Syntheses of Natural (+)-Phomalactone, (+)-Acetylphomalactone (+)-Asperlin and Their Isomers

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Received December 25, 1986

(+)-Phomalactone, (+)-acetylphomalactone, (+)-asperlin and their isomers were synthesized from 3-triethylsiloxypropyne and (*S*,*E*)-1-formyl-2-butenyl benzoate, which was easily prepared from (2*R*,3*S*,*E*)-1, 2-cyclohexylidenedioxy-4-hexene-3-ol.

(+)-Phomalactone (**1**), a 6-substituted-5,6-dihydro-5-hydroxy (or acyloxy)-2*H*-pyran-2-one, has been isolated from *Nigrospora* sp.[1] and *Phoma* sp.[2] This dihydropyranone has been considered to be a biosynthetically and synthetically important precursor of (+)-acetylphomalactone (**2**)[3] and (+)-asperlin (**3**),[3,4] isolated from *Asperillus* sp., which have antibiotic and antitumor activities. Furthermore, (+)-asperlin (**3**) was shown to have inhibitory activity against rice and lettuce seedlings. Recently, a 5-epimer (**4**) of (+)-asperlin (**3**) was isolated along with **2** and **3** from *Asp. caespitosus*.[3] The absolute configuration of (+)-asperlin (**3**) was established in 1978 by X-ray analysis.[5] Though the syntheses of a racemic form[6] and an antipode[7] of asperlin (**3**) have been reported, these optically active natural dihydropyranones have not been synthesized. We now wish to report the syntheses of these highly functional and optically active dihydropyranones in detail.[8]

It was thought that dihydropyranones **1**, **2** and **3** could be synthesized through the route shown in Fig. 2 which was applied for the syntheses of (−)-osmundalactone (**5**) and its epimer (**6**),[9] because all of the above compounds have the same absolute configuration at C-5. Coupling reaction of two fragments, a propargyl alcohol derivative and a (*S*,*E*)-2-hydroxy-3-pentenal derivative, could build up a dihydropyranone skeleton. Thus we first attempted the synthesis of an (*S*,*E*)-2-hydroxy-3-pentenal derivative.

As a starting material we used (2*R*,3*S*,*E*)-1,2-cyclohexylidenedioxy-4-hexene-3-ol (**8**),[10] which was prepared from (*R*)-2,3-*O*-cyclohexylidene-D-glyceraldehyde (**7**).[11] The hydroxyl group of **8** was protected as a benzoate group. Removal of the cyclohexylidene group of **9** with a catalytic amount of *p*-toluenesulfonic acid in aqueous methanol gave a diol, **10.** Cleavage of the *vic*-diol moiety of **10** with sodium metaperiodate afforded an al-

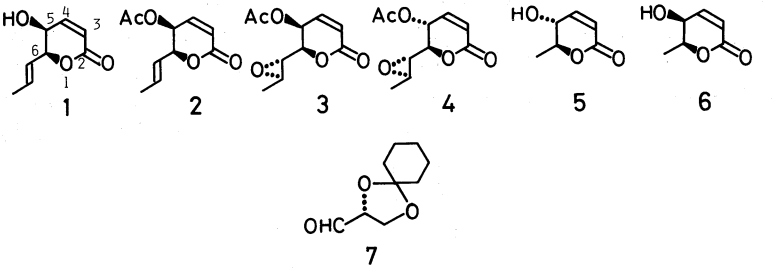

FIG. 1

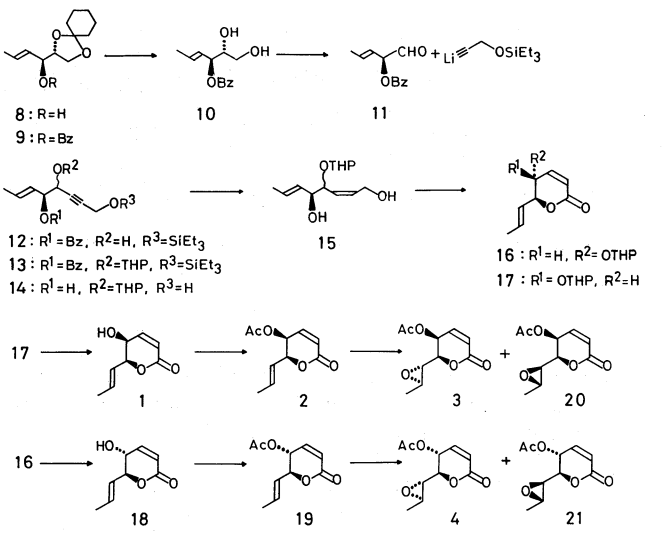

FIG. 2

dehyde, **11** (bp 120°C/0.8 mmHg). The optical purity of **11** was determined to be more than 95% *e.e.* by ^{1}H-NMR analysis using a chiral shift reagent (Eu(tfc)$_3$).

