The Components of *Petasites japonicus* Maxim. IV.[1] The Structure of Petasitin

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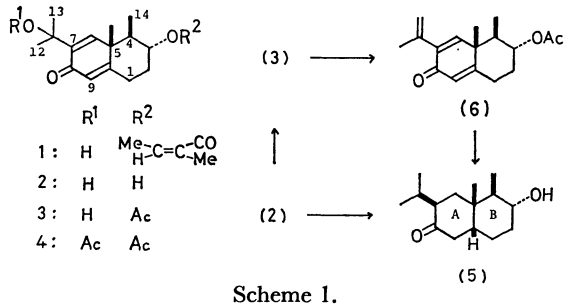
Petasitin, a component isolated from a wild variety of *Petasites japonicus* Maxim., has been shown to be 3α-[(*Z*)-2-methyl-2-butenoyloxy]-11-hydroxyeremophila-6,9-dien-8-one, and has been synthesized from the known isopetasin by photosensitized oxygenation.

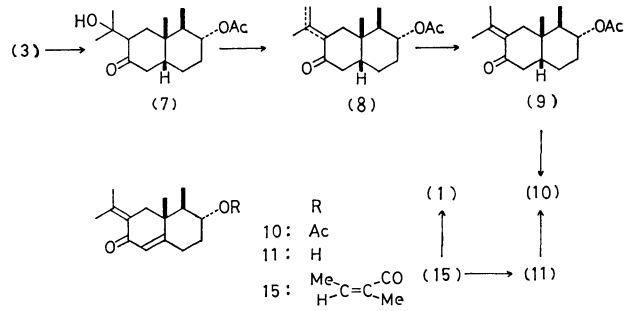
In an earlier communication,[2] we reported the structural proof of petasitin (**1**) isolated from the wild plant of *Petasites japonicus* Maxim. ("Fuki" in Japanese). We wish now to describe its isolation and structural determination, and also the synthesis of **1** from a known isopetasin (**15**).[3]

A methanol extract of the dried flower stalks of the plant was chromatographed repeatedly on alumina and silica gel, and from the polar part a component named petasitin (**1**) was obtained.



Scheme 1.

Petasitin (**1**), $C_{20}H_{28}O_4$ (bp 167.0—170 °C/2×10^{-4} mmHg, $[\alpha]_D$ −26.2°), is a colorless, highly viscous oil. Its IR and UV spectra show the presence of α,β-unsaturated carbonyl systems— a ketone (1665 cm^{-1} and λ_{max} 235 nm (ε, 14200)) and an ester (1710 and 1235 cm^{-1}). The spectral data also indicated that the fourth oxygen atom seemed to be a tertiary alcohol (3460 cm^{-1}) attached to the carbon atom bearing two methyls (δ 1.50, s, 6H). The existence of a (*Z*)-2-methyl-2-butenoate moiety as the ester group in petasitin, **1**, was inferred from the NMR signals, by analogy with those of the constituents[3-5] isolated from the same plant. In fact, the alkaline hydrolysis of **1** afforded (*Z*)-2-methyl-2-butenoic acid (angelic acid), accompanied by a small amount of the isomerization product, that is, the corresponding (*E*)-isomer (tiglic acid) and a diol, named petasitol (**2**), $C_{15}H_{22}O_3$ (mp 110.0—113.0 °C). In the UV spectrum of **2**, the intensity of the maximum at 244 nm (ε, 12700) suggests the presence of a cross-conjugated dienone system, and the IR spectrum exhibits bands at 3340 (hydroxyl), 1655 (α,β-unsaturated ketone), and 1610 cm^{-1} (double bond). In the NMR spectrum, petasitol, **2**, showed the signals due to four methyls, two vinyl protons (δ 6.12, t, J=1.0 Hz, 1H and 6.92, s, 1H), and a proton (δ 3.70, m, $W_{1/2}$=14 Hz) attached to a carbon atom carrying a newly appeared hydroxyl group. The acetylation of **2** with acetic anhydride–pyridine at room temperature gave a monoacetate (**3**) (mp 80.0—82.0 °C), which showed IR bands at 3420 (hydroxyl), 1735, 1240 (acetate), 1660 and 1610 cm^{-1} (α,β-unsaturated ketone), while acetylation with acetic anhydride–sodium acetate under reflux gave a mixture of monoacetate, **3**, and diacetate (**4**). The hydrogenation of **2** with 10% palladium charcoal in ethanol, followed by treatment with a catalytic amount of sodium methoxide in methanol, gave a dehydroxy-tetrahydro compound (**5**), $C_{15}H_{26}O_2$ (mp 103.0—103.5 °C), which was found to be identical with the known tetrahydroisopetasol (**5**)[3] (mp 103.0—104.0 °C), by a mixed-melting-point determination and a comparison of the spectral data. Thus, the one hydroxyl group lost by hydrogenolysis can be placed at an allylic position. This hydroxyl group in petasitol monoacetate, **3**, was readily dehydrated with phosphoryl chloride–pyridine to afford an anhydro derivative (**6**), whose spectra showed the NMR signals due to an *endo*-methylene group bearing a methyl (δ 5.11, d with allylic splittings, J=7.0 Hz, 2H and 1.97, d, J=1.0 Hz, 3H) and IR bands (3080, 920 cm^{-1}) attributable to the *exo*-methylene group. Tetrahydroisopetasol, **5**, was also obtained from the anhydro derivative, **6**, by hydrogenation with 10% palladium charcoal in ethanol, followed by stabilization in a basic medium. Thus, the **1** structure was assumed for petasitin on the basis of the above results.



