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A New 3-Arylcoumarin from Licorice Root[1]

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The structure of a new 3-arylcoumarin, glycyrin (I), isolated from the root of *Glycyrrhiza* spp. (Seihoku Kanzo) (Leguminosae) has been determined as 2′,4′-dihydroxy-5,7-dimethoxy-6-γ,γ-dimethylallyl-3-arylcoumarin on the basis of spectroscopic and chemical studies.

Keywords——licorice root; *Glycyrrhiza* spp.; glycyrin; 3-arylcoumarin; reductive cleavage; synthesis; lactone; 2-arylcoumarone; PMR; DDQ

Previously we reported the structure of a new flavonol, licoflavonol, isolated from a kind of Chinese licorice roots (*Glycyrrhiza* spp., Leguminosae), which is called Sipei licorice ("Seihoku Kanzo" in Japanese).[1] Further investigation on the same drug material afforded a new isoflavonoid compound, named glycyrin, with which the present paper is mainly concerned.

Glycyrin (I), $C_{22}H_{22}O_6$, yellow needles, mp 209—211°, gave a greenish yellow fluorescence under ultraviolet light. The proton magnetic resonance (PMR) spectrum showed the presence of two methoxyls, two hydroxyls, and one γ,γ-dimethylallyl group in addition to five aromatic protons. The infrared (IR) spectrum showed a band at 1665 cm^{-1} in the carbonyl region, and the ultraviolet (UV) spectrum exhibited an absorption maximum at 356 nm. Although these spectral data implied a structure of flavonol or flavone, it was incompatible with the negative Shinoda test (Mg–HCl). Methylation of I with diazomethane furnished glycyrin permethyl ether (III), $C_{24}H_{26}O_6$, mp 78—80°, which exhibited an intense blue fluorescence, characteristic of coumarin derivatives. Its carbonyl absorption in IR shifted to 1730 cm^{-1}, a reasonable value for a coumarin derivative. Reductive cleavage of III with AlH_3 afforded a diol (XI), $C_{24}H_{30}O_6$, mp 109—111°, whose PMR spectrum indicated the presence of allylic methylene (δ 4.31) and phenolic hydroxyl (δ 8.16), indicating that the diol was derived by a reductive cleavage of a lactone ring. Coumarins, coumestans, 3-aryl- and 4-arylcoumarins have already been known in nature of which only 3-arylcoumarin is adopted to glycyrin on the basis of its UV, PMR spectra and molecular weight. Especially the presence of an olefinic methine appeared as a singlet in the PMR of the diol excluded the possibility of 4-arylcoumarin, whose diol derived by the same reaction must show a signal coupled with the adjacent methylene protons.

The 4-proton of 3-arylcoumarins lacking O-functional group at 5- position appears at δ 7.5—7.6 region.[3,4] As for glycyrin, however, it was observed at δ 7.98. This indicates the presence of 5-O-functional group, since the lone pair of the oxygen atom deshields 4-proton magnetically to shift it lower. This effect has been observed in many compounds and characterized as "*peri* effect," which is diminished by acetylation of *peri*-hydroxyl,

1) Part XLII in the series of *Chemical Studies on the Oriental Plant Drugs*. Part XLI: T. Saitoh, T. Kinoshita and S. Shibata, *Chem. Pharm. Bull.* (Tokyo), **24**, 1242 (1976).

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3) M.A. Ferreira, M. Moir, and R.H. Thomson, *J. Chem. Soc. Perkin I*, **1974**, 2429.

4) D.M.X. Donnelly and P.J. Kavanagh, *Phytochemistry*, **13**, 2587 (1974).

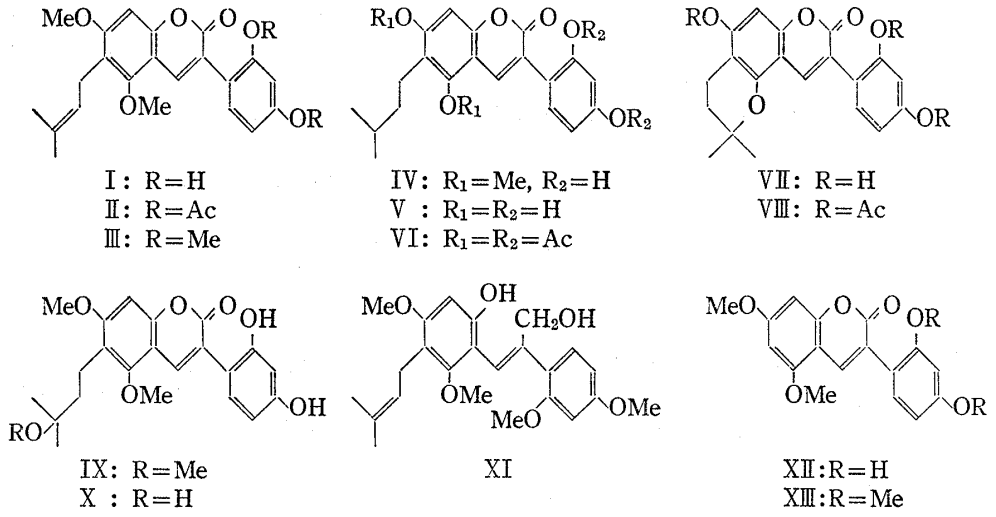

Chart 1

due to the electron induction of acetyl group.[5]

