[Chem. Pharm. Bull. 32(5)1754—1760(1984)]

Studies on the Constituents of the Seeds of *Hernandia ovigera* L. IV.[1] Syntheses of β-Peltatin-A and -B Methyl Ethers from Desoxypodophyllotoxin

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(Received September 5, 1983)

Two kinds of 4-aryltetralin type lignans, β-peltatin-A methyl ether (I-A) and β-peltatin-B methyl ether (I-B), were synthesized from desoxypodophyllotoxin (DPT), which is available in large quantities from the seeds of *Hernandia ovigera* L. (Hernandiaceae). The syntheses were achieved *via* demethylene-DPT (IV), 8-bromo-demethylene-DPT (V) and 8-bromo-DPT (VI). Methylenation of V was carried out successfully by using cesium fluoride and methylene iodide in DMF. Compound I-B was readily obtained by the reaction of VI with cuprous iodide and sodium methoxide in the presence of pyridine. Synthesis of I-A was only achieved by the reaction of lithiated VI with nitrobenzene at −100 °C in the presence of tetramethylethylene diamine, and I-A was obtained in low yield, together with I-B.

Keywords——*Hernandia ovigera*; 4-aryltetralin lignan; desoxypodophyllotoxin (DPT); desoxypicropodophyllin (DPP); 2′-bromo-desoxypodophyllotoxin; 8-bromo-desoxypodophyllotoxin; beta-peltatin-A methyl ether; beta-peltatin-B methyl ether; lithiated desoxypodophyllotoxin; lignan X-ray analysis

In the previous papers of this series,[1-3] the systematic isolation and structural determination of the lignans of *Hernandia ovigera* L. (Hernandiaceae) and various reactions of these lignans were reported.

In the present work, our aim was the syntheses of related 4-aryltetralin type lignans by utilizing desoxypodophyllotoxin (DPT), which is available in large quantities from the plant seeds. Here, we wish to describe the syntheses of β-peltatin-A methyl ether (I-A) and β-peltatin-B methyl ether (I-B)[4] from DPT. The synthetic route is shown in Chart 1.

Koford *et al.*[5] obtained a 2′-bromo-compound by direct bromination of podophyllotoxin. This suggests that the introduction of bromine at C-5 or C-8 of ring A is difficult by direct bromination of DPT. To confirm this, we carried out the direct bromination of DPT with *N*-bromosuccinimide (NBS) in dimethylformamide (DMF)[6] and obtained a monobromoderivative (II), $C_{22}H_{21}BrO_7$, mp 175—177 °C, $[\alpha]_D$ −106° ($CHCl_3$), in 83% yield. The cleavage of the methylenedioxy group of II with boron trichloride gave the corresponding dihydroxy compound (III), $C_{21}H_{21}BrO_7$, mp 224—226 °C, $[\alpha]_D$ −129° (EtOH). In the nuclear magnetic resonance (NMR) spectra of II and III, three aromatic protons were observed at δ 6.13—6.60 and three methoxy groups of ring C appeared independently as three singlet peaks (II, δ 3.63, 3.84, 3.90; III, δ 3.60, 3.75, 3.80). In usual 4-aryltetralin lignans, such as DPT, hernandin, I-A and I-B, which have no functional groups except for the three methoxy groups on ring C, the signals of the C-3′ and C-5′ methoxy groups appear as a singlet (6H) peak. These results lead to the presumption that the position of bromine of II was at C-2′.

In order to introduce bromine into ring A, demethylene-DPT (IV)[3] was used as a starting material in the expectation that an increment of the electron density on C-5 or C-8 would be produced by the phenolic hydroxy groups. Bromination of IV by NBS–DMF afforded a monobromocompound (V), mp 220—222 °C, $[\alpha]_D$ −131 ° (MeOH), in 80% yield. In the NMR spectrum of V, the C-3′ and C-5′ methoxy signals appeared at δ 3.68 as a singlet (6H) peak and two aromatic protons on C-2′ and C-6′ appeared at δ 6.37 as a singlet (2H) peak, suggesting that bromine had been introduced at C-5 or C-8 of ring A. However, it was difficult to determine whether the position of bromine was C-5 or C-8 from the NMR spectrum. X-Ray analysis could not be carried out because an attempt to get a suitable single crystal of V was unsuccessful.

