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Studies on the Constituents of Sophora Species. VI.[1] Constituents of the Root of *Sophora subprostrata* Chun et T. Chen. (4)[2]

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Three new flavonoids were isolated from the root of *Sophora subprostrata* Chun et T. Chen, and their structures were established from their spectral data and comparison with the corresponding synthesized derivatives as 6-[3-(2′,4′-dihydroxyphenyl)acryloyl]-7-hydroxy-2,2-dimethyl-8-(3-methyl-2-butenyl)-2*H*-benzopyran (I), 2-(2′,4′-dihydroxyphenyl)-8,8-dimethyl-10-(3-methyl-2-butenyl)-8*H*-pyrano[2,3-*d*]chroman-4-one (IV), and 2′,4′,7-trihydroxy-6,8-bis(3-methyl-2-butenyl)flavanone (VIII).

In previous papers we reported the isolation and the structure elucidation of four new flavonoids (sophoradin,[4] sophoranone,[4] sophoradochromene,[5] and sophoranochromene[5]) and the characterization of caffeic acid esters,[6] *l*-maackiain,[6] and genistein[6] as the constituents of the root of *Sophora subprostrata* Chun et T. Chen, a Chinese drug, Shan-Dou-Gen (山豆根).

Further studies on the constituents of this drug resulted in the isolation of three new flavonoids I, IV, and VIII from the ether-soluble fraction of the methanolic extract. The present paper deals with the structure of these flavonoids.

The compound (I) was obtained as orange-yellow needles, mp 176°, M^+ 406, $C_{25}H_{26}O_5$, with a positive ferric chloride reaction. It gave the absorption bands of hydroxyl, conjugated carbonyl, and benzene ring in the infrared (IR) spectrum. The ultraviolet (UV) spectrum (λ_{max}^{EtOH} nm: 403) suggested the presence of a chalcone ring. In the UV spectrum, bathochromic shifts of 67 and 62 nm were observed after the addition of aluminum chloride[7,8] and sodium ethoxide[7] respectively, indicating that the hydroxyl groups must be presented in positions 7 and 4′. The nuclear magnetic resonance (NMR) spectrum showed the presence of a 2,2-dimethylchromene[5] ring [δ 1.44 (6H, s), δ 5.65 (1H, J=9.8 Hz, d), δ 6.35 (1H, J=9.8 Hz, d)], an isoprenyl group [δ 1.63 (3H, s), δ 1.79 (3H, s), δ 3.31 (2H, J=8.3 Hz, d), δ 5.22 (1H, J=8.3 Hz, t)], three hydroxyl groups [δ 8.70—9.15 (2H), δ 14.18 (1H); both disappeared after the addition of D_2O)], and four aromatic protons [δ 7.70 (1H, s, C_5-H), δ 7.76 (1H, d, J=9.0 Hz, $C_{6'}$-H), δ 6.43 (1H, q, J=9.0 Hz, J=2.2 Hz, $C_{5'}$-H), δ 6.48 (1H, d, J=2.2 Hz, $C_{3'}$-H)].

On methylation, I gave a dimethyl ether, mp 123.5°, $C_{27}H_{30}O_5$ (II). II has a hydrogen-bonded hydroxyl group in position 7, according to the UV spectrum (bathochromic shift

1) Part V: K. Hatayama and M. Komatsu, *Chem. Pharm. Bull.* (Tokyo), **19**, 2126 (1971).
2) This work was reported at the 92th Annual Meeting of Pharmaceutical Society of Japan, Osaka, April 1972.
3) Location: *3-34-1, Takada, Toshima-ku, Tokyo, 171, Japan.*
4) M. Komatsu, T. Tomimori, K. Hatayama, and N. Mikuriya, *Chem. Pharm. Bull.* (Tokyo), **18**, 602 (1970).
5) M. Komatsu, T. Tomimori, K. Hatayama, Y. Makiguchi, and N. Mikuriya, *Chem. Pharm. Bull.* (Tokyo), **18**, 741 (1970).
6) M. Komatsu, T. Tomimori, K. Hatayama, and Y. Makiguchi, *Yakugaku Zasshi*, **90**, 459 (1970).
7) L. Jurd, "The Chemistry of Flavonoid Compounds," ed. by T.A. Geissman, Pergamon Press, London, 1962, pp. 141—147.
8) *a*) L. Jurd and T.A. Geissman, *J. Org. Chem.*, **21**, 1395 (1956); *b*) E.C. Bate-Smith and T. Swain, *J. Chem. Soc.*, **1953**, 2185; *c*) T.A. Geissman, J.B. Harborne, and M.K. Seikel, *J. Am. Chem. Soc.*, **78**, 825 (1956).

of 61 nm on the addition of aluminum chloride[7,8]) and the NMR spectrum [δ 13.85 (1H, s)]. Concerning the chemical shift of Ar-C$\underline{H}_2$- in II, a significant solvent effect[9]) was observed [NMR ($CDCl_3$): δ 3.33, (C_5H_5N): δ 3.61)], indicating that the isoprenyl group should be in position 8. Catalytic hydrogenation of II gave a hexahydro compound (III).

