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Studies on the Constituents of Ophiopogonis Tubers. VII.[1]
Synthetic Studies of Homoisoflavonoids. (3)

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Several homoisoflavonoidal compounds, namely the monomethyl ethers ((IIIb) and (IVb)) of methylophiopogonones A and B, isoophiopogonone A monomethyl ether (VIIIb) and desmethylisoophiopogonone B (IXa), which were derived from the constituents of Ophiopogonis tuber (tuber of *Ophiopogon japonicus* Ker-Gawler var. *genuinus* Maxim., Liliaceae), have been synthesized. The chemical and spectroscopical assignments reported in the previous papers have been confirmed by the synthesis of methylophiopogonone A (IIIa; 5,7-dihydroxy-6,8-dimethyl-3-(3,4-methylenedioxybenzyl)-chromone), methylophiopogonone B (IVa; 5,7-dihydroxy-3-(4-methoxybenzyl)-6,8-dimethyl-chromone), isoophiopogonone A (VIIIa; 5,7-dihydroxy-8-methyl-3-(3,4-methylenedioxybenzyl)-chromone) and desmethylisoophiopogonone B (IXa; 5,7-dihydroxy-3-(4-hydroxybenzyl)-8-methyl-chromone).

Keywords——homoisoflavonoids; total synthesis; Ophiopogonis tuber; chalcones; dihydrochalcones; methylophiopogonones A and B; isoophiopogonone A; desmethylisoophiopogonone B

We previously reported the isolation of eleven new homoisoflavonoids from Ophiopogonis tubers (tuber of *Ophiopogon japonicus* Ker-Gawler var. *genuinus* Maxim., Liliaceae) and the structural elucidation of nine compounds, methylophiogonanones A (I) and B (II), methylophiopogonones A (IIIa) and B (IVa), ophiopogonanone A (V), ophiopogonones A (VI) and B (VII), isoophiopogonone A (VIIIa) and desmethylisoophiopogonone B (IXa).[1,3] Among these compounds, I, II and V are classified as homoisoflavanones and the other six compounds as homoisoflavones. Compounds I, II and V correspond to dihydro derivatives of IIIa, IVa and VI, respectively, and VI is a positional isomer of VIIIa as regards a methyl group. The present paper is mainly concerned with syntheses of mono- and dimethyl ethers, (IIIb) and (IVb) of methylophiopogonones A and B, isoophiopogonone A monomethyl ether (VIIIb) and desmethylisoophiopogonone B (IXa).

The synthetic methods reported by Tamm *et al.*,[4] Farkas *et al.*[5] and Chatterjea *et al.*[6] for homoisoflavonoids are summarized in Chart 2. In general, 3-benzylidenechroman-4-one was obtained by the condensation of chromanone with benzaldehyde in boiling acetic anhydride, while 3-benzylchromone (homoisoflavone) was prepared *via* ring closure of 2′-hydroxy-dihydrochalcones using ethyl formate and sodium powder.

Syntheses of the homoisoflavonoidal compounds IIIb, IVb, VIIIb and IXa were achieved by the latter method. The syntheses of IIIb and IVb started from 2-hydroxy-4,6-dimethoxy-

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[1] Part VI: A. Tada, R. Kasai, T. Saitoh, and J. Shoji, *Chem. Pharm. Bull.*, **28**, 2039 (1980).

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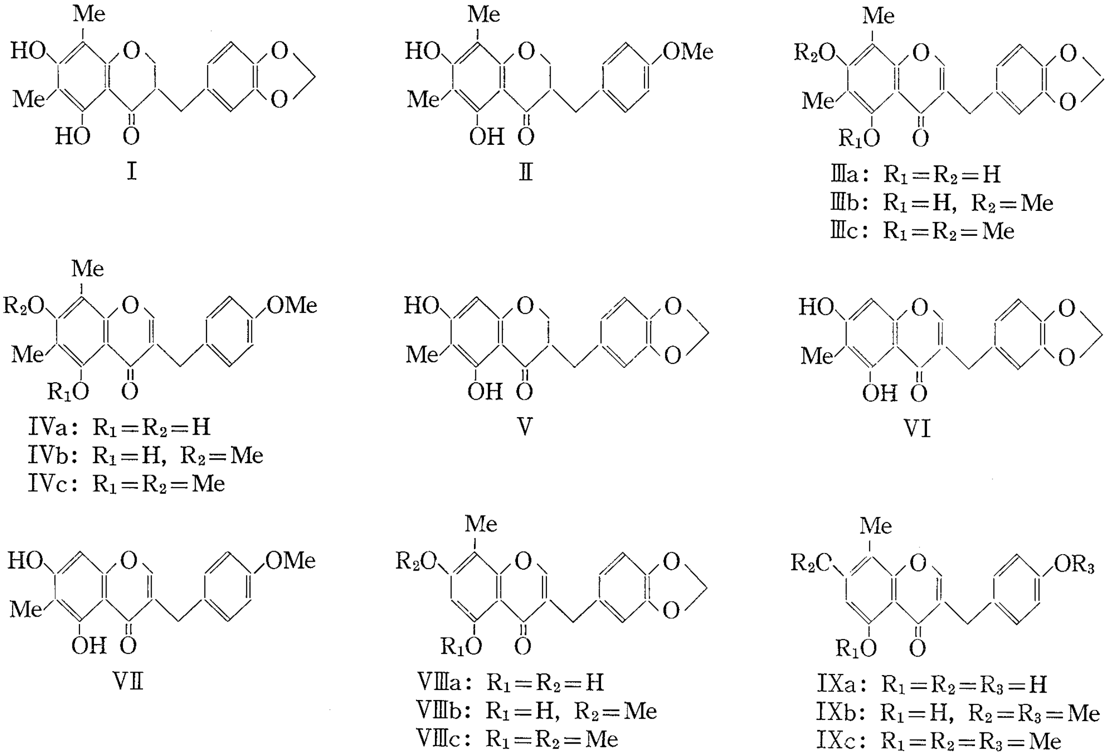
3,5-dimethylacetophenone (X),[7] while VIIIb and IXa were derived from 2-hydroxy-4,6-dimethoxy-3-methylacetophenone (XI).[8] Alkaline condensation of the ketones (X and XI) with piperonal or *p*-anisaldehyde was carried out at 45° for 1 hr[9] to give chalcones (XII—XV), which were catalyticaly hydrogenated to afford the corresponding dihydrochalcones