Scheme 2.

Furthermore, the location of a tertiary hydroxyl group was also confirmed by the following chemical reaction sequence— that is, by the conversion from petasitol monoacetate, **3**, to the known isopetasol acetate (**10**). The hydrogenation of **3** with Adams' catalyst in ethyl ether afforded a tetrahydroacetate (**7**),

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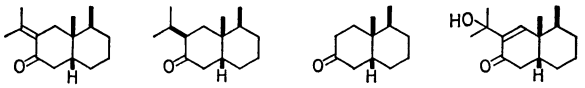
$C_{17}H_{28}O_4$ (mp 92.0—95.0 °C), without the loss of a hydroxyl group. Compound **7** was dehydrated with phosphoryl chloride–pyridine to give a mixture of olefinic isomers (**8**), which were isomerized to an α,β-unsaturated ketone (**9**) by column chromatography over alumina. The dehydrogenation of **9** with DDQ afforded isopetasol acetate (**10**), $C_{17}H_{24}O_3$ (mp 82.0—85.0 °C), which was identified by a mixed-melting-point determination and by a comparison of the spectra.

The steric course of the hydrogenation for the cross-conjugated dienone system in isopetasol (**11**) has already been clarified by the stereochemical correlation between isopetasol, **11**, and fukinone (**12**).[3] Therefore, the hydrogenation of petasitol, **2**, and the monoacetate, **3**, with another type of dienone system also proceeds predominantly to furnish two steroidal A/B *cis*-fused compounds, **5** and **7**. The above results clearly indicate that the stereochemical course of the hydrogenation of the α,β-α',β'-unsaturated dienone system in a neutral medium must be influenced by the presence of the C-7 substituent; this must be compared with the earlier generalization, based on the hydrogenation of Δ^4-3-keto steroid-type compounds,[6] that the product compositions with *cis*- and *trans*-fused A/B rings were approximately equal.