Coupling reaction of (*S*,*E*)-1-formyl-2-butenyl benzoate (**11**) and 1-lithio-3-triethylsiloxypropyne at −78°C gave a diastereomeric mixture, **12**, which was used without separation for several subsequent steps. Then **12** was protected by conversion to a tetrahydropyranyl ether (**13**) in a good yield. To avoid migration of the benzoyl group of **12** to a vicinal hydroxyl group, the tetrahydropyranylation should occur immediately. One-pot alkaline hydrolysis of a benzoyl and a triethylsiloxy group gave an acetylenic diol, **14**, in a good yield. Partial hydrogenation of compound **14** in the presence of Lindlar's catalyst afforded a (*Z*)-olefininc diol, **15.**

Lactonization of (*Z*)-olefinic compound **15** had to be performed under neutral conditions, because under acidic or basic conditions only five-membered lactones would be obtained. Oxidative lactonization of **15** with manganese dioxide in dichloromethane at room temperature afforded a separable mixture of dihydropyranones **16** and **17** without the production of five-membered lactones. Chromatographic separation of the diastereomeric mixture gave pure **16** (23%, *Rf*: 0.50) and **17** (42%, *Rf*: 0.45). The signal assigned to the α-proton of the lactone carbonyl in the ^{1}H-NMR spectrum showed d–d splitting (J=1.7 and 9.8 Hz) for **16**, while a simple doublet (J=9.8 Hz) was observed for **17.** The presence of allylic coupling (1.7 Hz) in **16** indicated the *trans* orientation of the substituents on the six-membered lactone ring, as reported by Perlin *et al.*[7] Therefore, **16** was determined to be a (5*R*,6*S*)-isomer, and **17** has the (5*S*,6*S*)-stereochemistry like the natural products. Deprotection of the tetrahydropyranyl ethers **17** and **16** with an ion exchange resin (Amberlyst-15) in dry methanol afforded (+)-phomalactone (**1**) and its 5-epimer (**18**) as crystals. The anhydrous conditions were necessary to prevent the conversion of the dihydropyranones into five-membered lactones during deprotection of the tetrahydropyranyl ethers. Acetylation of **1** and **18** was achieved in a usual manner to give (+)-acetylphomalactone (**2**) and its 5-epimer (**19**). Epoxidation of **2** with *m*-chloroperbenzoic acid in dry dichloromethane at room temperature afforded (+)-asperlin (**3**) and its (1′*R*,2′*S*)-isomer (**20**) in 44% and 11% yields, respectively. Similarly **19** gave a 5-epimer (**4**) of (+)-asperlin (**3**) and its isomer (**21**) in 23% and 28% yields,

TABLE I. THE PHYSICAL DATA FOR THE DIHYDROPYRANONES

(5*S*)-Dihydropyranones	$[\alpha]_D$ (°)	mp (°C)	(5*R*)-Dihydropyranones	$[\alpha]_D$ (°)	mp (°C)
1	+178 (+175	56.5 57.0)[2]	**18**	−68.6	77.0
2	+300 (+311	54.5 54.0)[3]	**19**	−175	—
3	+332 (+331	71.0 71.0)[3]	**4**	−185 (+224	81.5 64.0)[3]
20	+211	63.5	**21**	−240	83.0
6	+143	—	**5**	−70.3 (−70.6	82.5 82.5)[13]

Values in parentheses were reported in the literature.

respectively. These different diastereoselectivities resulted from the steric hindrance by an acetyl group in **2** and **19**.