Temporarily setting aside the problem of the bromine position, we turned our attention to the methylenation of V to prepare the corresponding DPT derivative (VI) by Miller's method[7] which consists of reaction with cesium fluoride (CsF) or potassium fluoride (KF) and methylene halide in DMF. In the preliminary experiment, the reaction of IV with CsF and methylene chloride in DMF afforded desoxypicropodophyllin (DPP) in 53% yield together with a trace of DPT. This result suggested that the *trans* (2-α-H, 3-β-H) configuration of the original IV had been converted to *cis* (2-α-H, 3-α-H). For the purpose of finding conditions under which the original 2,3-*trans* configuration could be retained, various methods were examined for the methylenation of IV. It was found that DPT was preferentially obtained in 43% yield by using methylene iodide in place of methylene chloride. On the basis of these preliminary experiments, the methylenation of V was examined under various conditions and two compounds, VI and VII, which had the same empirical formula, $C_{22}H_{21}BrO_7$, were isolated in every case. The ratio of the yields of these compounds depended markedly on the sort of methylene halide used. The reaction with CsF and methylene iodide or methylene bromide gave predominantly VI in 68—70% yield and VII in 10—12% yield. In

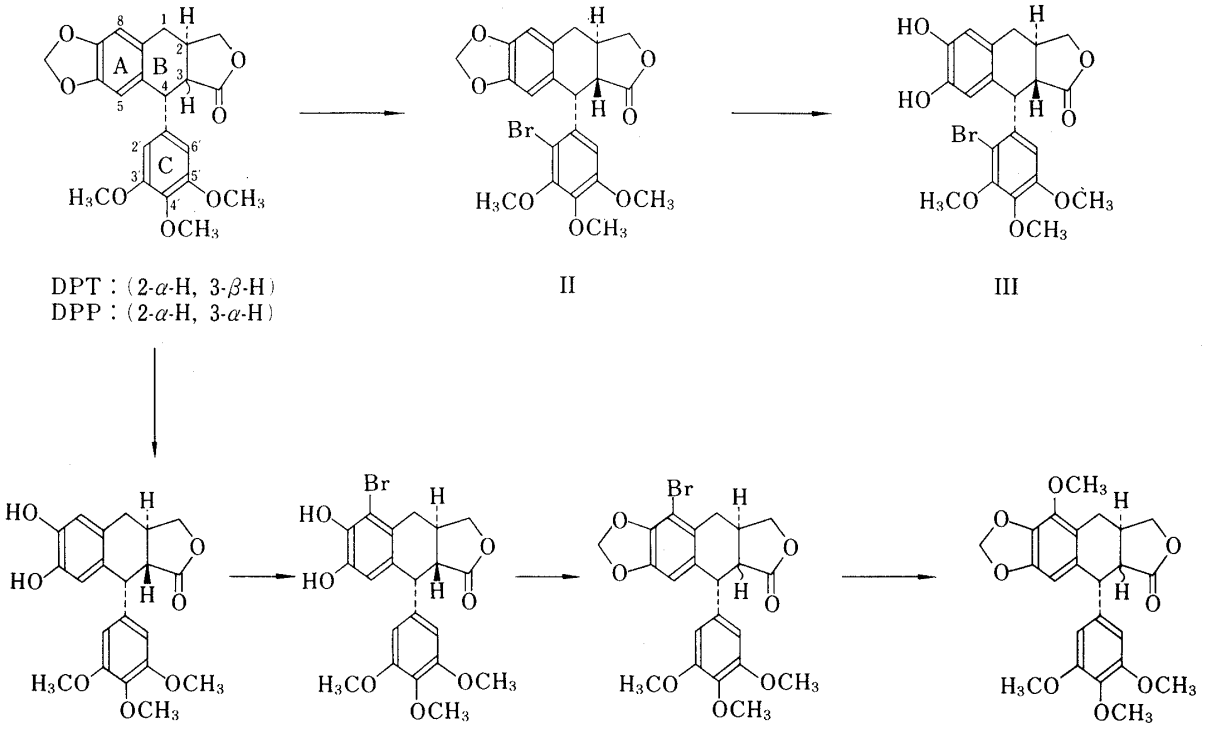

Chart 1

TABLE I. Yields of Methylenation Products from IV and V

Starting material	Metal halide (eq mol)	Methylene halide	Reaction conditions Temp. (°C)	Time (h)	Product yields (%)			
IV	CsF (5)	CH_2Cl_2	120	2	DPT	Trace	DPP	53
IV	CsF (5)	CH_2Br_2	120	2		39		15
IV	CsF (5)	CH_2I_2	120	2		43		12
V	CsF (3)	CH_2Br_2	60	3	VI	51	VII	9
V	CsF (5)	CH_2Br_2	60	3		68		10
V	CsF (5)	CH_2I_2	120	2		70		12
V	CsF (5)	CH_2Br_2	120	2		64		18
V	CsF (5)	CH_2Cl_2	120	2		16		58
V	CsF (10)	CH_2Br_2	60	3		62		12
V	KF (5)	CH_2I_2	120	2		52		4
V	KF (5)	CH_2Br_2	120	2		50		5