I

II

IIIa: $R_1=R_2=H$
IIIb: $R_1=H$, $R_2=Me$
IIIc: $R_1=R_2=Me$

IVa: $R_1=R_2=H$
IVb: $R_1=H$, $R_2=Me$
IVc: $R_1=R_2=Me$

V

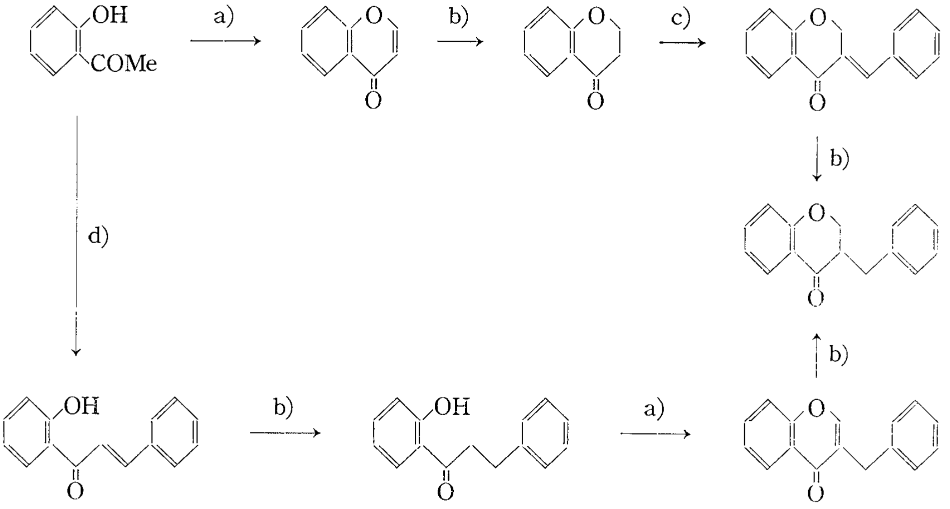
VI

VII

VIIIa: $R_1=R_2=H$
VIIIb: $R_1=H$, $R_2=Me$
VIIIc: $R_1=R_2=Me$

IXa: $R_1=R_2=R_3=H$
IXb: $R_1=H$, $R_2=R_3=Me$
IXc: $R_1=R_2=R_3=Me$

Chart 1



a) Ring closure with ethyl formate and powdered Na.
b) Catalytic hydrogenation.
c) Condensation with a benzaldehye in boiling acetic anhydride.
d) Alkali condensation with a benzaldehyde.