The optical rotations and melting points of the synthetic dihydropyranones are shown in Table I. The signs of the optical rotations of the dihydropyranones were largely dependent upon the absolute configuration at the 5-positions, that is, (5*S*)-dihydropyranones were dextrorotatory, while (5*R*)-dihydropyranones were levorotatory. The configurations of the epoxide ring of **4** and **21** were determined to be as follows. H-6 of **3** (δ 4.11, $J_{6\text{-}1'}=7.0$ Hz) is much more shielded than that of **20** (δ 4.36, $J_{6\text{-}1'}=4.9$ Hz) by the diamagnetic effect of the expoxide ring. On the other hand, H-6 of **4** is observed at δ 4.22 with $J_{6\text{-}1'}=6.6$ Hz, *i.e.*, a higher magnetic field resonance and a larger coupling constant than those in the case of H-6 of **21** (δ 4.66, $J_{6\text{-}1'}=2.9$ Hz). A quite similar tendency was observed between **3** and **20.** It was deduced from these result that the configuration of the epoxide ring is (1′*S*,2′*R*) for **4** and (1′*R*,2′*S*) for **21.** Comparison of the optical rotation values of **3**, **20**, **4** and **21**, as well as the behavior of the dihydropyranones on thin layer chromatography was also helpful as to the above conclusion.

Moreover, the following characteristics were seen in the ^{1}H-NMR spectra of the above dihydropyranones. Long-range couplings between H-3 and H-5 were dependent on the relative stereochemistry between H-5 and H-6. 5,6-*trans* Isomers (**4**, **5**, **18**, **19** and **21**) showed allylic couplings with $J_{3\text{-}5}$-values of 1.0∼1.8 Hz. The coupling constant between H-5 and H-6 were in the range of 2.7∼3.7 Hz for 5,6-*cis* isomers. On the other hand, those of *trans*-isomers depended on the substituents at the 5-positions, that is, $J_{5\text{-}6}$-values of 8.5∼9.0 Hz were obtained in the case of hydroxyl substituents (**5** and **18**) and ones of 4.6∼5.6 Hz for the 5-acetoxyl substituents (**4**, **19** and **21**). Some of the above observations agreed with data of Perlin,[7] Yamagiwa[12] and Yamamoto.[6]

The synthetic dihydropyranones, (+)-phomalactone (**1**), (+)-acetylphomalactone (**2**) and (+)-asperlin (**3**), were identical with the natural dihydropyranones in all spectral data optical rotations. The physical data (mp and $[\alpha]_D$) and ^{1}H-NMR spectrum of synthetic **4**, however, did not agree with those reported by Mizuba *et al.*[3] In the case of synthetic compound **4**, 1) the optical rotation was levotatory (−185°), 2) long range coupling between H-3 and H-5 ($J_{3\text{-}5}=1.0$ Hz) was observed, 3) the coupling constant between H-5 and H-6 was 4.6 Hz (5,6-*trans*) and 4) the melting point was 81.5°C. While in the case of the natural compound, 1) the potical rotation was dextrorotatory (+224°), 2) long range coupling between H-3 and H-5 was not observed, 3) the coupling constant between H-5 and H-6 was 3.5 Hz and 4) the melting point was 64.0°C.[3] All of these data indicated that

the natural compound was of *cis* orientation. Therefore, the chemical structure including the absolute configuration of the third dihydropyranone isolated along with **2** and **3** form *Asp. caespitosus* might not be **4** but **20**, which was obtained through the present synthetic study.

Through this work, we have developed a facile and efficient synthetic route to dihydropyranone with high optical purities. This methodology is thought to be promising for application to the synthesis of other polyfunctional dihydropyranones. The biological activities of the synthetic dihydropyranones will be published later.

EXPERIMENTAL

All boiling points and melting points were uncorrected. ^{1}H-NMR spectra were recorded on a JEOL JNM FX-100 spectrometer. IR spectra were recorded on a JASCO IR-810 infrared spectrometer. Optical rotations were measured with a JASCO DIP-4 polarimeter. Gas chromatographic analyses were performed with a YANACO G 3800 model with flame ionization detector, on a glass column (2m × 3mm) packed with 5% Carbowax (PEG) 20 M on Chromosorb W (AM) (column temp., 170°C;N_2 flow rate, 20 ml/min). The ^{1}H-NMR data for THP-ethers (**13**~**17**) refer to those of major isomers.