The negative *ortho*-diphenol reaction according to the UV spectrum of I (bathochromic shift was not shown on the addition of sodium acetate-boric acid[10]) suggested that a remaining hydroxyl group should be in position 2′ on the B-ring.

From these data, and biogenetical speculation on the chromene ring,[5]) the structure of compound I was assumed as in Chart 1.

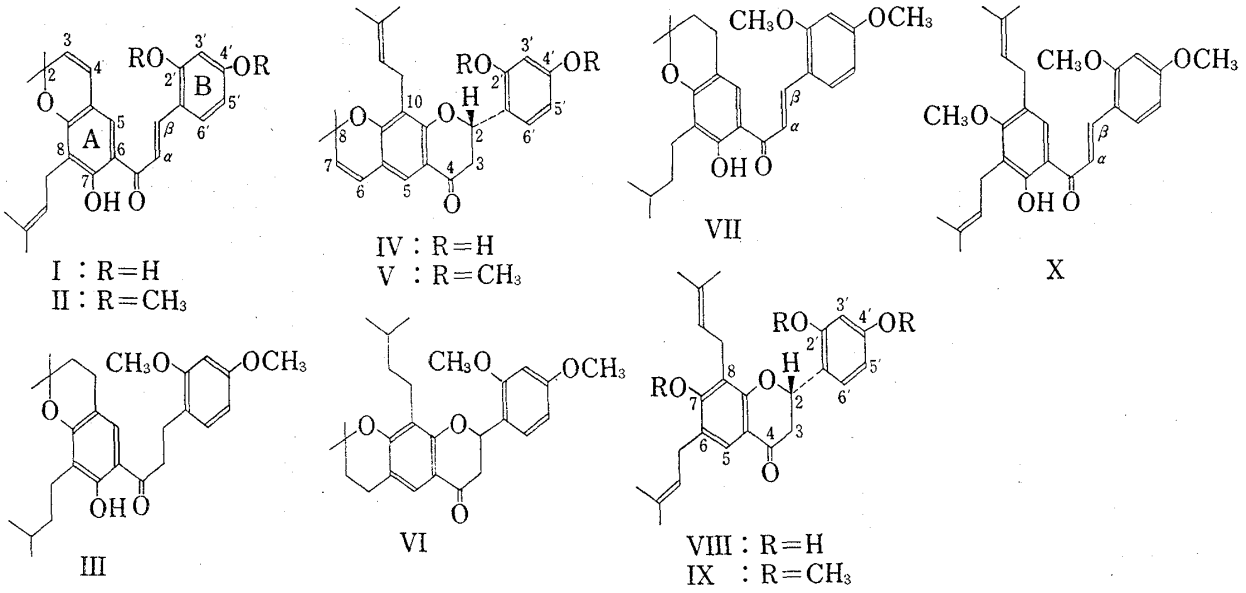

Chart 1

The compound (IV) was obtained as colorless needles, mp 173°, $[\alpha]_D^{25}$ −2.5° (EtOH), M^+ 406, $C_{25}H_{26}O_5$, with a positive ferric chloride reaction. It gave the absorption bands of hydroxyl group, conjugated carbonyl, and benzene ring in the IR spectrum. The NMR spectrum, as in the spectrum of I, exhibited the presence of a 2,2-dimethylchromene ring, an isoprenyl group. It also showed the presence of two hydroxyls [δ 8.00—8.45 (2H, br); disappeared by the addition of D_2O], four aromatic protons [δ 7.37 (1H, s, C_5-H), δ 6.39 (1H, q, J=9.0 Hz, J=2.2 Hz, $C_{5'}$-H), δ 6.47 (1H, d, J=2.2 Hz, $C_{3'}$-H), δ 7.30 (1H, d, J=9.0 Hz, $C_{6'}$-H)], C-2 proton [δ 5.68 (1H, q, J=10.5 Hz, J=5.0 Hz)] and C-3 protons [δ 2.50—3.00 (2H, m)] in the flavanone ring.[4])

On methylation, IV gave two dimethyl ethers, $C_{27}H_{30}O_5$, one of which had a flavanone ring (V) and the other was the above-mentioned dimethyl ether (II) obtained from I. Catalytic hydrogenation of V afforded a tetrahydro compound (VI), which gave the chalcone (VII) by alkali cleavage. Alkali cleavage of IV with 5% methanolic potassium hydroxide gave I.

From these data, the structure of compound (IV) was established as the flavanone corresponding to I.