Chart 2

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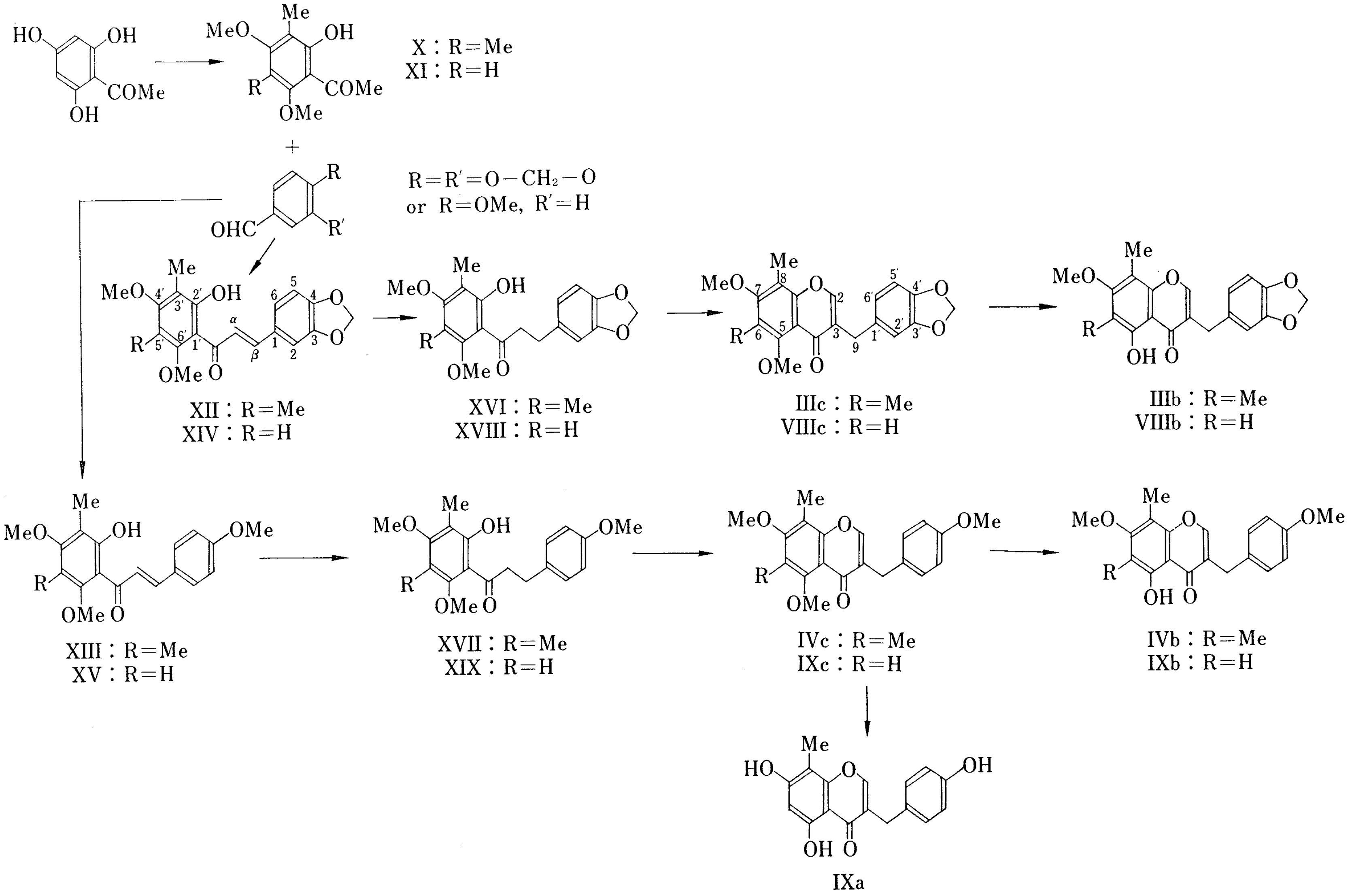
HO
OH
COMe
OH
MeO
Me
OH
R
COMe
OMe
X : R=Me
XI : R=H
+
R
R'
OHC
R=R'=O−CH₂−O
or R=OMe, R'=H
XII : R=Me
XIV : R=H
XVI : R=Me
XVIII : R=H
IIIc : R=Me
VIIIc : R=H
IIIb : R=Me
VIIIb : R=H
XIII : R=Me
XV : R=H
XVII : R=Me
XIX : R=H
IVc : R=Me
IXc : R=H
IVb : R=Me
IXb : R=H
IXa

Chart 3

(XVI—XIX). The ring closures of XVI—XIX with ethyl formate and powdered sodium[5,10] gave 3-benzylchromone permethyl ethers, (IIIc), (IVc), (VIIIc) and (IXc), respectively.

The dimethyl ether (IIIc) of methylophiopogonone A was obtained as colorless needles, this material was shown to be identical with an authentic sample derived from natural methylophiopogonone A (IIIa) by means of thin layer chromatography (TLC) and proton magnetic resonance (PMR) spectroscopy. In addition, IIIc was partially demethylated with $AlCl_3$ in acetonitrile[4,5] to give a monomethyl ether (IIIb) which was shown to be identical with that of the natural compound by means of mixed fusion, TLC, and infrared (IR) and PMR spectroscopies.

Methylophiopogonone B dimethyl ether (IVc) obtained by the synthesis mentioned above was partially demethylated with $AlCl_3$ in acetonitrile to give IVb, which was identical with an authentic sample as judged by TLC and IR and PMR spectroscopy.

Isoophiopogonone A dimethyl ether (VIIIc) was obtained as colorless needles, and demethylation of VIIIc gave isoophiopogonone A monomethyl ether (VIIIb). Compounds VIIIc and VIIIb were shown to be identical with those derived from natural isoophipogonone A (VIIIa) by means of spectroscopy, TLC and mixed fusion. As described in our preceding paper, the structure of isoophiopogonone A (VIIIa) was elucidated by comparison of the chemical shifts of aromatic methyl and ring protons with those of ophiopogonone A (VI). The present synthesis of isoophiopogonone A thus also supports the structure of ophiopogonone A proposed in our preceding paper.[1]

Desmethylisoophiopogonone B trimethyl ether (IXc) was obtained as a colorless syrup which was completely demethylated with $AlCl_3$ in benzene[11] to afford pale yellow plates. It was identified as desmethylisoophiopogonone B (IXa) by means of TLC, IR and PMR spectroscopy. This result also provides evidence for the structure of IXa presented on the basis of PMR and mass spectral analysis.[1]

In conclusion, the structures of desmethylisoophiopogonone B (IXa), methyl ethers of methylophiopogonone A (IIIa) and B (IVa) and isoophiopogonone A (VIIIa) have been established by the present syntheses.