(1S,1′R,E)-1-(1′2′-Cyclohexylidenedioxy)ethyl-2-butenyl benzoate (**9**). To a solution of 8.2 g of **8** (39 mmol)[10] in 50 ml of pyridine was added 6.0 g of benzoyl chloride (43 mmol) at 0°C, followed by stirring for 2 hr at 0°C. The reaction mixture was poured into water and extracted with ether, and then the extract was washed with 5% acetic acid, water, aq. $NaHCO_3$ and brine, and finally dried over anhyd. Na_2SO_4. After evaporating the ether *in vacuo*, the residue was subjected to column chromatography on alumina to give 13 g of **9** (99%). $[\alpha]_D^{20}$ −4.6° (*c*=0.88, $CHCl_3$). IR ν_{max} (film) cm^{-1}: 3075, 3040, 1720, 1675, 1605, 1585, 1450, 1365, 1270, 1160, 1110, 1100, 965, 915, 850, 815. ^{1}H-NMR ($CDCl_3$) δ: 1.57 (10H, m), 1.73 (3H, d, *J*=6.1 Hz), 3.99 (1H, dd, *J*=6.4, 8.0 Hz), 4.15 (1H, dd, *J*=6.1, 8.0 Hz), 4.31 (1H, dd, *J*=4.6, 6.1, 6.4 Hz), 5.40~6.00 (3H, m), 7.33~8.11 (5H, m). *Anal.* Found: C, 72.25; H, 7.73. Calcd. for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65%.

(1S,1′R,E)-1-(1′,2′-Dihydroxy)ethyl-2-butenyl benzoate (**10**). A solution of 11 g of **9** (35 mmol) and 1.0 g of *p*-TsOH in 50 ml of aq. MeOH was refluxed for 1 hr. The reaction mixture was cautiously poured into aq. $NaHCO_3$ and then extracted with ether. The extract was washed with saturated $NaHCO_3$ sol, and brine, and then dried over anhyd. Na_2SO_4. After evaporating the ether, the residue was subjected to column chromatography on silica gel to afford 7.4 g of **10** (89%). $[\alpha]_D^{20}$ −37.8°C (*c*=1.00, EtOH). IR ν_{max} (film) cm^{-1}: 3420, 3060, 3040, 1720, 1600, 1585, 1450, 1280, 1120, 1070, 1030, 970, 815. ^{1}H-NMR ($CDCl_3$) δ: 1.76 (3H, dd, *J*=1.0, 6.4 Hz), 2.68 (2H, br. s), 3.53~3.90 (3H, m), 5.47 (1H, dd, *J*=5.7, 7.0 Hz), 5.60 (1H, ddq, *J*=1.0, 7.0, 14.9 Hz), 5.88 (1H, dq, *J*=6.4, 14.9 Hz), 7.33~8.09 (5H, m). *Anal.* Found: C, 65.72; H, 6.81. Calcd. for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83%.

(S,E)-1-Formyl-2-butenyl benzoate (**11**). A mixture of 7.4 g of **10** (31 mmol), 8.0 g of $NaIO_4$ (37 mmol), 50 ml of water, 50 ml of THF and 100 ml of ether was stirred for 1 hr at room temperature. The reaction mixture was saturated with NaCl and then extracted with ether. The extract was washed with brine and then dried over Na_2SO_4. After evaporating the solvent, the residue was distilled *in vacuo* to afford 5.0 g of **11** (79%). bp 120°C (0.8 mmHg). $[\alpha]_D^{20}$ +103° (*c*=1.00, benzene). IR ν_{max}(film) cm^{-1}: 3060, 3040, 2725, 1720, 1670, 1600, 1450, 1275, 1110, 965, 715. ^{1}H-NMR ($CDCl_3$) δ: 1.83 (3H, d, *J*=6.4, Hz), 5.53~5.71 (2H, m), 6.11 (1H, dq, *J*=6.4, 14.1 Hz), 7.26~8.16 (5H, m). 9.67 (1H, s). *Anal.* Found: C, 70.84; H, 5.92. Calcd. for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92%.

(1S,2RS,E)-1-(1′-Propenyl)-2-tetrahydropyranyloxy-5-triethylsiloxy-3-pentynyl benzoate (**13**). To a solution of 4.5 g of 3-triethylsiloxypropyne (26 mmol) in 100 ml of dry THF was added 17 ml of 1.56 M *n*-Buli (27 mmol) at −78°C. After stirring for 1 hr, 5.0 g of **11** (24 mmol) was added to the reaction mixture at −78°C, followed by stirring for 3 hr. The reaction mixture was poured into water and then extracted with ether. The extract was washed with water and brine, and then dried over Na_2SO_4. After removal of the solvent, the residue was subjected to column chromatography on silica gel to afford 6.8 g of **12** (76%). Then **12** was converted into its THP ether (**13**) immediately. To a solution of 6.8 g of **12** (18 mmol) and 1.7 g of dihydropyran (20 mmol) in 50 ml of dry benzene was added a catalytic amount of *p*-TsOH, followed by stirring for 3 hr at room temperature. The reaction mixture was poured into aq. $NaHCO_3$ and then extracted with ether. The extract was washed with water and brine, and then dried over anhyd. Na_2SO_4. After evaporating the solvent, the residue was subjected to column chromatography on silica gel to give 6.5 g of **13** (79%). IR ν_{max} (film) cm^{-1}: 1730, 1680, 1635, 1440, 1380, 1255, 1120, 1080, 1030, 975, 920, 875, 820. ^{1}H-NMR ($CDCl_3$) δ: 0.67 (6H, m), 0.96 (9H, m), 1.40~1.90 (6H, m), 1.74 (3H, d, *J*=5.6 Hz), 3.40~3.93 (2H, m), 4.35 (2H, d, *J*=1.5 Hz), 4.68 (1H, m), 5.04 (1H, m), 5.57~5.94 (3H, m), 7.32~8.15 (5H, m). *Anal.* Found: C, 67.88; H, 8.46. Calcd. for $C_{26}H_{38}O_5Si$: C, 68.08; H, 8.36%.