Although the 4-proton of glycyrin diacetate (II) appeared at δ 7.85 without any significant shift, that of demethyldihydroglycyrin tetraacetate (VI), prepared from dihydroglycyrin (IV) by demethylation followed by acetylation, shifted remarkably to higher field (δ 7.48). This result supported that glycyrin (I) has a methoxyl at 5-position. Reflux of glycyrin (I) with hydroiodic acid yielded a chroman, demethylisoglycyrin (VII), whose acetyl derivative (VIII) exhibited no shift of 4-proton (δ 8.04), indicating that 6-position is substituted with a γ,γ-dimethylallyl group cyclized with 5-methoxyl after demethylation to form the chroman (VII). From the biogenetical point of view, O-functional group must be placed at 7-position. By reflux in methanolic hydrochloric acid glycyrin afforded the adducts (IX and X) of methanol and water respectively, to γ,γ-dimethylallyl group. This fact supported the presence of a methoxyl at 7-position.

On the basis of the above discussion glycyrin (I) possesses two methoxyls, two hydroxyls and one γ,γ-dimethylallyl group, and the two methoxyls have been assigned to 5- and 7-positions, the dimethylallyl to 6-position. Therefore, the remaining two hydroxyls must be located at B ring, probably at 2'- and 4'-positions from the biogenetical viewpoint.

These results led a structure (I) for glycyrin whose IR spectrum, however, showed a carbonyl absorption at 1665 cm^{-1}, an unusually lower wave number for a 3-arylcoumarin. In order to clarify this point, a model compound, 2',4'- dihydroxy-5,7-dimethoxyl-3-arylcoumarin (XII), was synthesized. Its UV spectrum was superimposable with that of glycyrin, and the IR spectrum showed a band at 1668 cm^{-1}, very similar value to that of glycyrin. It has now been confirmed that glycyrin is a 3-arylcoumarin having two methoxyls at 5- and 7-positions and two hydroxyls at 2'- and 4'-positions.

Recently, a new 3-arylcoumarin (XX) was reported[4] to show an IR band at 1680 cm^{-1}. As all these compounds possess a free hydroxyl at 2'-position, abnormal bathochromic shift of the IR absorption of a carbonyl would be caused by a hydrogen bonding between 2'-hydroxyl and 2-carbonyl group.

As mentioned above, the location of γ,γ-dimethylallyl group was assigned to the 6-position by the occurrence of demethylisoglycyrin (VII) on demethylation of glycyrin with hydroiodic acid. But the possibility of 8-position for γ,γ-dimethylallyl group was not excluded, since reflux under strong acid condition might cause Wessely-Moser rearrangement[6] to produce

5) G. Dudek, *Spectrochimica Acta*, **19**, 691 (1963), A. Arone, G. Gardillo, L. Merlini, and R. Mondelli, *Tetrahedron Lett.*, **1967**, 4201.
6) W. Baker, I. Dunstan, J.B. Harborne, W.D. Ollis, and R. Winter, *Chem. Ind.*, **1953**, 277.