contrast, the use of methylene chloride gave VI in 16% yield and VII in 58% yield. The use of KF with methylene iodide or methylene bromide afforded a mixture consisting of the same products. However the yields of methylenated products were inferior to those obtained with CsF for both VI and VII. The results are listed in Table I.

Compound VI had mp 207—209 °C, $[\alpha]_D$ −148° ($CHCl_3$) and VII showed mp 176—178 °C, $[\alpha]_D$ −12.5° ($CHCl_3$). The specific rotations of these two compounds indicated that VI is *x*-bromo-DPT and VII is *x*-bromo-DPP. In order to clarify the position of bromine and to confirm the absolute configurations of C-2 and C-3, X-ray diffraction analysis was applied to a single crystal of VI obtained from the ethanol solution by slow evaporation at room temperature.

A crystal with dimensions of 0.3 × 0.4 × 0.4 mm was used for the X-ray study. The crystal is orthorhombic, space group $P2_12_12_1$ with cell dimensions of $a=20.720$ (2), $b=10.322$ (2) and $c=9.686$ (2) Å. The observed density [$D_m=1.521$ (2) g·cm^{-3}] showed that there were four molecules in a unit cell [volume = 2072 (2) Å^3, $D_x=1.530$ g·cm^{-3}]. The intensity data were collected on a Rigaku automated four-circle diffractometer by using graphite-monochromated Cu-$K\alpha$ radiation ($\lambda=1.5418$ Å). By means of the $\omega-2\theta$ scanning technique, 2034 independent reflections at less than $\sin\theta/\lambda=0.589$ Å^{-1} were collected and used for the structure determination. Corrections were made for Lorentz and polarization effects. Although the linear absorption coefficient of this crystal is relatively large [μ(Cu-$K\alpha$) = 33.56 cm^{-1}], absorption correction was not made because of the small size of the crystal used. The structure was solved by a combination of the heavy atom and direct methods. The positional parameters were refined by the block-diagonal least-squares method with anisotropic temperature factors for nonhydrogen atoms and isotropic ones for hydrogen atoms. The final *R* value was 0.074. The atomic numbering of VI is shown in Fig. 1. The final atomic coordinates are listed in Table II.