(4RS,5S,E)-4-Tetrahydropyranyloxy-6-octen-2-yne-1,5-diol (**14**). A solution of 6.5 g of **13** (14 mmol) and 2.5 g of NaOH in 50 ml of aq. MeOH was stirred for 3 hr at room temperature. The reaction mixture was poured into 300 ml of water and then extracted several times with ether. The extracts were combined and washed with 5% acetic acid, water, saturated $NaHCO_3$ and brine, and then dried over Na_2SO_4. After evaporating the solvent, the residue was subjected to column chromatography on silica gel to afford 3.3 g of **14** (98%). IR ν_{max}(film) cm^{-1}: 3400, 1675, 1440, 1200, 1120, 1020, 975, 910, 870, 815. ^{1}H-NMR ($CDCl_3$) δ: 1.49 ~ 1.90 (6H, m), 1.74 (3H, d, J = 5.6 Hz), 2.64 (2H, br.s), 3.58 ~ 3.95 (2H, m), 4.19 ~ 4.94 (4H, m), 5.40 ~ 6.00 (2H, m). The diacetate of **14**: IR ν_{max}(film) cm^{-1}: 1750, 1675, 1440, 1370, 1230, 1120, 1025, 970, 910, 870, 815. ^{1}H-NMR ($CDCl_3$) δ: 1.31 ~ 1.93 (6H, m), 1.74 (3H, d, J = 6.4 Hz), 2.09 (6H, m), 3.48 ~ 3.93 (3H, m), 4.44 ~ 5.00 (3H, m), 5.25 ~ 6.08 (3H, m). *Anal.* Found: C, 63.17; H, 7.58. Calcd. for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46%.

(2Z,4RS,5S,6E)-4-Tetrahydropyranyloxy-2,6-octadiene-1,5-diol (**15**). A solution of 3.3 g of **14** (14 mmol), 0.1 g of Lindlar's catalyst and 0.1 ml of quinoline in 50 ml of ethanol was stirred under H_2. When 300 ml of H_2 had been absorded, the reaction was stopped. The reaction mixture was filtered and then washed sufficiently with ethanol. The filtrate and washings were combined and then concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to afford 2.8 g of **15** (82%). IR ν_{max}(film) cm^{-1}: 3390, 3020, 1675, 1440, 1200, 1115, 1030, 975, 910, 870, 815. ^{1}H-NMR ($CDCl_3$) δ: 150 ~ 2.00 (6H, m), 1.71 (3H, d, J = 6.4 Hz), 2.70 (2H, br. s), 3.45 ~ 3.85 (2H, m), 3.98 ~ 4.53 (4H, m), 4.85 (1H, m), 5.29 ~ 6.20 (4H, m). The diacetate of **15**: IR ν_{max}(film) cm^{-1}: 3020, 1740, 1675, 1440, 1370, 1230, 1120, 1020, 975, 905, 870, 815. ^{1}H-NMR ($CDCl_3$) δ: 1.40 ~ 1.90 (6H, m), 1.70 (3H, d, J = 6.6 Hz), 2.05 (6H, m), 3.40 ~ 4.20 (3H, m), 4.40 ~ 5.00 (3H, m), 5.33 ~ 5.90 (5H, m). *Anal.* Found: C, 63.03; H, 8.35. Calcd. for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03%.