Experimental

All melting points were determined on a Yanagimoto micro-melting point apparatus (hot-stage type) and are uncorrected. The UV spectra were recorded with a Hitachi EPS-3 spectrophotometer, IR spectra with a JASCO IRA-1 unit and PMR spectra with a Hitachi R-22 (90 MHz) spectrometer. Mass spectra were measured with a Hitachi RMS-4 machine.

2-Hydroxy-4,6-dimethoxy-3,5-dimethylacetophenone (X) and 2-Hydroxy-4,6-dimethoxy-3-methylacetophenone (XI)——A mixture of phloroacetophenone (3 g), MeI (10 ml), K_2CO_3 (9 g) and Me_2CO (30 ml) was refluxed for 3 hr.[8] After the solid had been filtered off, the filtrate was evaporated to dryness. The residue was crystallized from EtOH to give 2-hydroxy-4,6-dimethoxy-3-methylacetophenone (XI; 0.97 g), mp 142—143° (lit.[8] mp 141—142°). The mother liquor was subjected to silica gel column chromatography with benzene to afford 2-hydroxy-4,6-dimethoxy-3,5-dimethylacetophenone (X), pale yellow needles of mp 51—52° (recrystallized from petroleum benzene, yield 0.23 g) (lit.[7] mp 51°) and further XI (0.62 g).

2′-Hydroxy-4′,6′-dimethoxy-3′,5′-dimethyl-3,4-methylenedioxychalcone (XII)——A mixture of 2-hydroxy-4,6-dimethoxy-3,5-dimethylacetophenone (X) (1 mmol, 0.23 g), piperonal (1.1 mmol; 0.17 g), EtOH (5 ml) and 50% NaOH (1 ml) was stirred at 45° for 1 hr. The reaction mixture was acidified with dilute HCl under cooling, then extracted with Et_2O. After removal of the solvent, the residue was crystallized from EtOH to give reddish-yellow plates, mp 126—127° (yield; 0.35 g). UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 265 (4.09), 303 (4.21), 358 (4.60). $\lambda_{\max}^{\mathrm{EtOH+AlCl_3}}$ nm: 331, 370. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3450, 1621, 937. PMR (DMSO-d_6) δ: 2.09, 2.13 (3H each, s, arom. CH_3), 3.66, 3.73 (3H each, s, OCH_3), 6.10 (2H, s, O–CH_2–O), 6.98 (1H, d, J = 8 Hz, H-5), 7.25 (1H, q, J = 8 and 1.5 Hz, H-6), 7.32 (1H, d, J = 1.5 Hz, H-2), 7.51 (1H, d, J = 16 Hz, H-α),

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7.69 (1H, d, J = 16 Hz, H-β), 12.27 (1H, s, OH, disappeared upon addition of D_2O). *Anal.* Calcd for $C_{20}H_{20}O_6$: C, 67.40; H, 5.66. Found: C, 67.47; H, 5.66.

2′-Hydroxy-4,4′,6′-trimethoxy-3′,5′-dimethylchalcone (XIII)——A mixture of 2-hydroxy-4,6-dimethoxy-3,5-dimethylacetophenone (X) (1 mmol; 0.23 g), *p*-anisaldehyde (1.1 mmol; 0.15 g), EtOH (5 ml) and 50% NaOH (1 ml) was stirred at 55° for 1 hr. The reaction mixture was acidified with dilute HCl under cooling, then extracted with Et_2O. After removal of the solvent, the residue was crystallized from EtOH to give XIII, an orange-yellow powder, mp 83—84° (yield; 0.3 g). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 225 (sh., 4.36), 282 (3.88), 358 (4.32). $\lambda_{\max}^{\text{EtOH}+\text{AlCl}_3}$ nm: 320, 384. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3420, 1620. PMR (DMSO-d_6) δ: 2.09, 2.13 (3H each, s, arom. CH_3), 3.65, 3.73, 3.84 (3H each, s, OCH_3), 7.01 (2H, d, J = 8 Hz, H-3 and 5), 7.52 (1H, d, J = 18 Hz, H-α), 7.71 (2H, d, J = 8 Hz, H-2 and 6), 7.76 (1H, d, J = 18 Hz, H-β), 12.31 (1H, s, OH, exchangeable with D_2O). *Anal.* Calcd for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 69.81; H, 6.31.