All numerical calculations were carried out on an ACOS-900 computer at the Computation Center of Osaka University by using the UNICS program.[8] A stereoscopic view of the molecular conformation is shown in Fig. 2. The structure of VI was confirmed to be 8-bromo-DPT (VI).

The structure of VII as 8-bromo-DPP had not been proven at this stage, but was clarified by the fact that VI was converted to VII on treatment with basic reagents, as described later.

Subsequently, several methods were examined to convert VI into β-peltatin and its methyl ether (I-A, I-B) by direct substitution of the bromine with a hydroxy group and methoxy group, respectively. The attempt to convert VI to β-peltatin methyl ether (I-A, I-B)

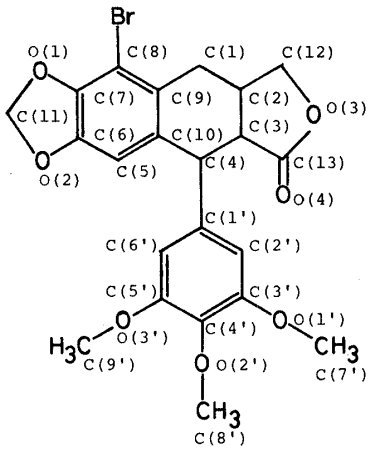

Fig. 1. Atomic Numbering of VI

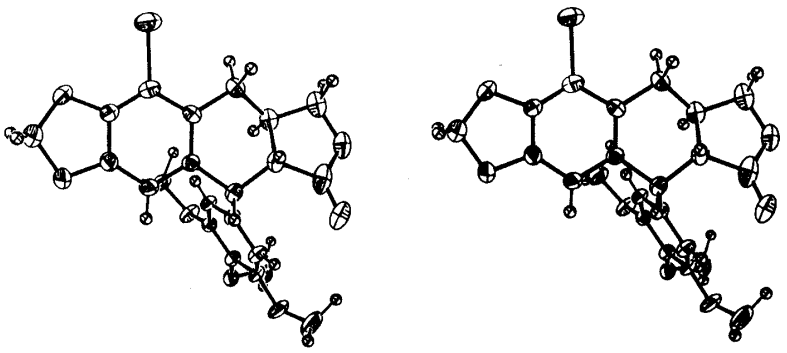

Fig. 2. ORTEP Drawing of VI

TABLE II. Atomic Coordinates ($\times 10^4$) with Their Estimated Standard Deviations in Parentheses

Atom	x	y	z
Br	7414 (0)	5125 (1)	4189 (1)
O(1)	7750 (2)	2791 (5)	6183 (6)
O(2)	7118 (2)	1511 (5)	7599 (6)
O(3)	4162 (2)	6282 (5)	4595 (5)
O(4)	3679 (2)	4432 (6)	5232 (6)
O(1′)	3316 (2)	3815 (6)	9736 (5)
O(2′)	4045 (2)	5168 (5)	11530 (4)
O(3′)	5233 (2)	5929 (5)	10894 (5)
C(1)	5918 (3)	5563 (6)	4635 (7)
C(2)	5245 (3)	5836 (6)	5115 (6)
C(3)	4862 (3)	4567 (6)	5135 (6)
C(4)	5078 (3)	3700 (6)	6321 (6)
C(5)	6097 (3)	2604 (6)	7042 (6)
C(6)	6743 (3)	2446 (6)	6959 (6)
C(7)	7119 (3)	3200 (6)	6122 (6)
C(8)	6870 (3)	4178 (6)	5388 (7)
C(9)	6197 (3)	4436 (5)	5456 (6)
C(10)	5818 (3)	3625 (6)	6279 (6)
C(11)	7747 (3)	1685 (9)	7037 (9)
C(12)	4812 (4)	6714 (7)	4255 (8)
C(13)	4163 (3)	5025 (8)	5028 (6)
C(1′)	4820 (3)	4133 (6)	7727 (6)
C(2′)	4188 (3)	3776 (6)	8069 (7)
C(3′)	3929 (3)	4139 (6)	9313 (7)
C(4′)	4288 (3)	4864 (6)	10251 (6)
C(5′)	4920 (3)	5211 (6)	9907 (5)
C(6′)	5181 (2)	4848 (6)	8645 (6)
C(7′)	2895 (4)	3276 (11)	8683 (10)
C(8′)	3608 (4)	6271 (9)	11515 (8)
C(9′)	5909 (3)	6169 (8)	10717 (8)