(5R,6S)- and (5S, 6S)-5,6-Dihydro-6-((E)-1'-propenyl)-5-tetrahydropyranyloxy-2H-pyran-2-ones (**16** *and* **17**). To a solution of 2.7 g of **15** (11 mmol) 100 ml of CH_2Cl_2 was added 19 g of MnO_2 (220 mmol), followed by shaking at 20°C. After 8 hr, the reaction mixture was filtered and washed several times with ether. The fltrate and washings were combined and then concentrated *in vacuo*. The residue was purified by preparative thin layer chromatography on silica gel developed with hexane–ether (1 : 2) to give 0.6 g of pure **16** (23%) and 1.1 g of pure **17** (42%). The physical data for **16**: IR ν_{max}(film) cm^{-1}: 1740, 1680, 1640, 1440, 1380, 1235, 1125, 1080, 1030, 970, 875, 820. ^{1}H-NMR ($CDCl_3$) δ: 1.60 ~ 1.90 (6H, m), 1.75 (3H, dd, J = 1.2, 6.4 Hz), 3.40 ~ 4.04 (2H, m), 4.25 (1H, ddd, J = 1.7, 3.2 7.6 Hz), 4.71 ~ 4.84 (2H, m), 5.52 (1H, ddq, J = 1.2, 6.8, 15.4 Hz), 5.88 (1H, dq, J = 6.4, 15.4 Hz), 5.99 (1H, dd, J = 1.7, 9.8 Hz), 6.91 (1H, dd, J = 2.9, 9.8 Hz). *Anal.* Found: C, 65.42; H, 7.95. Calcd. for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61%. The physical data for **17**: IR ν_{max}(film) cm^{-1}: 1730, 1720, 1670, 1630, 1440, 1375, 1250, 1115, 1070, 1020, 965, 930, 910, 870, 820. ^{1}H-NMR ($CDCl_3$) δ: 1.40 ~ 1.90 (6H, m), 1.78 (3H, d, J = 4.9 Hz), 3.45 ~ 3.95 (2H, m), 4.08 ~ 4.38 (1H, m), 4.71 ~ 4.95 (2H, m), 5.57 ~ 5.96 (2H, m), 6.08 (1H, d, J = 9.8 Hz), 6.96 (1H, dd, J = 5.1, 9.8 Hz). *Anal.* Found: C, 65.30; H, 7.67. Calcd. for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61%.

(5S,6S)-5,6-Dihydro-5-hydroxy-6-((E)-1'-propenyl)-2H-pyran-2-one (**1**). One gram of **17** (4.2 mmol) was dissolved in dry MeOH and then treated with a catalytic amount of Amberlyst-15 at room temperature. After stirring for 3 hr, the reaction mixture was filtered and the filter cake obtained was washed several times with ethyl acetate. The filtrate and washings were combined and then concentrated *in vacuo*. The residue was subjected to preparative TLC on silica gel developed with hexane–ether (1 : 2) to give 0.40 g of pure dihydropyranone (**1**) (62%). mp 56.0 ~ 56.5°C (lit.[1] 56.0 ~ 57.0°C). $[\alpha]_D^{20}$ +178° (c = 0.49, EtOH). (lit.[1] 179.3°) IR ν_{max} (KBr) cm^{-1}: 3510, 3360, 1720, 1700, 1665, 1620, 1380, 1255, 1150, 1100, 1065, 1020, 960, 870, 820, 805. ^{1}H-NMR ($CDCl_3$) δ: 1.80 (3H, dd, J = 1.2, 5.8 Hz), 2.50 (1H, br. s), 4.18 (1H, dd, J = 3.2, 5.4 Hz), 4.81 (1H, dd, J = 3.2, 6.1 Hz), 5.76 (1H, ddq, J = 1.2, 6.1, 15.4 Hz), 5.96 (1H, dq, J = 5.8, 15.4 Hz), 6.08 (1H, d, J = 9.8 Hz), 6.99 (1H, dd, J = 5.4, 9.8 Hz). *Anal.* Found: C, 61.99; H, 6.39. Calcd. for $C_8H_{10}O_3$: C, 62.32; H, 6.54%.