2′-Hydroxy-4′,6′-dimethoxy-3′-methyl-3,4-methylenedioxychalcone (XIV)——A mixture of piperonal (1.1 mmol; 0.17 g), XI (1 mmol; 0.21 g), EtOH (5 ml) and 50% NaOH (1 ml) was stirred at 45° for 1 hr, then the reaction mixture was acidified with dilute HCl. The precipitated chalcone was collected by filtration and crystallized from EtOH to give XIV, yellow needles, mp 193—195° (yield; 0.3 g). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 370 (4.48). $\lambda_{\max}^{\text{EtOH}+\text{AlCl}_3}$ nm: 418. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3450, 1620, 930. PMR (DMSO-d_6) δ: 1.96 (3H, s, arom. CH_3), 3.92, 3.98 (3H each, s, OCH_3), 6.09 (2H, s, O–CH_2–O), 6.23 (1H, s, H-5′), 6.93 (1H, d, J = 8 Hz, H-5), 7.19 (1H, q, J = 8 and 1.5 Hz, H-6), 7.25 (1H, d, J = 1.5 Hz, H-2), 7.58 (1H, d, J = 16 Hz, H-α), 7.78 (1H, d, J = 16 Hz, H-β), 14.01 (1H, s, OH, exchangeable with D_2O). MS *m/e*: 342 (M^+). *Anal.* Calcd for $C_{19}H_{18}O_6$: C, 66.66; H, 5.30. Found: C, 66.58; H, 5.36.

2′-Hydroxy-4,4′,6′-trimethoxy-3′-methylchalcone (XV)——A mixture of XI (1.4 mmol; 0.3 g), *p*-anisaldehyde (1.5 mmol; 0.2 g), EtOH (5 ml) and 50% NaOH (1 ml) was stirred at 45° for 30 min and the reaction mixture was acidified with dilute HCl. The precipitated chalcone was collected by filtration and crystallized from EtOH to give XV, yellow needles, mp 132—133° (lit.[8] mp 134—135°) (yield; 0.37 g). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 378 (4.67). $\lambda_{\max}^{\text{EtOH}+\text{AlCl}_3}$ nm: 412. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3500, 1660, 1618. PMR (DMSO-d_6) δ: 1.93 (3H, s, arom. CH_3), 3.82, 3.91, 3.98 (3H each, s, OCH_3), 6.26 (1H, s, H-5′), 6.98 (2H, d, J = 8 Hz, H-3 and 5), 7.66 (1H, d, J = 18 Hz, H-α), 7.68 (2H, d, J = 8 Hz, H-2 and 6), 7.82 (1H, d, J = 18 Hz, H-β), 14.06 (1H, s, OH, exchangeable with D_2O). MS *m/e*: 328 (M^+). *Anal.* Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.82; H, 6.27.

2′-Hydroxy-4′,6′-dimethoxy-3′,5′-dimethyl-3,4-methylenedioxydihydrochalcone (XVI)——XII (0.3 g) was hydrogenated in the presence of prereduced 10% Pd-C (0.2 g) in AcOEt (30 ml). After the solid had been filtered off, the mother liquor was concentrated and the residue was treated with EtOH to give a syrup. (yield; 0.3 g). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 219 (4.34), 279 (4.22). $\lambda_{\max}^{\text{EtOH}+\text{AlCl}_3}$ nm: 310. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3400, 1615. PMR ($CDCl_3$) δ: 2.14, 2.16 (3H each, s, arom. CH_3), 2.93 (2H, t, J = 7.5 Hz, H-β), 3.39 (2H, t, J = 7.5 Hz, H-α), 3.69, 3.75 (3H each, s, OCH_3), 5.91 (2H, s, O–CH_2–O), 6.71 (3H, bs, H-2, 5 and 6), 12.93 (1H, s, OH, exchangeable with D_2O). *Anal.* Calcd for $C_{20}H_{22}O_6$: C, 67.02; H, 6.19. Found: C, 66.74; H, 6.30.

2′-Hydroxy-4,4′,6′-trimethoxy-3′,5′-dimethyldihydrochalcone (XVII)——XIII (0.2 g) was hydrogenated in the presence of prereduced 10% Pd-C in AcOEt. The product was recrystallized from MeOH to give colorless needles, mp 85—86° (yield; 0.2 g). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 223 (4.76), 277 (4.49). $\lambda_{\max}^{\text{EtOH}+\text{AlCl}_3}$ nm: 309. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3450, 1610. PMR ($CDCl_3$) δ: 2.12, 2.14 (3H each, s, arom. CH_3), 2.98 (2H, t, J = 7.5 Hz, H-β), 3.40 (2H, t, J = 7.5 Hz, H-α), 3.68, 3.74, 3.94 (3H each, s, OCH_3), 6.83 (2H, d, J = 9 Hz, H-3 and 5), 7.16 (2H, d, J = 9 Hz, H-2 and 6), 12.96 (1H, s, OH, exchangeable with D_2O). *Anal.* Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.84; H, 6.97.