(12) (13) (14) (16)

In a previous paper,[2] we reported that tetrahydroisopetasol, **5** (mp 103.0—103.5 °C), derived from petasitol, **2**, showed a negative RD Cotton effect on the basis of the close resemblance to the RD curves of dihydro- (**13**) and desisopropylidene fukinone (**14**).[3] On the other hand, the pure tetrahydroisopetasol, **5**, has always been obtained as crystals after the crude hydrogenation product (**5a**) of isopetasol, **11**, has been subjected to isomerization with sodium methoxide–methanol or potassium hydroxide–methanol, that is, immediately after the hydrogenation product, **5a**, a viscous oil, showed a strong negative extreme, $[\theta]_{292}$ −1920, in the CD curve (Fig. 1). After all, the crystalline tetrahydroisopetasol, **5** (mp 103.0—104.0 °C), converted from isopetasol, **11**, has been found to show a weak positive Cotton effect, $[\theta]_{280}$ +460, by the reinvestigation of a part of the CD study of the eremophilan-8-one derivatives[7] (Fig. 1).

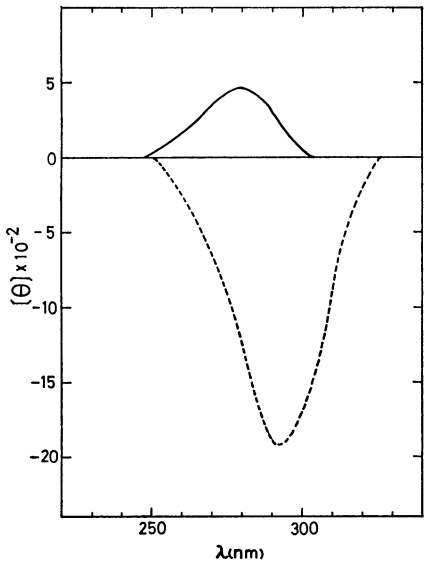


Fig. 1. CD curves of tetrahydroisopetasol: **5a** (an oily compd before isomerization; a dotted line) and **5** (a cryst compd after isomerization; a full line).

The final evidence for the stereochemistry of petasitin, **1**, was provided by the conversion of the known isopetasin (**15**) to **1** by means of photosensitized oxygenation in a manner similar to that in the case of the synthesis of petasitolone (**16**).[8]

Experimental

All the melting and boiling points are uncorrected. The IR, UV, ORD-CD, and mass spectra were taken with Jasco DS-402G, Cary Model 14, Jasco Model ORD-5, and Hitachi RMU-6 spectrophotometers respectively. The NMR spectra were recorded with JEOL C-60 and Hitachi R-20B (60 MHz) spectrophotometers, and the chemical shifts are reported in δ-values, with TMS as the internal reference. The optical rotations were measured with a Perkin-Elmer 141 polarimeter. The TLC were run on Kieselgel G (Merck). The analytical and preparative GLC were performed with a Shimadzu GC-1C apparatus on a stainless steel column (ϕ= 3 mm). The microanalyses were carried out in the microanalytical section of the Shionogi Research Laboratory, Shionogi and Co., Ltd.

Isolation of Petasitin (1). Dried flower stalks (34 kg) of *P. japonicus* Maxim. collected at Mt. Ioh in Ishikawa Prefecture, were extracted with methanol at room temperature. The extract was evaporated *in vacuo*, and the residue was dissolved in benzene. The benzene solution was washed with a saturated sodium hydrogencarbonate solution, dried over anhydrous sodium sulfate, and evaporated *in vacuo* to afford a dark green oil (2.4 kg). This oil was once chromatographed on alumina, and then repeatedly on silica gel. Subsequent elution with benzene–ethyl acetate (50: 1), gave petasitin (**1**) as a viscous oil (6.7 g) and almost a single spot on TLC (R_f, 0.2; benzene–ethyl acetate, 10: 1). This oil was purified by vacuum distillation and GLC for an analytical sample; bp 167.0—170.0 °C/2×10^{-4} mmHg; GLC: SF-96, 2 m, 60 ml/min H_2; column temperature, 240 °C; retention time, 16 min; $[\alpha]_D^{22}$ −26.2° (*c*, 1.0, MeOH); MS: *m/e* 332 M^+; IR (film): 3460, 1710, 1665, 1632, 1617, 1235 cm^{-1}; UV: λ_{max}^{EtOH} 235 nm (ε, 14200); NMR ($CDCl_3$): 6.93 (s, 6-H), 6.15 (t, J=1.0 Hz, 9-H), 6.13 (q, J=7.0 Hz, 3-H in an ester part), 4.95 (m, $W_{1/2}$=14 Hz, 3-H), 2.05 (d, J=7.0 Hz, 3-Me in an ester part), 1.90 (s, 2-Me in an ester part), 1.50 (s, 12- and 13-Me), 1.25 (s, 15-Me), 1.16 (d, J=7.0 Hz, 14-Me).