with potassium methoxide in the presence of dicyclohexyl-18-crown-6-ether[9] failed and afforded only VII in quantitative yield. This result shows that VII is a stereoisomer of VI. Introduction of a hydroxy group by means of the Grignard reaction[10] was also unsuccessful, affording merely the demethylated product since no Grignard reagent is formed even on treatment with active magnesium.[11]

The reaction of VI with cuprous iodide and sodium methoxide[12] furnished two substances, which were isolated by preparative thin layer chromatography (PTLC). One of them, mp 189—191 °C, $[\alpha]_D$ +9.1° ($CHCl_3$), was I-B in which the 2,3-configuration had been converted to *cis* type, although the introduction of a methoxy group had been achieved. The other one was DPP produced by debromination of the starting material VI together with conversion of the 2,3-configuration. Similar reaction of VII gave rise to I-B. This confirmed that the structure of VII was 8-bromo-DPP.

The above findings suggest that mild reaction conditions are required to obtain β-peltatin-A or I-A from VI without the conversion of the original 2,3-*trans* configuration.

Finally, an attempt was made by using Buck and Köbrich's method,[13] which yields phenols by the reaction of lithiated aryl compounds with nitrobenzene. Compound VI was treated with *n*-butyllithium at −100 °C in tetrahydrofuran (THF) in the presence of tetramethylethylenediamine (TMEDA) followed by the addition of nitrobenzene. The crude products, which were difficult to isolate as phenolic compounds, were immediately methylated with diazomethane in ether solution. The products were subjected to PTLC, affording two substances. One, obtained from the upper layer, was recrystallized from ethanol as colorless needles, mp 162.5—163.5 °C, $[\alpha]_D$ −110° ($CHCl_3$). The other one, isolated from the lower layer, was recrystallized from ethanol as colorless needles, mp 185—187 °C, $[\alpha]_D$ +11° ($CHCl_3$). These products were identified as I-A and I-B by direct comparison with corresponding authentic samples (infrared (IR) and NMR spectra and mixed melting point determination). Thus, syntheses of β-peltatin-A and -B methyl ethers were achieved from desoxypodophyllotoxin.

Experimental

All melting points are uncorrected. The instruments used in this study were as follows; IR spectra, Jasco IR-A-1; MS, Hitachi MU-6D; ^{1}H-NMR spectra, Hitachi R-40 (with tetramethylsilane as an internal standard; optical rotation, Jasco DIP-181. Precoated silica gel plates used in PTLC were Merck Kieselgel 60-F_{254}, 0.5 mm thickness.

2′-Bromo-DPT (II)——A solution of NBS (93 mg, 0.5 mmol) in dry DMF (10 ml) was added to a solution of DPT (200 mg, 0.5 mmol) in dry DMF (10 ml) and the whole was stirred at room temperature for 24 h, then poured into water (100 ml) and extracted with ether. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography in hexane–AcOEt (1 : 1) and recrystallized from EtOH. Colorless needles, mp 175—177 °C, 199 mg (83%), $[\alpha]_D^{25}$ −106.2° (c=1 in $CHCl_3$). *Anal.* Calcd for $C_{22}H_{21}BrO_7$: C, 55.36; H, 4.43. Found: C, 55.29; H, 4.23. MS *m/z*: 476, 478 (M^+). IR cm^{-1} (KBr): 1780 (C=O), 930 (–O–CH_2–O–). NMR ($CDCl_3$) δ ppm: 6.60 (1H, s, C_8–H), 6.36 (1H, s, C_5–H), 6.13 (1H, s, $C_{6'}$–H), 5.87 (2H, s, –O–CH_2–O–), 5.20—5.36 (1H, m, C_4–H), 3.90—4.60 (2H, m, lactone CH_2), 3.90 (3H, s, $C_{3'}$–OCH_3), 3.84 (3H, s, $C_{5'}$–OCH_3), 3.63 (3H, s, $C_{4'}$–OCH_3), 2.40—3.55 (4H, m, $C_{1,2,3}$–H).