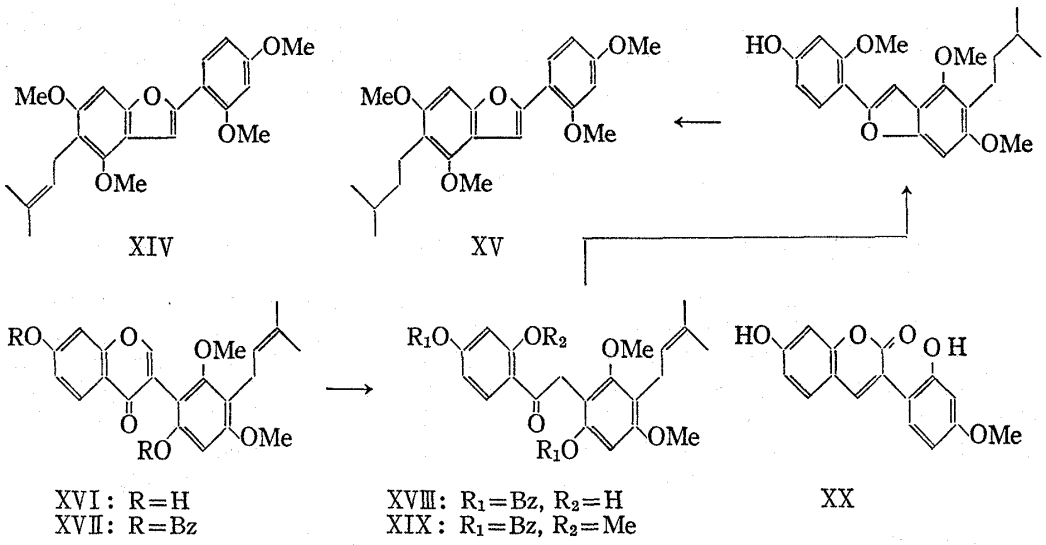

Chart 2

VII from the 8-substituted compound. If glycyrin were 8-substituted, diol (XI) prepared in the manner as has already been stated would yield a chroman under acidic condition or a chromene by dehydrogenated cyclization with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), since a free hydroxyl exists at the *ortho* position of γ,γ-dimethylallyl group. However, a chroman was not obtained because the diol was very sensitive even to a weak acid. Refluxing a mixture of the diol and DDQ in dry benzene did not produce any trace of chromene, but a 2-arylcoumarone (XIV) in a good yield. Therefore, the location of the dimethylallyl group at 8-position has been ruled out.

The structure of the 2-arylcoumarone (XIV) was established under the chemical correlation with licoricone (XVI) (Chart 2). The dihydro derivative (XV) of the 2-arylcoumarone (XIV) was synthesized *via* a deoxybenzoin (XIX) derived from licoricone dibenzyl ether (XVII) by the process already reported.[7] Since the structure of licoricone (XVI) has been established by X-ray analysis,[8] the structure of glycyrin (I) has unequivocally been proved.

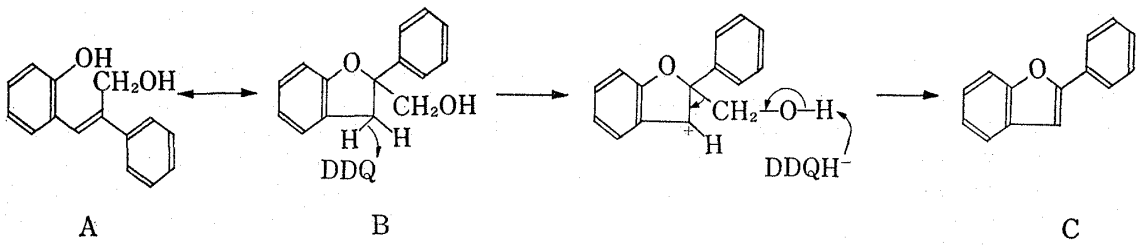

Chart 3. Possible Mechanism of Producing 2-Arylcoumarone (C) from Diol (A)

The formation of 2-arylcoumarone (XIV) from diol (XI) would be derived by hydride ion transfer from benzyl position of coumaran (B) to DDQ in the equilibrium between diol (A) and coumaran (B) resulting in the elimination of carbinol group to yield 2-arylcoumarone (C) (Chart 3). This reaction can be used as an efficient method for the synthesis of 2-arylcoumarones.

For many years the 3-arylcoumarin was represented in nature by only pachyrrhizin.[9]

7) W.B. Whalley and G. Lloyd, *J. Chem. Soc.*, **1956**, 3213.
8) M. Kaneda, T. Saitoh, Y. Iitaka, and S. Shibata, *Chem. Pharm. Bull.* (Tokyo), **21**, 1338 (1973).
9) E. Simonitsch, H. Frei, and H. Schmid, *Monatsh. Chem.*, **88**, 541 (1957).

Neofolin[10] and two other compounds[4] have since been reported as the members of this group. Glycyrin is the fifth naturally occurring 3-arylcoumarin. It would be noted that all these 3-arylcoumarins have so far been isolated from the Leguminoseous plants.

Experimental

The isolation and purification of glycyrin from licorice root were described in detail previously.[1] Glycyrin was tentatively designated "C-12" therein.