2′-Hydroxy-4′,6′-dimethoxy-3′-methyl-3,4-methylenedioxydihydrochalcone (XVIII)——XIV (0.4 g) was hydrogenated with prereduced 10% Pd-C (0.2 g) in AcOEt (20 ml). The product was crystallized from EtOH to give colorless needles, mp 171—173° (yield; 0.4 g). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 282 (4.28). $\lambda_{\max}^{\text{EtOH}+\text{AlCl}_3}$ nm: 318. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3400, 1630, 930. PMR ($CDCl_3$) δ: 2.06 (3H, s, arom. CH_3), 2.95 (2H, t, J = 7.5 Hz, H-β), 3.26 (2H, t, J = 7.5 Hz, H-α), 3.92 (3H × 2, s, OCH_3), 5.92 (2H, s, O–CH_2–O), 5.98 (1H, s, H-5′), 6.74 (3H, bs, H-2, 5 and 6), 13.90 (1H, s, OH, exchangeable with D_2O). MS *m/e*: 344 (M^+). *Anal.* Calcd for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.45; H, 5.97.

2′-Hydroxy-4,4′,6′-trimethoxy-3′-methyldihydrochalcone (XIX)——XV (0.5 g) was hydrogenated with prereduced 10% Pd-C (0.35 g) in AcOEt (20 ml). The product was crystallized from EtOH to give colorless needles, mp 116—117° (yield; 0.5 g). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 220 (4.34), 290 (4.32). $\lambda_{\max}^{\text{EtOH}+\text{AlCl}_3}$ nm: 317. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3450, 1630, 1612. PMR ($CDCl_3$) δ: 2.03 (3H, s, arom. CH_3), 2.98 (2H, t, J = 8 Hz, H-β), 3.30 (2H, t, J = 8 Hz, H-α), 3.80 (3H, s, OCH_3), 3.93 (3H × 2, s, OCH_3), 6.00 (1H, s, H-5′), 6.83 (2H, d, J = 8 Hz, H-3 and 5), 7.22 (2H, d, J = 8 Hz, H-2 and 6), 13.95 (1H, s, OH, exchangeable with D_2O). MS *m/e*: 330 (M^+). *Anal.* Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.06; H, 6.84.

5,7-Dimethoxy-6,8-dimethyl-3-(3,4-methylenedioxybenzyl)-chromone (IIIc) (Methylophiopogonone A Dimethyl Ether)——Powdered Na (13 mmol; 0.3 g) was added in small portions with cooling to a mixture of 2′-hydroxy-4′,6′-dimethoxy-3′,5′-dimethyl-3,4-methylenedioxydihydrochalcone (XVI) (1 mmol; 0.35 g) and ethyl formate (7 ml), and the mixture was allowed to stand at 0° for 24 hr. Excess Na was decomposed with ice-cold dilute HCl, then the reaction mixture was extracted with Et_2O. The ethereal solution was concentrated and the syrupy residue was chromatographed repeatedly on silicic acid using benzene and $CHCl_3$.

The product was crystallized from EtOH, mp 117—118° (colorless needles, yield; 0.1 g). UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 236 (4.58), 255 (sh., 4.38), 285 (4.06), 308 (3.91). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1640, 940. PMR ($CDCl_3$) δ: 2.15, 2.17 (3H each, s, arom. CH_3), 3.68 (2H, s, arom. –CH_2–), 3.74, 3.83 (3H each, s, OCH_3), 5.85 (2H, s, O–CH_2–O), 6.71 (3H, bs, H-2′, 5′ and 6′), 7.47 (1H, s, olefinic H). *Anal.* Calcd for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.21; H, 5.35. The product was identical with the dimethyl ether of natural IIIa as judged by TLC and PMR spectral comparison.

5,7-Dimethoxy-3-(4-methoxybenzyl)-6,8-dimethyl-chromone (IVc) (Methylophiopogonone B Dimethyl Ether)——Na powder (13 mmol; 0.3 g) was added to a solution of XVII (1 mmol; 0.35 g) in ethyl formate (5 ml), and the mixture was kept in a refigerator overnight. The reaction mixture was treated with ice-cold dilute HCl to decompose excess Na and extracted with Et_2O. After removal of the solvent the product was purified by repeated column chromatography on silicic acid using benzene and $CHCl_3$ to give a syrup (yield; 0.07 g). UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 230 (4.55), 235 (4.55), 250 (sh., 3.93), 284 (3.89), 310 (3.83). IR $\nu_{\max}^{\mathrm{film}}$ cm^{-1}: 1640, 1607. PMR ($CDCl_3$) δ: 2.27 (3H$\times$2, s, arom. CH_3), 3.72 (2H, s, arom. –CH_2–), 3.76, 3.77, 3.86 (3H each, s, OCH_3), 6.81 (2H, d, $J=9$ Hz, H-3′ and 5′), 7.20 (2H, d, $J=9$ Hz, H-2′ and 6′), 7.41 (1H, s, olefinic H). *Anal.* Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 71.10; H, 6.43.