(5R,6S)-5,6-Dihydro-6-hydroxy-6-((E)-1'-propenyl)-2H-pyran-2-one (**18**). Treatment of 0.60 g of dihydropyranone **16** with Amberlyst-15, as mentioned above gave 0.35 g of **18** (90%). mp 76.5 ~ 77.0°C. $[\alpha]_D^{20}$ −68.6°C (c = 0.58, EtOH). IR ν_{max} (KBr) cm^{-1}: 3450, 2860, 1700, 1680, 1630, 1240, 1100, 1060, 1010, 970, 820. ^{1}H-NMR ($CDCl_3$) δ: 1.78 (3H, dd, J = 1.4, 6.4 Hz), 2.80 (1H, br.s), 4.31 (1H, ddd, J = 1.7, 2.4, 8.5 Hz), 4.65 (1H, dd, J = 7.3, 8.5 Hz), 5.54 (1H, ddq, J = 1.4, 7.3, 16.0 Hz), 5.92 (1H, dd, J = 1.7, 9.8 Hz), 6.00 (1H, dq, J = 6.4, 16.0 Hz), 6.88 (1H, dd, J = 2.4, 9.8 Hz). *Anal.* Found: C, 62.50; H, 6.82. Calcd. for $C_8H_{10}O_3$: C, 62.32; H, 6.54%.

(5S,6S)-5-Acetoxy-5,6-dihydro-6-((E)-1'-propenyl)-2H-pyran-2-one ((+)-*acetylphomalactone* (**2**)). A solution of 260 mg of **1** (1.7 mmol), 1.0 ml of acetic anhydride and 1.5 ml of pyridine in 3.0 ml of CH_2Cl_2 was stirred for 8 hr at room temperature. The reation mixture was poured into water and then extracted with ether. The extracts were combined and then washed with water, 5% acetic acid, water, saturated $NaHCO_3$ sol. and brine successively. The ethereal layer was dried over anhyd. Na_2SO_4 and evaporated *in vacuo*. The residue was purified by preparative TLC on silica gel developed with ethyl acetate–hexane (1 : 1) to afford 200 mg of **2** (65%). mp 54.0 ~ 54.5°C (lit.[3])

56.0°C). $[\alpha]_D^{20}+300°$ ($c=0.44$, EtOH) (lit.[3] $+311.8°$). IR ν_{max} (KBr) cm^{-1}: 1735, 1720, 1635, 1370, 1255, 1230, 1160, 1075, 1030, 980, 820. ^{1}H-NMR ($CDCl_3$) δ: 1.78 (3H, dd, $J=1.2$, 6.4 Hz), 2.10 (3H, s), 4.99 (1H, dd, $J=2.9$, 6.8 Hz), 5.23 (1H, dd, $J=2.9$, 5.4 Hz), 5.59 (1H, ddq, $J=1.2$, 6.8, 15.1 Hz), 5.94 (1H, dq, $J=6.4$, 15.1 Hz), 6.20 (1H, d, $J=9.8$ Hz), 6.96 (1H, dd, $J=5.4$, 9.8 Hz). *Anal.* Found: C, 61.17; H, 6.32. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17%.

(5R,6S)-5-Acetoxy-5,6-dihydro-6-(E)-1'-propenyl)-2H-pyran-2-one (**19**). One hundred ten milligrams of dihydropyranone **18** (0.17 mmol) was acetylated as mentioned above to give 130 mg of **19** (94%). $[\alpha]_D^{20}$ $-175°$ ($c=0.53$, EtOH). IR ν_{max} (KBr) cm^{-1}: 1740, 1680, 1640, 1380, 1235, 1030, 975, 820. ^{1}H-NMR ($CDCl_3$) δ: 1.75 (3H, ddd, $J=0.7$, 1.5, 6.4 Hz), 2.11 (3H, s), 4.89 (1H, dddq, $J=0.5$, 0.7, 5.6, 6.8 Hz), 5.34 (1H, ddd, $J=1.2$, 3.9, 5.6 Hz), 5.51 (1H, ddq, $J=1.5$, 6.8, 15.1 Hz), 5.86 (1H, ddq, $J=1.0$, 6.4, 15.1 Hz), 6.13 (1H, dd, $J=1.2$, 9.8 Hz), 6.78 (1H, ddd, $J=0.5$, 3.9, 9.8 Hz). *Anal.* Found: C, 61.05; H, 6.45. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17%.