Glycyrin (I) was recrystallized from C_6H_6–$(CH_3)_2CO$ to form yellow needles, mp 209—211°. It gave no color reaction with Mg–HCl, and positive Gibbs test (purple). λ_{max}^{EtOH} nm (log ε): 250 (4.06), 257 (4.03), 356 (4.28). ν_{max}^{KBr} cm^{-1}: 3400, 2940, 1665, 1600, 1455. PMR (δ, d_6-$(CH_3)_2CO$, 100 MHz): 1.65 (3H, s, CH_3 of γ,γ-dimethylallyl), 1.77 (3H, s, CH_3 of γ,γ-dimethylallyl), 3.36 (2H, d, 7 Hz, $-CH_2$ of γ,γ-dimethylallyl), 3.87 and 3.95 (3H each, s, 5- and 7-OMe), 5.16 (1H, t, 7 Hz, –CH= of γ,γ-dimethylallyl), 6.4 (2H, 3′- and 5′-H), 6.76 (1H, s, 8-H), 7.21 (1H, d, 8 Hz, 6′-H), 7.96 (1H, s, 4-H), 8.31 and 8.39 (1H each, s, 2′- and 4′-OH, disappeared with the addition of D_2O). *m/e*; 382 (M^+). *Anal.* Calcd. for $C_{22}H_{22}O_6$: C, 69.10; H, 5.80. Found: C, 69.37; H, 5.90.

Glycyrin Diacetate (II)——A mixture of glycyrin (53 mg) dissolved in dry pyridine (1 ml) and acetic anhydride (1 ml) was allowed to stand overnight at room temperature, and then poured into ice-water (30 ml). White precipitates were collected and recrystallized from EtOH–H_2O to give a diacetate as colorless needles (50 mg), mp 140—142°. λ_{max}^{EtOH} nm (log ε): 246 (4.16, inf.), 255 (4.04, inf.), 345 (4.43). $\nu_{max}^{CHCl_3}$ cm^{-1}: 2900, 1768, 1725, 1614, 1376. PMR (δ, $CDCl_3$, 100 MHz): 1.68 (3H, s, CH_3 of γ,γ-dimethylallyl), 1.78 (3H, s, CH_3 of γ,γ-dimethylallyl), 2.17 and 2.31 (3H each, s, 2′- and 4′-OAc), 3.36 (2H, d, 7 Hz, $-CH_2$ of γ,γ-dimethylallyl), 3.82 and 3.90 (3H each, s, 5- and 7-OMe), 5.12 (1H, t, 7 Hz, –CH= of γ,γ-dimethylallyl), 6.63 (1H, s, 8-H), 7.0 (2H, 3′- and 5′-H), 7.43 (1H, d, 8 Hz, 6′-H), 7.85 (1H, s, 4-H). *m/e*: 466 (M^+). *Anal.* Calcd. for $C_{26}H_{26}O_8$: C, 66.94; H, 5.62. Found: C, 66.66; H, 5.61.

Glycyrin Permethyl Ether (III)——To a methanolic solution of glycyrin (50 mg), an excess amount of etherial diazomethane was added at 0° and allowed to stand overnight. The solvent was removed under reduced pressure and the residue was recrystallized from EtOH–H_2O to give colorless needles, mp 78—80° (43 mg). λ_{max}^{EtOH} nm (log ε): 247 (4.08, sh.), 256 (4.02, inf.), 290 (3.75, inf.), 347.5 (4.29). ν_{max}^{KBr} cm^{-1}: 2940, 1730, 1612, 1580, 1510, 1462, 1421. PMR (δ, $CDCl_3$, 100 MHz): 1.68 (3H, s, CH_3 of γ,γ-dimethylallyl), 1.78 (3H, s, CH_3 of γ,γ-dimethylallyl), 3.36 (2H, d, 7 Hz, $-CH_2$ of γ,γ-dimethylallyl), 3.78, 3.80, 3.82 and 3.86 (3H, each, s, 2′-, 4′-, 5- and 7-OMe), 5.12 (1H, t, 7 Hz, –CH= of γ,γ-dimethylallyl), 6.4—6.6 (3H, m, 3′-, 5′- and 8-H), 7.25 (1H, d, 8 Hz, 6′-H), 7.82 (1H, s, 4-H). *m/e*: 410 (M^+). *Anal.* Calcd. for $C_{24}H_{26}O_6$: C, 70.23; H, 6.39. Found: C, 70.08; H, 6.39.