5,7-Dimethoxy-8-methyl-3-(3,4-methylenedioxybenzyl)-chromone (VIIIc) (Isoophiopogonone A Dimethyl Ether)——Na powder (13 mmol; 0.3 g) was added to a mixture of XVIII (0.85 mmol; 0.3 g) and ethyl formate (5 ml) with cooling, and the reaction mixture was allowed to stand at 0° for 24 hr. After the decomposition of excess Na with ice-cold dilute HCl, the reaction mixture was extracted with Et_2O. The syrupy product was purified by column chromatography on silicic acid using benzene, and product was crystallized from EtOH to give colorless needles (yield; 0.2 g), mp 172—173°. UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 230 (4.47), 251 (4.49), 259 (4.53), 292 (4.09), 315 (inf., 3.86). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1645, 1626, 925. PMR ($CDCl_3$) δ: 2.17 (3H, s, arom. CH_3), 3.68 (2H, s, arom. –CH_2–), 3.96, 3.99 (3H each, s, OCH_3), 5.93 (2H, s, O–CH_2–O), 6.42 (1H, s, H-6), 6.72—6.85 (3H, m, H-2′, 5′ and 6′), 7.49 (1H, s, olefinic H). MS *m/e*: 354 (M^+). *Anal.* Calcd for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12. Found: C, 67.34; H, 5.10. It was identical with the dimethyl ether of natural VIIIa as judged by spectral comparisons, TLC and mixed fusion.

5,7-Dimethoxy-3-(4-methoxybenzyl)-8-methyl-chromone (IXc) (Desmethylisoophiopogonone B Permethyl Ether)——Na powder (13 mmol; 0.3 g) was added to a mixture of XIX (1.1 mmol; 0.36 g) and ethyl formate (20 ml) with cooling, and the reaction mixture was allowed to stand at 0° for 48 hr. After the addition of ice-cold dilute HCl, the reaction mixture was extracted with Et_2O. The solvent was removed and the product was subjected to repeated silicic acid column chromatography using benzene and $CHCl_3$ to give a syrup (yield; 0.1 g). UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 230 (4.76), 249 (4.64), 255 (4.66), 279 (sh., 4.20), 285 (4.21), 310 (inf., 4.01). IR $\lambda_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1640, 1600. PMR ($CDCl_3$) δ: 2.16 (3H, s, arom. CH_3), 3.71 (2H, s, arom. –CH_2–), 3.80, 3.92, 3.97 (3H each, s, OCH_3), 6.39 (1H, s, H-6), 6.83 (2H, d, $J=9$ Hz, H-3′ and 5′), 7.22 (2H, d, $J=9$ Hz, H-2′ and 6′), 7.42 (1H, s, olefinic H). *Anal.* Calcd for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92. Found: C, 70.53; H, 5.83.

5-Hydroxy-7-methoxy-6,8-dimethyl-3-(3,4-methylenedioxybenzyl)-chromone (IIIb) (Methylophiopogonone A Monomethyl Ether)——A mixture of IIIc (0.1 mmol; 37 mg), $AlCl_3$ (0.1 mmol; 14 mg) and MeCN (3 ml) was refluxed for 2 hr. After the addition of ice-cold dilute HCl the reaction mixture was extracted with Et_2O. The ethereal solution was concentrated and the residue was subjected to column chromatography to give IIIb as colorless needles from EtOH, mp 142—143° (yield; 30 mg). UV $\lambda_{\max}^{\mathrm{EtOH}}$nm (log ε): 230 (4.43), 245 (4.45), 265 (4.50), 341 (3.66). $\lambda_{\max}^{\mathrm{EtOH+AlCl_3}}$ nm: 276, 380. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3450, 1642, 1600, 931. PMR ($CDCl_3$) δ: 2.19, 2.23 (3H each, s, arom. CH_3), 3.71 (2H, s, arom. –CH_2–), 3.78 (3H, s, OCH_3), 5.92 (2H, s, O–CH_2–O), 6.75 (3H, bs, H-2′, 5′ and 6′), 7.61 (1H, s, olefinic H), 12.71 (1H, s, OH, exchangeable with D_2O). MS *m/e*: 354 (M^+). *Anal.* Calcd for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12. Found: C, 67.70; H, 5.10. It was identical with the monomethyl ether of natural IIIa as judged by mixed fusion, TLC, IR and PMR spectroscopy.

5-Hydroxy-7-methoxy-3-(4-methoxybenzyl)-6,8-dimethyl-chromone (IVb) (Methylophiopogonone B Monomethyl Ether)——A mixture of IVc (0.1 mmol; 0.35 mg) and $AlCl_3$ (0.1 mmol) in MeCN was refluxed for 2 hr. The reaction mixture was treated as described above to afford colorless needles from EtOH, mp 130—131° (yield; 27 mg). UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 230 (4.63), 245 (4.54), 265 (4.60), 341 (3.79). $\lambda_{\max}^{\mathrm{EtOH+AlCl_3}}$ nm: 277, 405. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3450, 1625. PMR ($CDCl_3$) δ: 2.23, 2.26 (3H each, s, arom. CH_3), 3.76 (2H, s, arom. –CH_2–), 3.79, 3.82 (3H each, s, OCH_3), 6.86 (2H, d, $J=9$ Hz, H-3′ and 5′), 7.19 (2H, d, $J=9$ Hz, H-2′ and 6′), 7.58 (1H, s, olefinic H), 12.71 (1H, s, OH, exchangeable with D_2O). MS *m/e*: 340 (M^+). *Anal.* Calcd for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92. Found: C, 70.71; H, 6.00. It was identical with the natural product as judged by mixed fusion, TLC, IR and PMR spectroscopy.

