (dd, 1H, J = 8.0, 1.5, Ar), 7.33 (s, 1H, vinyl), 7.35 (s, 1H, vinyl), 7.36 (d, 1H, J = 8.0, Ar), 7.39 (s, 1H, Ar)	350 (M$^+$, 100)
(*Z*, *E*)-**7**	48	130–132 (dec.)	1750, 1575, 1500, 1485, 1450, 1270	4.95 (d, 2H, J = 2.1, CH_2), 6.04 (s, 2H, OCH_2O), 6.09 (s, 2H, OCH_2O), 6.48 (s, 1H, vinyl), 6.96 (m, 4H, Ar), 7.02 (s, 1H, Ar), 7.46 (s, 1H, vinyl), 7.82 (d, 1H, J = 1.5, Ar)	350 (M$^+$, 100)
(*Z*, *Z*)-**7**	27	145–146	1745, 1625, 1570, 1505, 1490, 1450, 1265	5.30 (d, 2H, J = 2.2, CH_2), 6.06 (s, 2H, OCH_2O), 6.11 (s, 2H, OCH_2O), 6.87 (d, 1H, J = 8.2, Ar), 6.89 (s, 1H, Ar), 6.99 (d, 1H, J = 8.2, Ar), 7.02 (d, 1H, J = 8.2, Ar), 7.05 (s, 1H, vinyl), 7.53 (d, 1H, J = 8.2, Ar), 7.59 (s, 1H, vinyl), 8.05 (d, 1H, J = 8.2, Ar)	350 (M$^+$, 100)

[a] Satisfactory microanalyses obtained: C ± 0.27, H ± 0.04.

[b] Yield of pure isolated product.

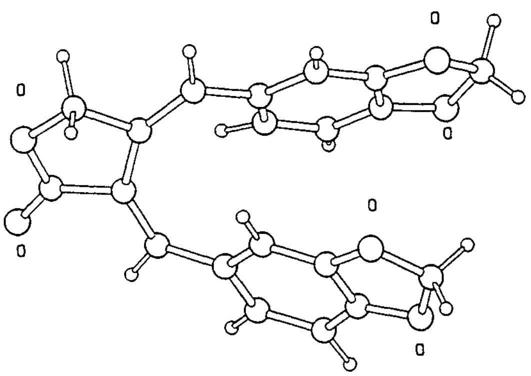


Figure 1. Parallel view of compound (*E*,*E*)-**7**.

1,1-Dibromo-2-(3,4-methylenedioxyphenyl)ethylene (2):
A mixture of CBr_4 (82.8 g, 0.25 mol) and PPh_3 (131 g, 0.50 mol) in CH_2Cl_2 (400 mL) was stirred under nitrogen at r.t. for 1 h. To this mixture was added piperonal (25 g, 0.167 mol) at 0 °C and the mixture was stirred for 16 h at r.t. The resulting precipitate was filtered off and the filtrate was concentrated in vacuo. The residue was chromatographed (silica gel; hexane/EtOAc, 10:1) to give **2** (47.6 g, 93 %) as a colorless oil.

IR (film): $\nu = 2895, 1605, 1500, 1490, 1445, 1260\ cm^{-1}$.

^{1}HNMR ($CDCl_3$): $\delta = 5.99$ (s, 2H, OCH_2O), 6.80 (d, 1H, $J = 8.1$ Hz, Ar), 6.95 (dd, 1H, $J = 8.1, 1.8$ Hz, Ar), 7.19 (d, 1H, $J = 1.8$ Hz, Ar), 7.37 (s, 1H, vinyl).

MS: $m/z = 308$ (31 %), 306 (62), 304 (M^+, 32), 146 (100).

Methyl 3-(3,4-Methylenedioxyphenyl)propynoate (3a):
To a solution of **2** (30.7 g, 0.10 mol) in dry THF (300 mL) was added BuLi (1.6 M in hexane) (138 mL, 0.22 mol) below −50 °C under nitrogen and the mixture was stirred at r.t. for 1 h. Then methyl chloroformate (9.3 mL, 0.12 mol) in dry THF (50 mL) was added below −50 °C and the resulting mixture was stirred at r.t. for 30 min. The reaction was quenched by addition of sat. aq NH_4Cl and the reaction mixture was extracted with EtOAc. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed (silica gel; hexane/EtOAc, 5:1) to give **3a** (15.9 g, 78 %); mp 81–82 °C.