Reductive Cleavage of Glycyrin Permethyl Ether (III) with AlH_3 (Formation of XI)——A solution of III (60 mg) in dry ether (12 ml) was added under stirring for 10 min to an ice-cold ether solution (15 ml) of AlH_3, prepared from $AlCl_3$ (133 mg) and $LiAlH_4$ (114 mg). The mixture was kept at 0° for 50 min, and then the excess AlH_3 was decomposed by portional addition of MeOH (2 ml), and then the solution was acidified with 2 N HCl (15 ml). The reaction mixture was extracted three times with ether. The combined extracts were washed with 2 N $NaHCO_3$, and dried over anhyd. Na_2SO_4. After the ether was removed, the residue was recrystallized from EtOH–H_2O to form colorless needles, mp 124—125° (XI) (52 mg). λ_{max}^{EtOH} nm (log ε): 267 (3.81), 286 (3.76). ν_{max}^{KBr} cm^{-1}: 3400, 2930, 1607, 1587, 1505, 1467, 1450, 1417. PMR (δ, d_6-$(CH_3)_2CO$, 100 MHz): 1.65 and 1.76 (3H each, s, CH_3 of γ,γ-dimethylallyl), 3.25 (2H, d, 7 Hz, $-CH_2$ of γ,γ-dimethylallyl), 3.67, 3.79, 3.81 and 3.85 (3H, each, s, OMe), 4.31 (2H, d, 6 Hz), 5.15 (1H, t, 7 Hz, –CH= of γ,γ-dimethylallyl), 6.34 (2H), 6.4—6.6 (2H), 7.29 (1H, d, 8 Hz, 6′-H), 8.16 (1H, s, OH, exchangeable with D_2O). *m/e*: 414 (M^+). *Anal.* Calcd. for $C_{24}H_{30}O_6$: C, 69.54; H, 7.30. Found: C, 69.63; H, 7.28.

Dihydroglycyrin (IV)——A mixture of glycyrin (50 mg), EtOH (25 ml) and PtO_2 (40 mg) was shaken in an atmosphere of H_2 for 2 hr. After filtration, the solvent was evaporated and crystallization of the residue from C_6H_6–$(CH_3)_2CO$ gave dihydroglycyrin (43 mg), mp 186—188°. PMR (δ, d_6-$(CH_3)_2CO$, 100 MHz): 0.93 (6H, d, 7 Hz, CH_3 of 3-methylbutyl), 1.3—1.6 (3H, 2- and 3-H of 3-methylbutyl), 2.6—2.8 (2H, m, 1-H of 3-methylbutyl), 3.86 and 3.94 (3H each, s, 5- and 7-OMe), 6.3—6.4 (2H, 3′- and 5′-H), 6.71 (1H, s, 8-H), 7.23 (1H, d, 8 Hz, 6′-H), 7.92 (1H, s, 4-H), 8.25 (2H, broad s, 2′- and 4′-OH, disappeared by the addition of D_2O). *m/e*: 384 (M^+).

Demethyldihydroglycyrin Tetraacetate (VI)——A mixture of dihydroglycyrin (40 mg) and HI (4 ml, 57%) was refluxed for 30 min, and then poured into 2 N $Na_2S_2O_7$ (30 ml). The precipitates were collected, dried *in vacuo* and acetylated in the usual manner. Crystallization of the crude acetate from EtOH–H_2O afforded demethyldihydroglycyrin tetraacetate (22 mg) as colorless prisms, mp 165—166°. λ_{max}^{EtOH} nm (log ε):

10) c.v.d. M. Brink, W. Nel, G.J.H. Rall, J.C. Weitz, and K.G.R. Pachler, *J. South African Chem. Inst.*, **19**, 24 (1966).

236 (4.12, inf.), 313 (4.25), 325 (4.24, sh.). $\nu_{max}^{CHCl_3}$ cm^{-1}: 2960, 1774, 1740, 1620, 1582, 1503, 1470, 1440, 1374. PMR (δ, $CDCl_3$' 100 MHz): 0.95 (6H, d, 7 Hz, CH_3 of 3-methylbutyl), 1.3—1.4 (2H, m, 2-H_2 of 3-methylbutyl), 1.60 (1H, t, 7 Hz, 3-H of 3-methylbutyl), 2.18, 2.30, 2.36 and 2.42 (3H, each, s, OAc), 2.5 (2H, m, 1-H_2 of 3-methylbutyl), 7.0—7.4 (4H), 7.48 (1H, s, 4-H). *m/e*: 524 (M^+). *Anal.* Calcd. for $C_{28}H_{28}O_{10}$: C, 64.11; H, 5.38. Found: C, 63.81; H, 5.32.

Demethylisoglycyrin Triacetate (VIII)——Glycyrin (40 mg) was demethylated, followed by acetylation with dry pyridine and acetic anhydride in the manner described above. The crude acetate was crystallized from EtOH–H_2O to give demethylisoglycyrin triacetate (26 mg) as colorless prisms, mp 215—217°. λ_{max}^{EtOH} nm (log ε): 255 (4.04), 328 (4.31). $\nu_{max}^{CHCl_3}$ cm^{-1}: 2980, 1768, 1732, 1624, 1613, 1587, 1500, 1374. PMR (δ, $CDCl_3$, 100 MHz): 1.36 (6H, s, CH_3 of dimethylchroman), 1.82 (2H, t, 7 Hz, 2-H of dimethylchroman), 2.16, 2.29 and 2.33 (3H each, s, 7-, 2'- and 4'-OAc), 2.57 (2H, t, 7 Hz, 1-H of dimethylchroman), 6.66 (1H, s, 8-H), 7.1 (2H, 3'- and 5'-H), 7.49 (1H, d, 8 Hz, 6'-H), 8.0 (1H, s, 4-H). *m/e*: 480 (M^+). *Anal.* Calcd. for $C_{26}H_{24}O_9$: C, 64.99; H, 5.04. Found: C, 65.08; H, 5.10.