2′-Bromo-demethylene-DPT (III)——A solution of II (954 mg, 2 mmol) in CH_2Cl_2 (9 ml) was added to a solution of BCl_3 (937 mg, 8 mmol) in CH_2Cl_2 at −50 °C with stirring. After 2 h, the reaction mixture was added to a saturated solution of $NaHCO_3$ (16 ml) mixed with ice (16 g) under vigorous stirring. After 30 min, the mixture was extracted with AcOEt. The extract was washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure at below 30 °C. A mixture of acetone (40 ml), water (40 ml) and $CaCO_3$ (4 g) was added to the residue and the mixture was refluxed for 2 h with stirring. After cooling, the whole was acidified with dil. HCl and extracted with AcOEt. The extract was washed with water, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was recrystallized from $CHCl_3$. 487 mg, 52% yield. mp 224—226 °C, $[\alpha]_D^{25}$ −129° (c=0.5 in EtOH). *Anal.* Calcd for $C_{21}H_{21}BrO_7$: C, 54.21; H, 4.55. Found: C, 54.17; H, 4.64. IR cm^{-1} (KBr): 3360 (OH), 1760 (C=O). NMR (DMSO-d_6) δ ppm: 8.75 (2H, br s, OH, disappeared on addition of D_2O), 6.60 (1H, s, C_8–H), 6.23 (2H, s, $C_{5,6'}$–H), 4.90—5.10 (1H, m, C_4–H), 3.85—4.70 (2H, m, lactone CH_2), 3.80 (3H, s, $C_{3'}$–OCH_3), 3.75 (3H, s, $C_{5'}$–OCH_3), 3.60 (3H, s, $C_{4'}$–OCH_3), 2.65—3.15 (4H, m, $C_{1,2,3}$–H).

8-Bromo-demethylene-DPT (V)——A solution of NBS (356 mg, 2 mmol) in dry DMF (10 ml) was added to a solution of IV (772 mg, 2 mmol) in dry DMF (10 ml) and the mixture was stirred at room temperature for 24 h, then poured into water (350 ml) and extracted with AcOEt. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by polyamide column chromatography with MeOH–H_2O (7 : 3). Recrystallization from EtOH afforded 741 mg (80% yield) of colorless crystals, mp 220—222 °C, $[\alpha]_D^{25}$ −131° (c=0.5 in MeOH). *Anal.* Calcd for $C_{21}H_{21}BrO_7$: C, 54.21; H, 4.55. Found: C, 54.18; H, 4.82. IR cm^{-1} (KBr):

3420 (OH), 1770 (C=O). NMR (DMSO-d_6) δ ppm; 9.25 (2H, br s, OH, disappeared on addition of D_2O), 6.47 (1H, s, C_5–H), 6.37 (2H, s, $C_{2',6'}$–H), 4.50 (1H, m, C_4–H), 3.96—4.43 (2H, m, lactone CH_2), 3.68 (6H, s, $C_{3',5'}$–OCH_3),3.65 (3H, s, $C_{4'}$–OCH_3), 2.78—3.50 (4H, m, $C_{1,2,3}$–H).