The compound (VIII) was obtained as colorless needles, mp 102°, $[\alpha]_D^{25}$ −42.6° (EtOH), M^+ 408, $C_{25}H_{28}O_5$, with a positive ferric chloride reaction. It gave the absorption bands of hydroxyl group, conjugated carbonyl, and benzene ring in the IR spectrum. The UV spectrum (λ_{max}^{EtOH} nm: 285) suggested the presence of a flavanone ring. In the UV spectrum,

9) P.V. Demarco, E. Farkas, D. Doddrel, B.L. Mylari, and E. Wenkert, *J. Am. Chem. Soc.*, **90**, 5480 (1968).
10) T.J. Mabry, K.R. Markham, and M.B. Thomas, "The Systematic Identification of Flavonoids," Springer-Verlag, New York Inc. 1970, pp. 228—229.

a bathochromic shift of 74 nm was observed on the addition of sodium hydroxide,[11] indicating that a hydroxyl must be in position 7. The NMR spectrum showed the presence of two isoprenyl groups [δ 1.63, 1.71 (each 6H, each s), δ 5.05—5.45 (2H, m), δ 3.23—3.45 (4H, m)], three hydroxyl groups [δ 7.90—8.60 (3H, br); shifted to δ 7.80—8.40 at 48°], and, as in the spectrum of IV, exhibited the presence of four aromatic protons, C-2 proton and C-3 protons.

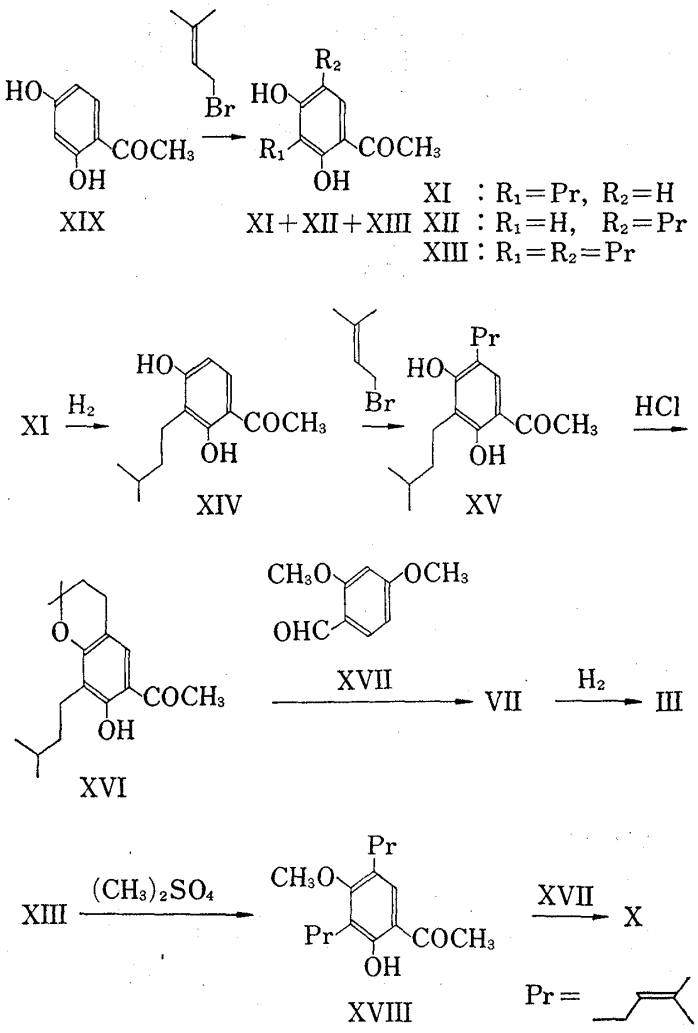

Chart 2

On methylation, VIII gave two trimethyl ethers, one of which was the flavanone (IX) (M^+ 450, UV: λ_{max}^{EtOH} nm: 269, 328, NMR: $-OCH_3\times3$), the other was the chalcone (X) [UV: λ_{max}^{EtOH} nm: 383, NMR: δ 7.77 (1H, d, J=15.0 Hz, C_α-H), δ 8.08 (1H, d, J=15.0 Hz, C_β-H)], as in compound IV.

III, VII, and X were synthesized by the route shown in Chart 2. Treatment of resacetophenone (XIX) with 3,3-dimethylallyl bromide in alkali solution gave XI, XII, and XIII. Catalytic hydrogenation of XI furnished the dihydro compound (XIV) which was converted to XV by treatment with 3,3-dimethylallyl bromide. Cyclization of XV was accomplished by boiling XV in methanolic hydrochloric acid to produce XVI. Condensation of XVI with XVII[12] in alkali solution[13] gave the chalcone (VII). On catalytic hydrogenation, VII afforded a dihydro derivative (III). Methylation of XIII gave a monomethyl ether (XVIII). The chalcone (X) was obtained by condensation of XVIII and XVII in alkali solution.

III, VII, and X thus obtained were identified with the respective compounds derived from natural sources by thin-layer chromatography (TLC), and by UV, IR, and NMR spectra.