IR (KBr): $\nu = 2210, 1700, 1505, 1305, 1240\ cm^{-1}$.

^{1}HNMR ($CDCl_3$): $\delta = 3.83$ (s, 3H, CO_2CH_3), 6.02 (s, 2H, OCH_2O), 6.80 (d, 1H, $J = 8.1$ Hz, Ar), 7.00 (d, 1H, $J = 1.4$ Hz, Ar), 7.16 (dd, 1H, $J = 8.1, 1.4$ Hz, Ar).

MS: $m/z = 204$ (M^+, 100 %).

Anal. Calc. for $C_{11}H_8O_4$: C, 64.71; H, 3.95. Found: C, 64.76; H, 3.86.

Methoxymethyl 3-(3,4-Methylenedioxyphenyl)propynoate (3b):
To a solution of **2** (17.6 g, 57.5 mmol) in dry THF (150 mL) was added BuLi (1.6 M in hexane) (79 mL, 127 mmol) below −50 °C under nitrogen and the mixture was stirred at r.t. for 1 h. Then CO_2 gas was bubbled in below 0 °C for 30 min. The reaction mixture was acidified to pH 1 with 10 % aq HCl and extracted with $CHCl_3$. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (100 mL). To this solution were successively added *i*-Pr_2NEt (12.0 mL, 69 mol) and MOMCl (5.2 mL, 69 mol) below 10 °C. After stirring at r.t. for 30 min, the mixture was poured into ice-water and extracted with EtOAc. The organic layer was washed with 10 % aq HCl, sat. aq $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed (silica gel; hexane/EtOAc, 4:1) to give **3b** (11.0 g, 82 %) as a pale yellow oil.

IR (film): $\nu = 2215, 1710, 1505, 1490, 1445, 1300, 1240\ cm^{-1}$.

^{1}HNMR ($CDCl_3$): $\delta = 3.54$ (s, 3H, OCH_2OCH_3), 5.36 (s, 2H, OCH_2OCH_3), 6.03 (s, 2H, OCH_2O), 6.81 (d, 1H, $J = 8.1$ Hz, Ar), 7.02 (d, 1H, $J = 1.6$ Hz, Ar), 7.18 (dd, 1H, $J = 8.1, 1.6$ Hz, Ar).

MS: $m/z = 234$ (M^+, 27 %), 146 (100).

Methyl (*E*)-3-(3,4-Methylenedioxyphenyl)-2-(tributylstannyl)propenoate [(*E*)-4a]:
To a solution of **3a** (5.0 g, 24.5 mmol) and $Pd(PPh_3)_4$ (0.5 g, 0.43 mmol) in dry THF (30 mL) was added dropwise Bu_3SnH (6.6 mL, 24.5 mmol) in dry THF (20 mL) over 2 h under nitrogen and stirred at r.t. for 1 h. Solvent was removed in vacuo and the residue was diluted with hexane. The resulting precipitate was filtered off and the filtrate was concentrated in vacuo. The residue was chromatographed (silica gel; hexane/EtOAc, 20:1) to give (*E*)-**4a** (7.4 g, 61 %) as a colorless oil.

IR (film): $\nu = 2955, 1705, 1590, 1500, 1490, 1440, 1255\ cm^{-1}$.

^{1}HNMR ($CDCl_3$): $\delta = 0.90$ (t, 9H, $J = 7.1$ Hz, $CH_2CH_2CH_2CH_3$), 1.04 (t, 6H, $J = 7.8$ Hz, $CH_2CH_2CH_2CH_3$), 1.20–1.70 (m, 12H, $CH_2CH_2CH_2CH_3$), 3.71 (s, 3H, CO_2CH_3), 5.95 (s, 2H, OCH_2O), 6.58 (s, 1H, vinyl), 6.74 (d, 1H, $J = 8.0$ Hz, Ar), 6.80 (d, 1H, $J = 8.0$ Hz, Ar), 6.83 (s, 1H, Ar).