5-Hydroxy-7-methoxy-8-methyl-3-(3,4-methylenedioxybenzyl)-chromone (VIIIb) (Isoophiopogonone A Monomethyl Ether)——A mixture of VIIIc (0.14 mmol; 50 mg), $AlCl_3$ (0.14 mmol; 19 mg) and MeCN (2 ml) was refluxed for 2 hr and the reaction mixture was treated as described above. The crude product was subjected to column chromatography to give VIIIb as colorless needles from EtOH (yield; 40 mg), mp 166—167°. UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε): 229 (4.22), 248 (4.28), 256 (4.37), 263 (4.42), 290 (3.92), 331 (3.64). $\lambda_{\max}^{\mathrm{EtOH+AlCl_3}}$ nm: 273, 315, 370. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3450, 1650, 1605, 930. PMR ($CDCl_3$) δ: 2.12 (3H, s, arom. CH_3), 3.71 (2H, s, arom. –CH_2–), 3.91 (3H, s, OCH_3), 5.96 (2H, s, O–CH_2–O), 6.43 (1H, s, H-6), 6.78 (3H, bs, H-2′, 5′ and 6′), 7.57 (1H, s, olefinic H), 12.67 (1H, s, OH, exchangeable with D_2O). *Anal.* Calcd for $C_{19}H_{16}O_6$: C, 67.05;

H, 4.75. Found: C, 66.85; H, 4.61. It was identical with the monomethyl ether of natural VIIIa as judged by mixed fusion, TLC, IR and PMR spectroscopy.

5-Hydroxy-7-methoxy-3-(4-methoxybenzyl)-8-methyl-chromone (IXb) (Desmethylisoophiopogonone B Dimethyl Ether)——A mixture of IXc (0.12 mmol; 40 mg), $AlCl_3$ (0.12 mmol; 16 mg) and MeCN (3 ml) was refluxed for 2 hr and the reaction mixture was treated as described above. The product was extracted with Et_2O and crystallized from EtOH to afford colorless needles, mp 132—133° (yield; 32 mg). UV λ_{max}^{EtOH} nm (log ε): 224 (4.38), 244 (sh., 4.29), 256 (sh., 4.41), 263 (4.46), 285 (3.80), 298 (3.73), 333 (3.64). $\lambda_{max}^{EtOH+AlCl_3}$ nm: 273, 315, 390. IR ν_{max}^{KBr} cm^{-1}: 3500, 1660, 1618. PMR ($CDCl_3$) δ: 2.14 (3H, s, arom. CH_3), 3.76 (2H, s, arom. $-CH_2-$), 3.83, 3.92 (3H each, s, OCH_3), 6.42 (1H, s, H-6), 6.89 (2H, d, $J=9$ Hz, H-3′ and 5′), 7.23 (2H, d, $J=9$ Hz, H-2′ and 6′), 7.57 (1H, s, olefinic H), 12.73 (1H, s, OH, exchangeable with D_2O). MS *m/e*: 326 (M^+). *Anal.* Calcd for $C_{19}H_{18}O_5$: C, 69.92; H, 5.56. Found: C, 69.60; H, 5.48.

5,7-Dihydroxy-3-(4-hydroxybenzyl)-8-methyl-chromone (IXa) (Desmethylisoophiopogonone B)——A mixture of IXc (0.12 mmol; 40 mg), $AlCl_3$ (0.9 mmol; 120 mg) and benzene (2 ml) was refluxed for 3 hr and the reaction mixture was treated as described above. The crude product was purified by column chromatography to afford pale yellow plates from EtOH (yield; 20 mg), mp 215—217° (the natural product reported in the previous paper[1] was a pale yellow powder, mp 208—210°). UV λ_{max}^{EtOH} nm (log ε): 222 (4.34), 264 (4.44), 297 (3.78), 325 (inf., 3.94). $\lambda_{max}^{EtOH+NaOAc}$ nm: 332. $\lambda_{max}^{EtOH+AlCl_3}$ nm: 316, 364. IR ν_{max}^{KBr} cm^{-1}: 3400, 1650. PMR (acetone-d_6) δ: 2.16 (3H, s, arom. CH_3), 3.68 (2H, s, arom. $-CH_2-$), 6.36 (1H, s, H-6), 6.80 (2H, d, $J=9$ Hz, H-3′ and 5′), 7.20 (2H, d, $J=9$ Hz, H-2′ and 6′), 8.00 (1H, s, olefinic H), 8.15, 9.48 (1H each, bs, OH, exchangeable with D_2O), 12.74 (1H, s, OH, exchangeable with D_2O). MS *m/e*: 298 (M^+). *Anal.* Calcd for $C_{17}H_{14}O_6$: C, 68.45; H, 4.73. Found: C, 67.99; H, 4.73. It was identical with the natural product as judged by TLC, IR and PMR spectroscopy.

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