Found: C, 72.63; H, 8.56%. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.56%.

Alkaline Hydrolysis of Petasitin (1). A solution of petasitin, **1** (1.26 g), in 5% ethanolic potassium hydroxide (20 ml) was allowed to stand at room temperature for 2 days. After the removal of the solvent, the aqueous solution of the residue was extracted with ether. The extract was washed with water and dried over anhydrous sodium sulfate. The evaporation of the solvent gave petasitol (**2**) (760 mg) as a semisolid, which was then crystallized from ethyl acetate–

light petroleum as colorless prisms; mp 110.0—113.0 °C, $[\alpha]_D^{21}$ −1.2 ° (*c*, 1.1, $CHCl_3$); $[\alpha]_D^{21}$ −5.5 ° (*c*, 1.0, MeOH); MS: *m/e* 250 M^+; IR (KBr): 3340, 1655, 1610 cm^{-1}; UV: λ_{max}^{EtOH} 244 nm (ε, 12700); NMR ($CDCl_3$): 6.92 (s, 6-H), 6.12 (t, J=1.0 Hz, 9-H), 3.70 (m, $W_{1/2}$=14 Hz, 3-H), 1.50 (s, 12- and 13-Me), 1.18—1.30 (partly superimposed two methyls).

Found: C, 67.01; H, 8.97%. Calcd for $C_{15}H_{22}O_3 \cdot H_2O$: C, 67.13; H, 9.09%.

The 2,4-dinitrophenylhydrazone was prepared as usual and crystallized from ethanol as red needles; mp 230.0—232.0 °C (dec).

Found: C, 58.71; H, 6.10; N, 13.24%. Calcd for $C_{21}H_{26}O_6N_4$: C, 58.59; H, 6.06; N, 13.02%.

The above alkaline solution was acidified with 3 M sulfuric acid and extracted with ether. The ethereal extract was washed with water and dried. The solvent was removed to give a crude acidic part (310 mg); IR (film): 3500—2400 (broad), 1685, 1655 cm^{-1}. The above residue was transformed to the *p*-phenylphenacyl ester in the usual manner, using *p*-phenylphenacyl bromide. The product (550 mg) was chromatographed with light petroleum–benzene (10: 1) on silica gel (10 g) to give *p*-phenylphenacyl (*Z*)-2-methyl-2-butenoate (220 mg), which was crystallized from methanol as colorless prisms; mp 88.0—89.5 °C.

Found: C, 77.54; H, 6.20%. Calcd for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16%.

The subsequent elution on the above chromatography gave *p*-phenylphenacyl (*E*)-2-methyl-2-butenoate (30 mg), which was crystallized from methanol as colorless prisms (mp 104.5—106.5 °C). The two esters were identified by a mixed-melting-point determination with authentic samples.

Acetylation of Petasitol (2). a) A solution of petasitol, **2** (510 mg), in pyridine (2 ml) and acetic anhydride (2 ml) was left at room temperature for 20 h. The reaction mixture was then worked up in the usual manner to afford a crude monoacetate (**3**) as a solid, which was subsequently crystallized from acetone–light petroleum as prisms; mp 80.0—82.0 °C, $[\alpha]_D^{21}$ −17.9 ° (*c*, 1.0, $CHCl_3$), $[\alpha]_D^{21}$ −12.9 ° (*c*, 1.0, MeOH); MS: *m/e* 292 M^+; IR (KBr): 3420, 1735, 1660, 1616, 1240 cm^{-1}; UV: λ_{max}^{EtOH} 242 nm (ε, 14700); NMR ($CDCl_3$): 6.88 (s, 6-H), 6.10 (t, J=1.0 Hz, 9-H), 4.90 (m, $W_{1/2}$=14 Hz, 3-H), 2.06 (s, AcO), 1.48 (s, 12- and 13-Me), 1.20 (s, 15-Me), 1.10 (d, J=7.0 Hz, 14-Me).