Methylenation of Demethylenated Compounds——The general procedure for the methylenation is as follows. A suspension of IV or V and anhydrous CsF or KF in DMF was stirred for 30 min at room temperature, then excess methylene halide was added and the mixture was heated at 60—120 °C for 2—4 h with stirring. After cooling, the mixture was poured into water and extracted with ether. The extract was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was fractionated by silica gel chromatography using hexane–AcOEt (1 : 1) to give two products. Each was recrystallized from EtOH to afford a methylenated compound. The results are listed in Table I. DPT, mp 167—168 °C, $[\alpha]_D^{25}$ −116° (c=2 in $CHCl_3$), and DPP, mp 172—173 °C, $[\alpha]_D^{25}$ +33° (c=0.5 in $CHCl_3$), were identified conclusively by direct comparison with authentic samples (IR and NMR spectra).[2] VI: needles, mp 207—209 °C, $[\alpha]_D^{25}$ −148° (c=0.5 in $CHCl_3$). *Anal.* Calcd for $C_{22}H_{21}BrO_7$: C, 55.36; H, 4.43. Found: C, 55.50; H, 4.39. IR cm^{-1} (KBr): 1780 (C=O), 930 (–O–CH_2–O–). NMR ($CDCl_3$) δ ppm: 6.50 (1H, s, C_5–H), 6.43 (2H, s, $C_{2',6'}$–H), 6.02 (2H, s, –O–CH_2–O–), 4.59 (1H, m, C_4–H), 3.98—4.51 (2H, m, lactone CH_2), 3.80 (3H, s, $C_{4'}$–OCH_3), 3.75 (6H, s, $C_{3',5'}$–OCH_3), 2.05—3.43 (4H, m, $C_{1,2,3}$–H). VII: needles, mp 176—178 °C, $[\alpha]_D^{25}$ −12.5° (c=1 in $CHCl_3$). *Anal.* Calcd for $C_{22}H_{21}BrO_7$: C, 55.36; H, 4.43. Found: C, 55.27; H, 4.27. IR cm^{-1} ($CHCl_3$): 1770 (C=O), 920 (–O–CH_2–O–). NMR ($CDCl_3$) δ ppm: 6.55 (1H, s, C_5–H), 6.30 (2H, s, $C_{2'6'}$–H), 6.00 (2H, s, –O–CH_2–O–), 3.90—4.60 (2H, m, lactone CH_2), 4.40 (1H, m, C_4–H), 3.83 (3H, s, $C_{4'}$–OCH_3), 3.80 (6H, s, $C_{3',5'}$–OCH_3), 2.77—3.50 (4H, m, $C_{1,2,3}$–H).

Reaction of VI and VII with Cuprous Iodide and Sodium Methoxide——a) Reaction of VI: The reaction was carried out under a stream of dry N_2. Anhydrous pyridine (4 ml) was added to a methanolic sodium methoxide solution (23 mg Na, 0.6 ml MeOH). To this, VI (238.5 mg, 0.5 eq mol) and dried CuI (67 mg, 0.35 mol) were added. The whole was refluxed for 50 h. The reaction mixture was filtered through celite and the filtrate was acidified with dil. HCl then stirred at room temperature for 6 h. It was then poured into water and extracted with ether. The extract was washed with brine, dried over Na_2SO_4 and evaporated *in vacuo*. The residue was subjected to PTLC in hexane–AcOEt (1 : 1) to provide two components. PTLC was repeated several times. The upper layer was extracted with $CHCl_3$–acetone (9 : 1) and evaporated *in vacuo* to give I-B as a crystalline solid (98 mg, 48% yield). Recrystallized from EtOH, fine needles, mp 189.5—191 °C, $[\alpha]_D^{25}$ +9.1° (c=0.5 in $CHCl_3$), (lit.,[4b] mp 184 °C, $[\alpha]_D^{21}$ +10.9° (in $CHCl_3$)). *Anal.* Calcd for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65. Found: C, 64.22, H, 5.79. IR cm^{-1} ($CHCl_3$): 1770 (C=O), 940 (–O–CH_2–O–). NMR ($CDCl_3$) δ ppm: 6.33 (3H, s, $C_{5,2',6'}$–H), 5.89 (2H, s, –O–CH_2–O–), 4.35 (1H, m, C_4–H), 3.88—4.60 (2H, m, lactone CH_2), 3.99 (3H, s, C_8–OCH_3), 3.81 (3H, s, $C_{4'}$–OCH_3), 3.77 (6H, s, $C_{3',5'}$–OCH_3), 2.65—3.40 (4H, m, $C_{1,2,3}$–H). The lower layer was worked up in the same manner to give DPP as a colorless solid (65 mg, 33% yield). Recrystallized from EtOH, mp 172—175 °C, $[\alpha]_D^{25}$ +34° (c=0.5 in $CHCl_3$). Both substances were identified conclusively by spectral (IR and NMR) comparison and mixed melting point determination with corresponding authentic samples.