Methoxyglycyrin (IX) and Hydroxyglycyrin (X)——A mixture of glycyrin (50 mg), MeOH (6 ml) and conc. HCl (2 ml) was refluxed for 4 hr, and the solvent was removed under reduced pressure. The products were separated by preparative thin-layer chromatography (TLC) on silica gel to afford hydroxyglycyrin (23 mg) and methoxyglycyrin (19.5 mg).

Methoxyglycyrin (IX) was recrystallised from C_6H_6–$(C_2H_5)_2O$ to give yellow needles of mp 140—142°. ν_{max}^{KBr} cm^{-1}: 3280, 2980, 1680, 1606, 1462, 1375. PMR (δ, d_6-$(CH_3)_2CO$, 100 MHz): 1.20 (6H, s, CH_3 of 3-methoxy-3-methylbutyl), 1.68 (2H, m, 2-H of 3-methoxy-3-methylbutyl), 2.68 (2H, m, 1-H of 3-methoxy-3-methylbutyl), 3.21 (3H, s, OMe of 3-methoxy-3-methylbutyl), 3.91 and 3.96 (3H each, s, 5- and 7-OMe), 6.4—6.5 (2H, 3'- and 5'-H), 6.77 (1H, s, 8-H), 7.25 (1H, d, 8 Hz, 6'-H), 8.00 (1H, s, 4-H), 8.38 and 8.46 (1H each, s, 2'- and 4'-OH, disappeared by the addition of D_2O). *m/e*: 414 (M^+, base peak), 382 (M-32, 68%).

Hydroxyglycyrin (X) was recrystallized from ether to give yellow granules, mp 180—182°. ν_{max}^{KBr} cm^{-1}: 3380, 2960, 1670, 1604, 1510, 1454, 1415, 1377. PMR (δ, d_6-$(CH_3)_2CO$, 100 MHz): 1.27 (6H, s, CH_3 of 3-hydroxy-3-methylbutyl), 1.70 (2H, m, 2-H of 3-hydroxy-3-methylbutyl), 2.76 (2H, m, 1-H of 3-hydroxy-3-methylbutyl), 3.34 (1H, s, OH of 3-hydroxy-3-methylbutyl, exchangeable with D_2O), 3.92 and 3.99 (3H each, s, 5- and 7-OMe), 6.4—6.5 (2H, 3'- and 5'-H), 6.79 (1H, s, 8-H), 7.25 (1H, d, 8 Hz, 6'-H), 8.00 (1H, s, 4-H), 8.37 and 8.42 (1H each, s, 2'- and 4'-OH, disappeared by the addition of D_2O). *m/e*: 400 (M^+, base peak), 382 (M-18, 33%).

Synthesis of 2',4'-Dihydroxy-5,7-dimethoxy-3-arylcoumarin (XII)——A mixture of 2,4-dihydroxyacetophenone (7.6 g), benzyl bromide (18 g), anhyd. K_2CO_3 (15 g) and N,N-dimethylformamide (50 ml) was heated at 70° for 10 hr, and then the solvent was removed under reduced pressure. The residue gave 2,4-dibenzyloxyacetophenone (12.5 g), mp 74—76° on crystallization from EtOH. A mixture of 2,4-dibenzyloxyacetophenone (5.1 g), morpholine (5.9 g) and sulphur (1.62 g) was refluxed for 8 hr. The product was taken up in $CHCl_3$ and washed with 2 N HCl, then with H_2O. The chloroform layer was evaporated to dryness, and heated under reflux in EtOH (100 ml) and H_2O (30 ml) containing KOH (17 g) for 13 hr. The solution was cooled, filtered and concentrated. The reaction mixture was acidified with 2 N HCl and extracted with ether. The ether solution was washed with 2 N $NaHCO_3$, then with H_2O, dried over Na_2SO_4 and evaporated to give 2,4-dibenzyloxyphenylacetic acid (4.1 g), mp 132—134° on crystallization from EtOH. ν_{max}^{KBr} cm^{-1}: 3300, 3000, 1699, 1615, 1592, 1510. PMR (δ, $CDCl_3$, 100 MHz): 3.60 (2H, s, $ArCH_2COOH$), 4.97 (4H, s, $ArCH_2O$–), 6.4—6.6 (2H, 3- and 5-H), 7.04 (1H, d, 8 Hz, 6-H), 7.26 and 7.32 (5H each, s, aromatic protons of benzyloxy).