(5S,6R,1'S,2'R)- and (5S,6R,1'R,2'S)-5-Acetoxy-5,6-dihydro-6-(1',2'-epoxypropyl)-2H-pyran-2-ones ((+)-*asperlin* (**3**) *and* **20**). A solution of 100 mg of **2** (0.51 mmol) and 150 mg of 80% *m*CPBA (0.70 mmol) in dry CH_2Cl_2 was stirred for 48 hr at room temperature. The reaction mixture was subjected to rapid column chromatography on alumina and then washed with a sufficient amount of ether. After evaporating the solvent, the residue was purified by preparative TLC on silica gel developed with hexane–ethyl acetate (1 : 1) to give 48 mg of **3** (44%, *Rf*: 0.45) and 12 mg of **20** (11%, *Rf*: 0.40). The physical data for **3**: mp 70.5~71.0°C (lit.[3] 69.5~71.0°C). $[\alpha]_D^{20}$ $+332°$ ($c=0.47$, EtOH) (lit.[3] $+331°$). IR ν_{max} (KBr) cm^{-1}: 3080, 1740, 1720, 1635, 1440, 1380, 1250, 1220, 1145, 1100, 1035, 945, 870, 825. ^{1}H-NMR ($CDCl_3$) δ: 1.39 (3H, d, $J=4.9$ Hz), 2.14 (3H, s), 3.01~3.20 (2H, m), 4.11 (1H, dd, $J=2.9$, 7.0 Hz), 5.32 (1H, dd, $J=2.9$, 5.9 Hz), 6.22 (1H, d, $J=9.8$ Hz), 7.08 (1H, dd, $J=5.9$, 9.8 Hz). *Anal.* Found: C, 56.40; H, 5.81. Calcd. for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70%. The physical data for **20**: mp 63.0~63.5°C. $[\alpha]_D^{20}+211°$ ($c=0.35$, EtOH), IR ν_{max} (KBr) cm^{-1}: 3070, 1735, 1635, 1440, 1370, 1240, 1225, 1100, 1030, 945, 845, 820. ^{1}H-NMR ($CDCl_3$) δ: 1.34 (3H, d, $J=4.9$ Hz), 2.15 (3H, s), 2.99~3.14 (2H, m), 4.36 (1H, dd, $J=3.7$, 4.9 Hz), 5.51 (1H, ddd, $J=0.5$, 3.7, 5.2 Hz), 6.21 (1H, dd, $J=0.5$, 9.8 Hz), 6.87 (1H, dd, $J=5.2$, 9.8 Hz). *Anal.* Found: C, 56.85; H, 5.91. Calcd. for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70%.

(5R,6R,1'S,2'R)- and (5R,6R,1'R,2'S)-5-Acetoxy-5,6-dihydro-6-(1',2'-epoxypropyl)-2H-pyran-2-ones (**4** *and* **21**). One hundred twenty milligrams of dihydropyranone **19** (0.61 mmol) was epoxidized as mentioned above to give 30 mg of **4** (23%, *Rf*: 0.45) and 36 mg of **21** (28%, *Rf*: 0.40). The physical data for **4**: mp 81.0~81.5°C. $[\alpha]_D^{20}-185°$ ($c=0.50$, EtOH). IR ν_{max} (KBr) cm^{-1}: 3080, 1735, 1635, 1240, 1110, 1030, 980, 950, 920, 880, 960, 820. ^{1}H-NMR ($CDCl_3$) δ: 1.35 (3H, d, $J=5.1$ Hz), 2.13 (3H, s), 2.85 (1H, dd, $J=2.2$, 6.6 Hz), 3.05 (1H, dq, $J=2.2$, 5.1 Hz), 4.22 (1H, dd, $J=5.1$, 6.6 Hz), 5.52 (1H, ddd, $J=1.0$, 4.1, 5.1 Hz), 6.18 (1H, dd, $J=1.0$, 9.8 Hz), 6.88 (1H, dd, $J=4.1$, 9.8 Hz). *Anal.* Found: C, 56.75; H, 6.01. Calcd. for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70%. The physical data for **21**: mp 82.5~83.0°C. $[\alpha]_D^{20}-240°$ ($c=0.50$, EtOH). IR ν_{max} (KBr) cm^{-1}: 3075, 1740, 1720, 1635, 1395, 1375, 1350, 1240, 1105, 1030, 985, 960, 940, 915, 880, 820. ^{1}H-NMR ($CDCl_3$) δ: 1.33 (3H, d, $J=5.4$ Hz), 2.14 (3H, s), 2.91 (1H, dd, $J=2.2$, 2.9 Hz), 3.13 (1H, dq, $J=2.2$, 5.4 Hz), 4.64 (1H, ddd, $J=1.0$, 2.9, 4.6 Hz), 5.46 (1H, ddd, $J=1.0$, 4.3, 4.6 Hz), 6.16 (1H, dd, $J=1.0$, 10.0 Hz), 6.77 (1H, ddd, $J=1.0$, 4.3, 10.0 Hz). *Anal.* Found: C, 56.18; H, 5.79. Calcd. for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70%.

Acknowledgments. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan. We also wish to thank Mr. Izumi Sasaki, Shiseido Co., for his cooperation in our earlier study.

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