MS (SIMS): $m/z = 495$ ($M^+ + 1$, 4 %), 177 (100).

Methoxymethyl (*E*)-3-(3,4-Methylenedioxyphenyl)-2-(tributylstannyl)propenoate [(*E*)-4b]:
Under the same reaction conditions as describd for the preparation of (*E*)-**4a**, (*E*)-**4b** (6.5 g, 58 %) was obtained from **3b** (5.0 g, 21.3 mmol) as a colorless oil.

IR (film): $\nu = 2955, 1710, 1590, 1500, 1490, 1440, 1255\ cm^{-1}$.

^{1}HNMR ($CDCl_3$): $\delta = 0.90$ (t, 9H, $J = 7.1$ Hz, $CH_2CH_2CH_2CH_3$), 1.07 (t, 6H, $J = 7.8$ Hz, $CH_2CH_2CH_2CH_3$), 1.20–1.70 (m, 12H, $CH_2CH_2CH_2CH_3$), 3.40 (s, 3H, OCH_2OCH_3), 5.27 (s, 2H, OCH_2OCH_3), 5.94 (s, 2H, OCH_2O), 6.61 (s, 1H, vinyl), 6.75 (d, 1H, $J = 7.9$ Hz, Ar), 6.84 (dd, 1H, $J = 7.9, 1.6$ Hz, Ar), 6.90 (d, 1H, $J = 1.6$ Hz, Ar).

MS (SIMS): $m/z = 525$ ($M^+ + 1$, 2 %), 177 (100).

Methyl (*Z*)-3-(3,4-Methylenedioxyphenyl)-2-(tributylstannyl)propenoate [(*Z*)-4a]:
To a solution of **3a** (0.5 g, 2.5 mmol) and Bu_3SnH (0.7 mL, 2.6 mmol) in benzene (5 mL) was added AIBN (10 mg, 0.06 mmol) under nitrogen and the mixture was stirred at r.t. for 1 h. Solvent was removed in vacuo and the residue was chromatographed (silica gel; hexane/EtOAc, 20:1) to give (*Z*)-**4a** (0.96 g, 79 %) as a colorless oil.

IR (film): $\nu = 2955, 1705, 1585, 1500, 1485, 1215\ cm^{-1}$.

^{1}HNMR ($CDCl_3$): $\delta = 0.70$–1.00 (m, 15H, $CH_2CH_2CH_2CH_3$), 1.14–1.46 (m, 12H, $CH_2CH_2CH_2CH_3$), 3.76 (s, 3H, CO_2CH_3), 5.98 (s, 2H, OCH_2O), 6.79 (s, 3H, Ar), 8.26 (s, 1H, vinyl).

MS (SIMS): $m/z = 495$ ($M^+ + 1$, 8 %), 177 (100).

Methoxymethyl (*Z*)-3-(3,4-Methylenedioxyphenyl)-2-(tributylstannyl)propenoate [(*Z*)-4b]:
Under the same reaction conditions as described for the preparation of (*Z*)-**4a**, (*Z*)-**4b** (3.0 g, 44 %) was obtained from **3b** (3.0 g, 12.8 mmol) as a colorless oil.

IR (film): $\nu = 2955, 1700, 1580, 1500, 1490, 1205\ cm^{-1}$.

^{1}HNMR ($CDCl_3$): $\delta = 0.70$–1.00 (m, 15H, $CH_2CH_2CH_2CH_3$), 1.14–1.48 (m, 12H, $CH_2CH_2CH_2CH_3$), 3.51 (s, 3H, OCH_2OCH_3), 5.33 (s, 2H, OCH_2OCH_3), 5.99 (s, 2H, OCH_2O), 6.80 (s, 3H, Ar), 8.32 (s, 1H, vinyl).

MS (SIMS): $m/z = 525$ ($M^+ + 1$, 2 %), 177 (100).