Since the specific optical rotation of IV and VIII had a minus (−) sign, as in other natural flavanones,[14] IV and VIII most probably have an (*S*)-configuration at C-2.

From these data, compounds I, IV, and VIII were assinged the following formulae: 6-[3-(2′,4′-dihydroxyphenyl)acryloyl]-7-hydroxy-2,2-dimethyl-8-(3-methyl-2-butenyl)-2*H*-benzopyran (I), 2-(2′,4′-dihydroxyphenyl)-8,8-dimethyl-10-(3-methyl-2-butenyl)-8*H*-pyrano-[2,3-*d*]chroman-4-one (IV), 2′,4′,7-trihydroxy-6,8-bis(3-methyl-2-butenyl)flavanone (VIII).

11) Y. Tomita, "Jikken Kagaku Koza, (Experimental Chemistry), *Suppl.* Vol.," Vol. 5, ed. by the Chemical Society of Japan, Maruzen Co., Ltd., Tokyo, 1966, pp. 940—942.
12) Ludwig Gatterman, *Chem. Ber.*, **31**, 1152 (1898).
13) M. Vandewalle, *Bull. Soc. Chim.* (Belges), **70**, 163 (1961).
14) W.B. Whalley, "The Chemistry of Flavonoid Compound," ed. by T.A. Geissman, Pergamon Press, London, 1962, pp. 441—467.

Experimental

All the melting points were uncorrected. UV spectra were measured using a Hitachi Recording Spectrophotometer EPS-2U type. IR spectra were measured using a JASCO DS-301 Spectrophotometer. NMR spectra were taken at 60 MHz with TMS as an internal standard using a Hitachi Perkin-Elmer Spectrometer (Model R-20). The chemical shifts were given in δ values. The unit (Hz) of coupling constant (J Hz) was abbreviated. The developing solvents of TLC[6] were acetone–hexane (1: 2) (solv. 1), $CHCl_3$–MeOH (9: 1) (solv. 2), benzene–isopropyl ether (1: 1) (solv. 3), benzene (solv. 4).

Isolation of Flavonoids——The roots of *Sophora subprostrata* Chun et T. Chen (100 kg) were extracted three times with boiling MeOH. The ether-soluble part (1 kg) of the MeOH extract was chromatographed on silica gel (100 kg) using acetone–hexane (1: 5) as eluent, and each fraction was checked by TLC. Neutral compounds (not investigated further), caffeic acid esters, sophoradochromene, the mixture of sophoradin and sophoradochromene, sophoranone, *l*-maackiain, the mixture of compounds I and IV, compound VIII, and genistein were eluted in that order. The mixture of compounds I and IV was subjected to rechromatography on silica gel, using benzene–isopropyl ether (3: 1). Then, I, IV, and VIII were submitted to rechromatography on silica gel to yield I (1 g), IV (1 g), and VIII (0.3 g), respectively.

Compound I——I was recrystallized from benzene as orange-yellow needles, mp 176°, M^+ 406, $FeCl_3$ (+). TLC (*Rf*): 0.38 (solv. 1), 0.43 (solv. 2), 0.33 (solv. 3). *Anal.* Calcd. for $C_{25}H_{26}O_5$: C, 73.85; H, 6.45. Found: C, 73.93; H, 6.42. UV λ_{max}^{EtOH} nm (log ε): 403 (4.49), $\lambda_{max}^{EtOH\text{-}AlCl_3}$ nm (log ε): 470 (4.56), $\lambda_{max}^{EtOH\text{-}NaOEt}$ nm (log ε): 465 (4.63), $\lambda_{max}^{EtOH\text{-}NaOAc\text{-}H_3BO_3}$ nm (log ε): 403 (4.46). IR ν_{max}^{KBr} cm^{-1}: 3333 (OH), 2950, 2890 (CH_3), 1613 (conjugated CO), 1535 (arom. C=C). NMR [$(CD_3)_2CO$]: 1.44 (6H, s, $\overset{-}{\underset{-O}{C}}\rangle C(C\underline{H}_3)_2$), 1.63, 1.79 (each 3H, each s, $-CH=C(C\underline{H}_3)_2$), 3.31 (2H, d, J=8.3, Ar-$C\underline{H}_2$-CH=), 5.22 (1H, t, J=8.3, Ar-CH_2-$C\underline{H}$=), 5.65 (1H, d, J=9.8, $^{=C\underline{H}}_{-O}\times$), 6.35 (1H, d, J=9.8, $^{=C\underline{H}}_{-O}\times$), 6.43 (1H, q, J=9.0, J=2.2, $C_{5'}$-H), 6.48 (1H, d, J=2.2, $C_{3'}$-H), 7.70 (1H, s, C_5-H), 7.73 (1H, d, J=15.0, C_α-H), 7.76 (1H, d, J=9.0, $C_{6'}$-H), 8.18 (1H, d, J=15.0, C_β-H), 8.70—9.15 (2H, br, OH×2; disappeared by addition of D_2O), 14.18 (1H, s, C_7-OH; disappeared by addition of D_2O).