A mixture of 2,4-dibenzyloxyphenylacetic acid (3.5 g), 2,4,6-trihydroxybenzaldehyde (1.5 g), anhyd. KOAc (2 g) and acetic anhydride (4 ml) was refluxed for 6 hr. After cooling, the reaction mixture was diluted with H_2O, and stirred overnight. The precipitate was collected and crystallized from EtOH to give 5,7-diacetoxy-2',4'-dibenzyloxy-3-arylcoumarin (1.7 g), mp 203—205°. ν_{max}^{KBr} cm^{-1}: 2900, 1780, 1734, 1619, 1606, 1575, 1504. *m/e*: 550 (M^+). *Anal.* Calcd. for $C_{33}H_{26}O_8$: C, 71.99; H, 4.76. Found: C, 71.49; H, 4.77.

Deacetylation of 5,7-diacetoxy-2',4'-dibenzyloxy-3-arylcoumarin (1.0 g) in dioxane (40 ml) and conc. NH_4OH (10 ml), followed by methylation with CH_2N_2 afforded the crude solid of 2',4'-dibenzyloxy-5,7-dimethoxy-3-arylcoumarin. Without purification, the crude material was warmed at 60 under stirring in a mixture of conc. HCl (6 ml) and AcOH (9 ml). The reaction mixture was diluted with ether. After removal of the solvent, the residue was subjected to column chromatography on silica gel to give 2',4'-dihydroxy-5,7-dimethoxy-3-arylcoumarin (0.3 g) (XII) as yellow needles, mp 261° (dec.), on crystallization from C_6H_6–$(CH_3)_2CO$. λ_{max}^{EtOH} nm (log ε): 252 (4.10, inf.), 259 (4.13), 353 (4.28). ν_{max}^{KBr} cm^{-1}: 3380, 2940, 1668, 1603, 1512, 1460, 1381. PMR (δ, d_6-$(CH_3)_2CO$, 100 MHz): 3.85 and 3.89 (3H each, s, 5- and 7-OMe), 6.24 (1H, d.d, 8 and 2 Hz, 5'-H), 6.34 (1H, d, 2 Hz, 3'-H), 6.47 (1H, d, 2 Hz, 6-H), 6.57 (1H, d, 2 Hz, 8-H), 7.05 (1H, d, 8 Hz, 6'-H), 7.85 (1H, s, 4-H), 9.21 (2H, broad s, 2'- and 4'-OH, exchangeable with D_2O). *m/e*: 314 (M^+). *Anal.* Calcd. for $C_{17}H_{14}O_6$: C, 64.96; H, 4.49. Found: C, 65.50; H, 4.51.

2',4',5,7-Tetramethoxy-3-arylcoumarin (XIII)——2',4'-Dihydroxy-5,7-dimethoxy-3-arylcoumarin (50 mg) was methylated with CH_2N_2 in the usual manner. After removal of solvent, the residue was recrystallized from EtOH–H_2O to afford 2',4',5,7-tetramethoxy-3-arylcoumarin (47 mg), mp 164—165°. ν_{max}^{KBr} cm^{-1}: 2960, 1720, 1624, 1602, 1525, 1438. *m/e*: 342 (M^+). *Anal.* Calcd. for $C_{19}H_{18}O_6$: C, 66.66; H, 5.30. Found:

C, 66.78; H, 5.34.

2-(2′,4′-Dimethoxyphenyl)-4,6-dimethoxy-5-(γ,γ-dimethylallyl)-coumarone (XIV)——The diol (XI) (50 mg) and DDQ (2,3-dichloro-5,6-dicyanobenzoquinone-1,4) (30 mg) were heated under reflux in dry C_6H_6 (30 ml) for 2 hr. The mixture was filtered, and after the removal of the solvent the residue was crystallized from MeOH–H_2O to give 2-(2′,4′-dimethoxyphenyl)-4,6-dimethoxy-5-(γ,γ-dimethylallyl)-coumarone (37 mg) as colorless prisms, mp 114—115°. λ_{max}^{EtOH} nm (log ε): 251 (3.94, inf.), 288 (4.17, sh.), 297 (4.26, inf.), 310 (4.42, inf.), 322 (4.60), 338 (4.54). ν_{max}^{KBr} cm^{-1}: 2900, 1612, 1584, 1505, 1470, 822. PMR (δ, d_6-$(CH_3)_2CO$, 100 MHz): 1.64 and 1.78 (3H each, s, CH_3 of γ,γ-dimethylallyl), 3.38 (2H, d, 7 Hz, $-CH_2$ of γ,γ-dimethylallyl), 3.85, 3.87, 4.00 and 4.02 (3H each, s, 2′,4′,4- and 6-OMe), 5.18 (1H, t, 7 Hz, –CH= of γ,γ-dimethylallyl), 6.6 (2H, 3′- and 5′-H), 6.88 (1H, s, 7-H), 7.29 (1H, s, 3-H), 7.83 (1H, d, 8 Hz, 6′-H). *m/e*: 382 (M^+). *Anal.* Calcd. for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.21; H, 6.87.