Methyl (*E*)-3-(3,4-Methylenedioxyphenyl)-2-bromopropenoate [(*E*)-5a]; Typical Procedure:
To a stirred solution of (*E*)-**4a** (1.0 g, 2.0 mmol) in dry CH_2Cl_2 (15 mL) was added dropwise bromine (0.1 mL, 2.0 mmol) in dry CH_2Cl_2 (20 mL) over 1 h under nitrogen below 10 °C. Solvent was removed in vacuo. Et_2O and aq KF (10 mmol) were added to the residue and the mixture was stirred for 1 h. The insoluble material was filtered off and the filtrate was extracted with Et_2O. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated in

vacuo. The residue was chromatographed (silica gel; hexane/EtOAc, 4:1) to give (*E*)-**5a** (0.52 g, 90%).

Methoxymethyl Methyl (2*E*,3*E*)-2,3-Bis(3,4-methylenedioxybenzylidene)succinate [(*E*,*E*)-6]; Typical Procedure:

A solution of (*Z*)-**4a** (1.1 g, 2.2 mmol), (*Z*)-**5b** (0.7 g, 2.2 mmol) and $PdCl_2(PPh_3)_2$ (78 mg, 0.11 mmol) in DMF (7 mL) was stirred under nitrogen at 60 °C for 72 h. Solvent was removed in vacuo. EtOAc and aq KF (11 mmol) was added to the residue and the mixture was stirred for 1 h. The insoluble material was filtered off and the filtrate was extracted with EtOAc. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed (silica gel; hexane/EtOAc, 2:1) to give (*E*,*E*)-**6** (0.49 g, 50%).

(2*E*,3*E*)-2,3-Bis(3,4-methylenedioxybenzylidene)-γ-butyrolactone [(*E*,*E*)-7]; Typical Procedure:

To a solution of (*E*,*E*)-**6** (0.6 g, 1.36 mmol) in THF (10 mL) was added conc. HCl (1 mL) and the mixture was stirred at r.t. for 30 min. To this solution, water was added and the mixture was extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$) and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (10 mL). To this solution was added diisobutylaluminum hydride (1.5 M in toluene) (2.5 mL, 3.8 mmol) under nitrogen below 10 °C and the mixture was stirred at r.t. for 1 h. To this solution, 10% aq HCl was added carefully until pH 1, below 10 °C, and the mixture was extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$) and concentrated in vacuo. The residue was dissolved in THF (5 mL). To this solution were successively added Et_3N (0.7 mL, 5.0 mmol) and ethyl chloroformate (0.24 mL, 2.5 mmol) under nitrogen below 10 °C. After stirring at 0 °C for 1 h, water was added and the mixture was extracted with EtOAc. The organic layer was washed with 10% aq HCl, sat. aq $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed (silica gel; hexane/EtOAc, 2:1) to give (*E*,*E*)-**7** (0.22 g, 46%).

X-Ray Structural Analysis of Compound (*E*,*E*)-7:

A plate orange crystal of $C_{20}H_{14}O_6$ of dimensions 0.30 × 0.20 × 0.05 mm was mounted on a Rigaku AFC-5R diffractometer. Cell constants were obtained from a least-squares fit of the setting angles of 25 reflections in the range $85° < 2\theta < 90°$. The compound crystallized in the tricyclic system, space group $P21/c$ with $a = 7.751(3)$, $b = 9.172(3)$, $c = 22.324(1)$ Å; $\alpha = 90.00(0)$, $\beta = 96.91(1)$, $\gamma = 90.00(0)°$, $V = 1575.4(61)$ Å^3, $Z = 4$; $F(000) = 728$, d calc. = 1.477 g cm^{-3}.

Three-dimensional reflections were recorded, using Cu-Kα radiation (graphite-monochromated), ω-2θ scan mode. The structure was solved by direct methods using the SHELXS86 program. The full-matrix least-squares refinement converged to $R = 0.0672$ and $R_w = 0.1158$. All non-hydrogen atoms were refined anisotropically.[15]

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