Found: C, 65.79; H, 8.45%. Calcd for $C_{17}H_{24}O_4 \cdot H_2O$: C, 65.78; H, 8.44%.

b) A mixture of petasitol, **2** (44 mg), acetic anhydride (1.5 ml), and sodium acetate (70 mg) was refluxed for 8 h. Working-up as usual gave a crude product (63 mg), which was subsequently chromatographed on silica gel (5 g); elution with benzene–ethyl acetate (30: 1) then afforded diacetate (**4**) as a viscous oil (18 mg); MS: *m/e* 334 M^+, *m/e* 274 M^+ −60, *m/e* 214 M^+ −120, *m/e* 59 base peak; IR (film): 1735—1725, 1660, 1240 cm^{-1}.

Further elution with the same solvent gave monoacetate, **3** (20 mg), which was crystallized as has been described above and identified with the above monoacetate by a mixed-melting-point determination.

Hydrogenation of Petasitol (2). Petasitol, **2** (95 mg), was hydrogenated with 10% palladium charcoal (40 mg) in ethanol (3 ml). After the hydrogen-uptake (2 mol, 1 h) had ceased, the filtrate was evaporated *in vacuo* to furnish an oil (93 mg). The residue was chromatographed on silica gel (10 g), after which elution with benzene–ethyl acetate (15: 1) gave a viscous oil (74 mg) as a single spot on TLC (R_f, 0.56; benzene–ethyl acetate, 5: 1).

The above oil (60 mg) was refluxed with a catalytic amount of sodium under a nitrogen atmosphere in methanol for 2.5 h. After working-up as usual, the crystalline product (**5**) (63 mg) was crystallized from light petroleum as leaflets; mp 103.0—103.5 °C, $[\alpha]_D^{22}$ +39.2 ° (*c*, 2.56, MeOH).

Found: C, 75.50; H, 11.05%. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00%.

The 2,4-dinitrophenylhydrazone was prepared in the usual manner and then crystallized from ethanol as yellow needles; mp 165.5—167.0 °C.

Found: C, 60.18; H, 7.14; N, 13.48%. Calcd for $C_{21}H_{30}O_5N_4$: C, 60.27; H, 7.23; N, 13.39%.

The semicarbazone was prepared in the usual manner and crystallized from methanol as needles; mp 188.0—189.5 °C.

Found: C, 65.06; H, 10.00; N, 13.95%. Calcd for $C_{16}H_{29}O_2N_3$: C, 65.05; H, 9.90; N, 14.23%.

The above substance and its derivatives were found by a mixed-melting-point determination and a comparison of the spectra, to be identical in all respects with those[3] of tetrahydroisopetasol (**5**) obtained from isopetasin (**12**).

Dehydration of Monoacetate (3). Monoacetate, **3** (550 mg), in pyridine (10 ml) was treated with phosphoryl chloride (10 ml) at room temperature for 44 h. The reaction mixture was then poured onto ice and extracted with ether. The extract was washed successively with a saturated sodium hydrogencarbonate solution and water. The dried solvent was removed to give a crude product (330 mg), which was then chromatographed on silica gel (30 g). Elution with benzene–ethyl acetate (50: 1) afforded the anhydro derivative (**6**) (145 mg) as an oil; MS: *m/e* 274 M^+, *m/e* 84 base peak; IR (film): 3080, 3040, 1737, 1664, 1637, 1242, 920 cm^{-1}; UV: λ_{max}^{EtOH} 240 nm (ε, 12500), ε, 9800/220 nm; NMR ($CDCl_3$): 6.82 (s, 6-H), 6.04 (t, J=1.0 Hz, 9-H), 5.11 (d, J=7.0 Hz, 12-C=CH_2), 4.87 (m, $W_{1/2}$=14 Hz, 3-H), 2.06 (s, AcO), 1.97 (d, J=1.0 Hz, 13-Me), 1.22 (s, 15-Me), 1.10 (d, J=7.0 Hz, 14-Me).