b) Reaction of VII: The reaction was carried out as described for the case of VI. I-B (99 mg) was obtained from 238 mg of VII. mp 182—184 °C, $[\alpha]_D^{25}$ +10.4° (c=0.5 in $CHCl_3$), and it was identified conclusively by direct comparison with an authentic sample (IR and NMR spectra and mixed melting point determination).

Reaction of Lithiated VI with Nitrobenzene——A solution of VI (119 mg, 0.25 mmol) in THF (2 ml) was added to a solution of *n*-butyllithium (0.34 ml of 1.55 M hexane solution) and TMEDA (0.075 ml, 0.5 mmol) in THF (0.3 ml). The mixture was stirred for 15 min at −100 °C. Then nitrobenzene (0.5 ml) was added to the reaction mixture at the same temperature. Stirring was continued for 2 h. Then the mixture was brought up to room temperature and acidified with dil. HCl. The mixture was extracted with ether and the extract was washed with brine, dried over Na_2SO_4 and evaporated *in vacuo*. The residue, which was purified once by PTLC (hexane–AcOEt (1 : 1)), was then immediately methylated with diazomethane in ether solution for 24 h. The ethereal solution was worked up in the usual manner. The product obtained was subjected to PTLC (hexane–AcOEt (1 : 1)) to provide two components. The upper layer was extracted with $CHCl_3$–acetone (9 : 1) and the extract was evaporated *in vacuo* to afford a yellow-green solid, which was recrystallized from EtOH to give I-A as colorless needles (6 mg), mp 162.5—163.5 °C, $[\alpha]_D^{25}$ −110° (c=0.14 in $CHCl_3$), (lit.,[4b] mp 162.6—163.6 °C, $[\alpha]_D^{20}$ −120° (c=0.98 in $CHCl_3$)). *Anal.* Calcd for $C_{23}H_{24}O_8 \cdot H_2O$: C, 61.87; H, 5.87. Found: C, 62.04, H, 5.98. MS m/z: 428 (M^+). IR cm^{-1} ($CHCl_3$): 1780 (C=O), 930 (–O–CH_2–O–). NMR ($CDCl_3$) δ ppm: 6.32 (2H, s, $C_{2',6'}$–H), 6.24 (1H, s, C_5–H), 5.87 (2H, s, –O–CH_2–O–), 4.55 (1H, m, C_4–H), 4.40—3.90 (2H, m, lactone CH_2), 4.03 (3H, s, C_8–OCH_3), 3.77 (3H, s, $C_{4'}$–OCH_3), 3.72 (6H, s, $C_{3',5'}$–OCH_3), 2.20—3.30 (3H, m, $C_{1,2,3}$–H). The lower layer was worked up in the same manner. The colorless solid obtained was recrystallized from ethanol, affording I-B (9 mg), mp 185—187 °C, $[\alpha]_D^{25}$ +11° (c=0.3 in $CHCl_3$). The I-A and I-B thus obtained were identified conclusively by direct comparison with corresponding authentic samples (IR and NMR spectra and mixed melting point determination).

References and Notes

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