2-(2′,4′-Dimethoxyphenyl)-4,6-dimethoxy-5-(3-methylbutyl)-coumarone (XV)——A solution of coumarone (XIV) (20 mg) in EtOH (20 ml) was hydrogenated with Pd–C (10 mg, 10%) for 3 hr. After filtration, the solvent was removed and the residue was crystallized from MeOH–H_2O to give 2-(2′,4′-dimethoxyphenyl)-4,6-dimethoxy-5-(3-methylbutyl)-coumarone (XV) (17 mg) as colorless plates, mp 81—82°. ν_{max}^{KBr} cm^{-1}: 2940, 1617, 1590, 1508, 1471, 1432. PMR (δ, $CDCl_3$′ 100 MHz): 0.94 (6H, d, 7 Hz, CH_3 of 3-methylbutyl), 1.3—1.7 (3H, 2- and 3-H of 3-methylbutyl), 2.62 (2H, m, 1-H of 3-methylbutyl), 3.82, 3.92 and 4.01 (6H, 3H and 3H each, OMe), 6.5 (2H, 3′- and 5′-H), 6.72 (1H, s, 7-H), 7.20 (1H, s, 3-H), 7.80 (1H, d, 8 Hz, 6′-H). *m/e*: 384 (M^+). *Anal.* Calcd. for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.73; H, 7.37.

Synthesis of 2-(2′,4′-Dimethoxyphenyl)-4,6-dimethoxy-5-(3-methylbutyl)-coumarone (XV) from Licoricone (XVI)——A solution of licoricone dibenzyl ether (XVII) (93 mg) in EtOH (20 ml) and H_2O (6 ml) containing KOH (2 g) was refluxed for 15 hr, cooled, acidified with 2 N HCl, and extracted with ether three times. The combined ether layer was washed with 2 N Na_2CO_3, then with H_2O, and the solvent was removed. The residue was crystallized from EtOH–H_2O to give 2′,4-dibenzyloxy-2-hydroxy-4′,6′-dimethoxy-5′-(γ,γ-dimethylallyl)-deoxybenzoin (XVIII) (77 mg) as colorless prisms of mp 93—95°. It exhibited a positive ferric reaction (purple). ν_{max}^{KBr} cm^{-1}: 3400, 2900, 1635, 1604, 1571, 1503, 1456. *Anal.* Calcd. for $C_{35}H_{36}O_6$: C, 76.06; H, 6.57. Found: 76.20; H, 6.69.

Methylation of this deoxybenzoin (50 mg) with Me_2SO_4 and anhyd. K_2CO_3 in $(CH_3)_2CO$ in the usual manner gave 2′,4-dibenzyloxy-2,4′,6′-trimethoxy-5′-(γ,γ-dimethylallyl)-deoxybenzoin (XIX) as colorless oil. It gave negative ferric reaction. PMR (δ, $CDCl_3$′ 60 MHz): 1.67 and 1.75 (3H each, s, CH_3 of γ,γ-dimethylallyl), 3.28 (2H, d, 7 Hz, $-CH_2$ of γ,γ-dimethylallyl), 3.63, 3.72 and 3.77 (3H each, s, OMe), 4.27 (2H, s, ArCO–CH_0–Ar), 4.92 and 5.02 (2H each, s, Ar–CH_2–O), 5.17 (1H, t, 7 Hz, –CH= of γ,γ-dimethylallyl), 6.30 (1H, s, 3′-H), 6.50 (2H, m, 6- and 8-H), 7.15 and 7.30 (5H each, broad s, arom-Hs of benzyl), 7.72 (1H, d, 8 Hz, 5-H).

A mixture of this oily deoxybenzoin, acetic acid (15 ml) and Pd–C (15 mg, 10%) was shaken in the atmosphere of H_2. After removal of the solvent under reduced pressure, the residue was methylated with diazomethane to afford a coumarone (17 mg) as colorless plates of mp 81—82° on crystallization from dil. MeOH. This synthetic coumarone was identified with XV derived from glycyrin (I) by mixed mp and IR spectrum. *Anal.* Calcd. for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.33; H, 7.30.

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