Hydrogenation of Anhydromonoacetate (6). Anhydroacetate, **6** (122 mg), in ethanol (3 ml) was hydrogenated with 10% palladium charcoal (23 mg). Hydrogen-uptake ceased after 10 h. The filtrate was evaporated *in vacuo* to leave an oil (137 mg). The residue (103 mg) was refluxed in methanol (4 ml) with sodium metal (28 mg) under a nitrogen atmosphere for 3 h. Working-up as usual gave a product (94 mg) which was chromatographed on silica gel (6 g) with benzene–ethyl acetate (5: 1) and then crystallized from aqueous ethanol as leaflets (mp 101.0—103.0 °C). This was found to be identical with tetrahydroisopetasol (**5**) by a mixed-melting-point determination and a comparison of the IR spectra.

Isomerization of Tetrahydroisopetasol (5) with a Base. Isopetasol, **11** (3.03 g), in ethanol (45 ml) was hydrogenated with 10% palladium charcoal (600 mg) at room temperature for 6 h. The subsequent working-up as usual gave a viscous oil, which was then chromatographed on silica gel (64 g). Elution with benzene–ethyl acetate (20: 1) gave tetrahydroisopetasol (**5a**) (3.01 g) as a colorless oil; $[\alpha]_D^{24}$ −19.1° (*c*, 1.26, MeOH); IR (film): 3380, 1695, 1380, 1360, 1020 cm^{-1}; ORD (*c*, 0.1025, MeOH): $[\phi]_{391}$ 0, $[\phi]_{325}$ −600, $[\phi]_{307}$ −1160 (trough), $[\phi]_{289}$ 0, $[\phi]_{265}$ +1330; CD (*c*, 0.1025, MeOH): Fig. 1; NMR ($CDCl_3$): 3.58 (m, $W_{1/2}$=18 Hz, 3-H), 1.08 (s, 15-Me), 0.98 and 0.88 (each d, J=7.0 Hz, 12- and 13-Me), 0.82 (d, J=6.5 Hz, 14-Me).

The above product (3.01 g) was dissolved in methanol (10 ml) and refluxed with 0.2 M potassium hydroxide–methanol (40 ml) under a nitrogen atmosphere for 5 h. The subsequent working-up as noted above gave a partially crystallized product, which was crystallized from ethyl acetate to afford tetrahydroisopetasol (**5**)[3] as leaflets; mp 103.0—104.0

°C, $[\alpha]_D^{25}$ +34.3° (*c*, 1.01, MeOH); IR (CCl_4): 3610, 3450, 1720, 1390, 1375, 1035 cm^{-1}; ORD (*c*, 0.0937, MeOH): $[\phi]_{375}$ +200, $[\phi]_{325}$ +330, $[\phi]_{288}$ +710, $[\phi]_{275}$ +530, $[\phi]_{258}$ +380, $[\phi]_{225}$ +1040; CD (*c*, 0.0937, MeOH): Fig. 1; NMR ($CDCl_3$): 3.53 (m, $W_{1/2}$=18 Hz, 3-H), 1.01 and 0.83 (each d, J=7.0 Hz, 12- and 13-Me), 0.93 (s, 15-Me), 0.91 (d, J=6.0 Hz, 14-Me).