Methylation of I (Formation of II)——A mixture of I (300 mg), Me_2SO_4 (500 mg), anhyd. K_2CO_3 (1.5 g), and acetone (20 ml) was refluxed for 2 hr, filtered, and the solvent was evaporated *in vacuo*. H_2O was added to the residue which was extracted with ether. The ether layer was washed with H_2O and dried over Na_2SO_4. After evaporation of ether, the residure was chromatographed over silica gel with benzene giving II. II was recrystallized from MeOH as yellow needles, mp 123.5°. *Anal.* Calcd. for $C_{27}H_{30}O_5$: C, 74.63; H 6.96. Found: C, 74.82; H, 7.08. UV λ_{max}^{EtOH} nm: 392, $\lambda_{max}^{EtOH\text{-}AlCl_3}$ nm: 453. IR ν_{max}^{KBr} cm^{-1}: 1630 (conjugated CO), 1611, 1550 (arom. C=C). NMR ($CDCl_3$): 3.33 (2H, d, J=7.5, Ar-$C\underline{H}_2$-CH=), 3.82, 3.87 (each 3H, each s, $-OCH_3$), 13.85 (1H, s, C_7-OH). NMR(C_5D_5N): 3.61 (2H d, J=7.5, Ar-$C\underline{H}_2$-CH=).

Catalytic Hydrogenation of II (Formation of III)——II (100 mg) in EtOH (200 ml) was hydrogenated over PtO_2 (30 mg) as a catalyst. Three moles of H_2 were absorbed during 50 min. After removal of the catalyst, the solvent was evaporated *in vacuo* and the residue was chromatographed over silica gel with benzene, from which a hexahydro product (III) was obtained. III showed one spot on TLC. M^+ 440. UV λ_{max}^{EtOH} nm: 288. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1630 (conjugated CO), 1620 (sh), 1590 (arom. C=C). NMR (CCl_4): 0.94 (6H, d, J=6.0, $-CH(C\underline{H}_3)_2$), 1.33 (6H, s, $\overline{\underset{-O}{}}\rangle C(C\underline{H}_3)_2$), 1.50—1.90 (5H, br, m, Ar-CH_2-$C\underline{H}_2$-$C\underline{H}$ and $^{-C\underline{H}_2}_{-O}\times$), 2.30—3.00 (8H, br, m, Ar-$C\underline{H}_2$- ×2 and Ar-CO-$C\underline{H}_2$-$C\underline{H}_2$-Ar).

Compound (IV)——IV was recrystallized from benzene as colorless needles, mp 173°, $[\alpha]_D^{25}$ −2.5° (c=5, EtOH), M^+ 406, $FeCl_3$ (+). TLC (*Rf*): 0.38 (solv. 1), 0.43 (solv. 2), 0.26 (solv. 3). *Anal.* Calcd. for $C_{25}H_{26}O_5$: C, 73.86; H, 6.45. Found: C, 74.09; H, 6.39. UV λ_{max}^{EtOH} nm (log ε): 257 (4.48). IR ν_{max}^{KBr} cm^{-1}: 3210 (OH), 1661 (conjugated CO), 1605, 1510 (arom. C=C). NMR [$(CD_3)_2CO$]: 1.43 (6H, s, $\overline{\underset{-O}{}}\rangle C(C\underline{H}_3)_2$), 1.62, 1.67 (each 3H, each s, $-CH=(C\underline{H}_3)_2$), 2.50—3.00 (2H, m, C_3-H_2), 3.30 (2H, d, J=7.5, Ar-CH_2–), 5.18 (1H, t, J=7.5, Ar-CH_2-$C\underline{H}$=), 5.65 (1H, d, J=9.8, $^{=C\underline{H}}_{-O}\times$), 5.68 (1H, q, J=10.5, J=5.0, C_2-H), 6.34 (1H, d, J=9.8, $^{-C\underline{H}=}_{-O}\times$), 6.39 (1H, q, J=9.0, J=2.2, $C_{5'}$-H), 6.47 (1H, d, J=2.2, $C_{3'}$-H), 7.30 (1H, d, J=9.0, $C_{6'}$-H), 7.37 (1H, s, C_5-H), 8.00—8.45 (2H, OH×2, disappeared by addition of D_2O).

Methylation of IV (Formation of II and V)——A mixture of IV (300 mg), Me_2SO_4 (500 mg), anhyd. K_2CO_3 (1.5 g), and acetone (20 ml) was refluxed for 2 hr, then extraction and chromatography were carried out as described in methylation of I, giving two products.

The first product [TLC (*Rf*): 0.17 (solv. 4)] was recrystallized from EtOH as colorless needles (V), mp 118.5°. *Anal.* Calcd. for $C_{27}H_{30}O_5$: C, 74.63; H, 6.96. Found: C, 74.75; H, 6.89. UV λ_{max}^{EtOH} nm: 257. IR ν_{max}^{KBr} cm^{-1}: 1680 (conjugated CO), 1610, 1590 (arom. C=C). NMR (CCl_4): 3.73, 3.79 (each 3H, each s, $-OCH_3$).

The second product [TLC (*Rf*): 0.56 (solv. 4)] was recrystallized from MeOH as colorless needles, mp 123.5°, the melting point of which was not decreased on admixture with II, in addition, the TLC and UV, IR, and NMR spectra of this product were identical with those of II.

Catalytic Hydrogenation of V (Formation of VI)——V (100 mg) in EtOH (20 ml) was hydrogenated over PtO_2 (30 mg) as a catalyst. Two moles of H_2 were absorbed during 40 min. Chromatography of the product was carried out as described for catalytic hydrogenation of II to give a compound (VI), M^+ 440, showing one spot on TLC. UV λ_{max}^{EtOH} nm: 285. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1681 (conjugated CO), 1608, 1591 (sh) (arom. C=C). NMR ($CDCl_3$): 0.90 (6H, d, J=6.0, $-CH(C\underline{H}_3)_2$), 1.34 (6H, s, $\begin{matrix}-C\\-O\end{matrix}\rangle C(CH_3)_2$), 1.22—2.15 (5H, br, m, Ar-CH_2-$C\underline{H}_2$-$C\underline{H}$ and $\begin{matrix}-CH_2\\-O\end{matrix}\times$), 2.47—2.90 (6H, m, Ar-$CH_2$- ×2 and C_3-H_2).

Alkali Cleavage of VI (Formation of VII)——A mixture of VI (50 mg) and 5% EtOH–KOH (10 ml) was refluxed for 30 min. After addition of H_2O (100 ml), EtOH was evaporated. The reaction mixture was acidified to pH 2 with dil. HCl, extracted with ether, and the ether layer was washed with H_2O and dried over Na_2SO_4. Evaporation of the solvent left a residue which was recrystallized from MeOH as yellow needles (VII), mp 132.5°. *Anal.* Calcd. for $C_{27}H_{34}O_5$: C, 73.94; H, 7.82. Found: C, 73.89; H, 7.90. UV λ_{max}^{EtOH} nm: 383. IR ν_{max}^{KBr} cm^{-1}: 1630 (conjugation CO), 1612, 1550 (arom. C=C). NMR ($CDCl_3$): 7.58 (1H, d, J=15.0, C_α-H), 8.10 (1H, d, J=15.0, C_β-H), 13.48 (1H, s, OH).

Alkali Cleavage of IV (Formation of I)——A mixture of IV (100 mg) and 5% EtOH–KOH (20 ml) was refluxed for 30 min. After addition of H_2O (200 ml), EtOH was evaporated. Then, the same procedures described for alkali cleavage of VI were carried out till the evaporation of the solvent. The product obtained was recrystallized from benzene to give orange-yellow needles, mp 176°, the melting point of which was not depressed on admixture with I, in addition, its TLC, UV and NMR spectra were identical to those of I.

Compound (VIII)——VIII was recrystallized from benzene as colorless fine needles, mp 102°, $[\alpha]_D^{25}$ −42.6° (c=5, EtOH), M^+ 408, $FeCl_3$ (+). TLC (*Rf*): 0.31 (solv. 1), 0.43 (solv. 2), 0.28 (solv. 3). *Anal.* Calcd. for $C_{25}H_{28}O_5$: C, 73.51; H 6.91. Found: C, 73.78; H, 6.88. UV λ_{max}^{EtOH} nm (log ε): 285 (4.19), $\lambda_{max}^{EtOH\text{-}NaOH}$ nm (log ε): 359 (partially opened to a chalcone ring). IR ν_{max}^{KBr} cm^{-1}: 3230 (OH), 1660 (conjugated CO), 1604, 1517 (arom. C=C). NMR [$(CD_3)_2CO$]: 1.63, 1.71 (each 6H, each s, $=C(C\underline{H}_3)_2$), 2.52—3.10 (2H, m, C_3-H_2), 3.23—3.45 (4H, m, Ar-$C\underline{H}_2$-CH= ×2), 5.05—5.45 (2H, m, Ar-CH_2-$C\underline{H}$= ×2), 5.65 (1H, q, J=11.3, J=5.3, C_2-H), 6.38 (1H, q, J=9.0, J=2.2, $C_{5'}$-H), 6.43 (1H, d, J=2.2, $C_{3'}$-H), 7.27 (1H, d, J=9.0, $C_{6'}$-H), 7.47 (1H, s, C_5-H), 7.90—8.60 (3H, br, OH×3, shifted to 7.80—8.40 at 48°).

Methylation of VIII (Formation of IX and X)——A mixture of VII (100 mg), Me_2SO_4 (700 mg), anhyd. K_2CO_3 (2 g), and acetone (30 ml) was refluxed for 2 hr, and the process described for methylation of I was carried out till the chromatography, giving IX and X.

Compound IX showed one spot on TLC. M^+ 450. UV λ_{max}^{EtOH} nm: 269, 328. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1692 (conjugated CO), 1594, 1546 (sh) (arom. C=C). NMR ($CDCl_3$): 3.73, 3.76, 3.78 (each 3H, each s, $-OCH_3$).

Compound X was recrystallized from EtOH as yellow needles, mp 55°, M^+ 450. *Anal.* Calcd. for C_{28}-$H_{34}O_5$: C, 74.64; H, 7.61. Found: C, 74.80; H, 7.66. UV λ_{max}^{EtOH} nm: 383. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1632 (conjugated CO), 1605, 1549 (arom. C=C). NMR [$(CD_3)_2CO$]: 3.76, 3.84, 3.95 (each 3H, each s, $-OCH_3$), 7.77 (1H, d, J=15.0, C_α-H), 8.08 (1H, d, J=15.0, C_β-H), 13.56 (1H, s, OH).

Isoprenylation of Resacetophenone (Formation of XI, XII, and XIII)——3,3-Dimethylallyl bromide (40.7g) was added dropwise, under agitation at room temp., into resacetophenone (XIX) (41.5 g) in 6.7% KOH solution (163 ml) and the mixture was agitated for 3 hr. After addition of H_2O (500 ml), the solution was acidified to pH 2 with dil. HCl and extracted with ether. The ether layer was washed with H_2O, dried over Na_2SO_4, the solvent was evaporated, and the residue was chromatographed on silica gel using benzene to elute XIII, XI, and XII in that order.

Compound XI was recrystallized from benzene to give colorless needles, mp 162°. *Anal.* Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.98; H, 7.25. IR ν_{max}^{KBr} cm^{-1}: 3150 (OH), 1622 (conjugated CO). NMR ($CDCl_3$): 1.73, 1.80 (each 3H, each s, $=C(CH_3)_2$), 2.53 (3H, s, $-COCH_3$), 3.42 (2H, d, J=7.5, Ar-$C\underline{H}_2$-CH=), 5.26 (1H, t, J=7.5, Ar-CH_2-$C\underline{H}$=C), 6.13 (1H, s, C_4-OH), 6.37 (1H, d, J=9.0, C_5-H), 7.50 (1H, d, J=9.0, C_6-H), 13.02 (1H, s, C_2-OH).

Compound XII was recrystallized from benzene to give colorless needles, mp 146°. *Anal.* Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.90; H, 7.30. IR ν_{max}^{KBr} cm^{-1}: 3210 (OH), 1628 (conjugated CO), NMR [$(CD_3)_2CO$]: 1.72 (6H, s, $=C(CH_3)_2$), 2.51 (3H, s, Ar-$COCH_3$), 3.23 (2H d, J=7.5, Ar-$C\underline{H}_2$-CH=), 5.28 (1H, t, J=7.5, Ar-CH_2-$C\underline{H}$=), 6.31 (1H, s, C_3-H), 7.52 (1H, s, C_6-H), 9.21 (1H, s, C_4-OH), 12.54 (1H, s, C_2-OH).

Compound XIII was recrystallized from MeOH to give colorless needles, mp 117°. *Anal.* Calcd. for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 75.11; H 8.31. IR ν_{max}^{KBr} cm^{-1}: 3170 (OH), 1633 (conjugated CO). NMR [$(CD_3)_2CO$]: 1.60—1.80 (12H, m, $=C(CH_3)_2$ ×2), 2.49 (3H, s, Ar-$COCH_3$), 3.21—3.45 (4H, m, Ar-$C\underline{H}_2$-CH= ×2), 5.05—5.40 (2H, m, Ar-CH_2-$C\underline{H}$= ×2), 7.42 (1H, s, C_6-H), 7.69 (1H, br, C_4-OH), 13.91 (1H, s, C_2-OH).

Catalytic Hydrogenation of XI (Formation of XIV)——Compound (XI) (1 g) dissolved in EtOH (50 ml) was hydrogenated over PtO_2 (200 mg) as a catalyst. One mol of H_2 was absorbed during 3 hr. After removal of the catalyst, the solvent was evaporated *in vacuo* and the residue was recrystallized from MeOH as colorless needles (XIV), mp 115°. *Anal.* Calcd. for $C_{13}H_{18}O_3$: C, 70.24: H, 8.16. Found: C, 70.16; H, 8.15. IR ν_{max}^{KBr} cm^{-1}: 3190 (OH), 1620 (conjugated CO). NMR ($CDCl_3$): 0.96 (6H, d, J=5.3, $-CH(C\underline{H}_3)_2$), 1.20—1.80 (3H, br, m, Ar-CH_2-$C\underline{H}_2$-$C\underline{H}$), 2.68 (2H, t, J=6.8, Ar-CH_2-).

Isoprenylation of XIV (Formation of XV)——3,3-Dimethylallyl bromide (0.4 g) was added dropwise, under agitation at room temp., into a solution of XIV (500 mg) dissolved in 6.7% KOH solution (2 ml), and the mixture was agitated for 3 hr. The same process as the isoprenylation of resacetophenone was carried out till the evaporation of the solvent. The compound XV thus obtained was submitted to chromatography on silica gel using benzene as an eluent, and recrystallized from MeOH to give colorless needles, mp 113.5°. *Anal.* Calcd. for $C_{18}H_{26}O_3$: C, 74.44; H, 9.03. Found: C, 74.05; H, 8.83. IR ν_{max}^{KBr} cm^{-1}: 3320 (OH), 1632 (conjugated CO). NMR (CCl_4): 1.78 (6H, s, $=C(CH_3)_2$), 3.20 (2H, d, $J=7.5$, Ar-CH_2-), 5.20 (1H, t, $J=7.5$, Ar-CH_2-C<u>H</u>=).

Conversion of XV to XVI——A mixture of XV (100 mg), MeOH (16 ml), and conc. HCl (2.2 ml) was refluxed for 2 hr. H_2O (200 ml) was added, and MeOH was evaporated *in vacuo*. The residue was extracted with ether, the ether layer was washed with H_2O, and dried over Na_2SO_4. Evaporation of the solvent left a product which was recrystallized from MeOH as colorless needles (XVI), mp 102°. *Anal.* Calcd. for $C_{18}H_{26}O_3$: C, 74.44; H, 9.03. Found: C, 74.44; H, 8.79. IR ν_{max}^{KBr} cm^{-1}: 1626 (conjugated CO). NMR (CCl_4): 0.92 (6H, d, $J=5.3$, $-CH(C\underline{H}_3)_2$), 1.33 (6H, s, $\overline{}\!\!>C(CH_3)_2$), 1.20—1.90 (5H, m, Ar-$CH_2$-C<u>H</u>$_2$-C<u>H</u> and $^{-CH_2}_{-O}\!\!>$), 2.40—2.85 (4H, m, Ar-CH_2- $\times 2$).

Methylation of XIII (Formation of XVIII)——A mixture of XIII (200 mg), Me_2SO_4 (200 mg), anhyd. K_2CO_3 (600 mg), and acetone (20 ml) was refluxed for 2 hr, and the process as for methylation of I was carried out till the chromatography step to give one spot on TLC (XVIII). NMR (CCl_4): 1.60—1.75 (12H, m, $=C(CH_3)_2$ $\times 2$), 2.46 (3H, s, Ar-$COCH_3$), 3.05—3.35 (4H, m, Ar-C<u>H</u>$_2$-CH= $\times 2$), 3.66 (3H, s, -OCH_3), 4.95—5.30 (2H, br, m, Ar-CH_2-C<u>H</u>= $\times 2$), 7.20 (1H, s, C_6-H), 12.39 (1H, s, C_2-OH).

Condensation of XVI and XVII (Formation of VII)——To a solution of XVI (80 mg) and XVII (45 mg) dissolved in EtOH (1 ml), 40% KOH solution (2 g) was added, and the mixture was agitated for 3 hr at room temp. After the addition of H_2O (100 ml), the solution was acidified to pH 2 with dil. HCl and extracted with ether. The ether layer was washed with H_2O and dried over Na_2SO_4. Evaporation of the solvent left a residue which was recrystallized from MeOH to form yellow needles, mp 132.5°. The melting point of this compound was not depressed on admixture with VII, and TLC, UV, and NMR features of this compound were identical with those of VII.

Catalytic Hydrogenation of VII (Formation of III)——VIII (50 mg) dissolved in EtOH (10 ml) was hydrogenated over PtO_2 (20 mg) as a catalyst. One mole of H_2 was absorbed during 30 min and, after removal of the catalyst, the solvent was evaporated *in vacuo*. The residue was chromatographed on silica gel using benzene as a solvent to give a final product, which showed one spot on TLC, and was identified with III by TLC, and UV, IR, and NMR spectral comparison.

Condensation of XVIII and XVII (Formation of X)——To a solution of XVIII (150 mg) and XVII (85 mg) dissolved in EtOH (1.5 ml), 40% KOH solution (4 g) was added and the mixture was agitated for 3 hr at room temperature. The same process as for the condensation of XVI and XVII was then carried out till the evaporation of the solvent. The residue obtained was recrystallized from EtOH–H_2O mixture as yellow needles, mp 55°, M^+ 450. This compound was identified with X by TLC, and UV, IR, and NMR spectra.

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