Hydrogenation of Monoacetate (3). Monoacetate, **3** (1.03 g), was dissolved in ether (30 ml) and hydrogenated with Adams' catalyst (111 mg). Hydrogen-uptake (2.2 mol) ceased after 30 min. Working-up as usual gave a crude product, which was chromatographed on silica gel (22 g) with benzene–ethyl acetate (10: 1) to afford the tetrahydro compound (**7**) (687 mg) (mp 92.0—95.0 °C) as needles (from light petroleum); IR (KBr): 3490, 1710, 1263 cm^{-1}; IR (CCl_4): 3500, 1735, 1700, 1240 cm^{-1}; NMR ($CDCl_3$): 4.81 (m, 3-H), 4.28 (br s, OH), 2.05 (s, AcO), 1.23 (s, 12- and 13-Me), 1.18 (s, 15-Me), 0.95 (d, J=7.0 Hz, 14-Me).

Found: C, 68.89; H, 9.57%. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52%.

Dehydration of Tetrahydromonoacetate (7). The above product, **7** (565 mg), was treated with pyridine (8 ml) and phosphoryl chloride (6.5 ml) at room temperature for 20 h. Working-up as usual gave a mixture of a dehydration product (**8**) (438 mg); IR (film): 1735, 1717 (sh), 1687 (sh), 1645, 1633, 1245 cm^{-1}.

The above product, **8** (430 mg), was chromatographed on alumina (10 g); subsequent elution with light petroleum–ethyl acetate (50: 1) gave a sole product (**9**) (360 mg); IR (film): 1735, 1682, 1630, 1240 cm^{-1}; UV: λ_{max}^{EtOH} 251 nm (ε, 5160); NMR ($CDCl_3$): 4.80 (m, 3-H), 2.05 (s, AcO), 1.98 and 1.81 (each s, 12- and 13-Me), 1.04 (s, 15-Me), 0.90 (d, J=7.0 Hz, 14-Me).

The 2,4-dinitrophenylhydrazone was prepared as usual and crystallized from ethanol (mp 168 °C) as deep red needles.

Found: N, 12.54%. Calcd for $C_{23}H_{30}O_6N_4$: N, 12.22%.

Dehydrogenation of Unsaturated Monoacetate (9). Into a stirred solution of the acetate, **9** (320 mg), and DDQ (2,3-dichloro-5,6-dicyano-*p*-benzoquinone) (292 mg) in dry dioxane (4 ml) anhydrous hydrogen chloride was bubbled at room temperature over a 30-s period. After further stirring for 40 min, crystals were separated, after which the stirring was continued for 8 h. After subsequent filtration and concentration, the residue was diluted with ether, washed successively with a 1% aqueous sodium hydroxide solution and water, and dried over anhydrous sodium sulfate. The removal of the solvent gave a product (290 mg) which was later chromatographed on silica gel (8 g). Elution with benzene gave a fraction (R_f, 0.35; benzene–ethyl acetate, 10: 1) which was subsequently crystallized from aqueous methanol to afford a pure acetate (**10**) as prisms; mp 82.0—85.0 °C; IR (Nujol): 1735, 1662, 1630, 1245 cm^{-1}; IR (CCl_4): 1740, 1666, 1631, 1244 cm^{-1}; UV: λ_{max}^{EtOH} 242 nm (ε, 7550), 278 (sh) nm (ε, 2900). This was found to be identical with the isopetasol acetate (**10**) converted from isopetasol (**11**) by a mixed-melting-point determination and a comparison of the IR spectra.

Acetylation of Isopetasol (11).[3] Isopetasol, **11** (106 mg), was acetylated with pyridine (1 ml) and acetic anhydride (0.5 ml). A subsequent working-up in the usual manner afforded the acetate (**10**) (98 mg), which was subsequently crystallized from aqueous methanol as prisms; mp 86.0—87.0 °C, $[\alpha]_D^{25}$ +80° (*c*, 0.97, $CHCl_3$); IR (KBr): 1735, 1660, 1630, 1245 cm^{-1}; IR (CCl_4): 1740, 1660, 1630, 1245 cm^{-1}; UV: λ_{max}^{EtOH} 243 nm (ε, 8400), 278 (sh) nm (ε, 3100); NMR (CCl_4): 5.65 (d, J=1.0 Hz, 9-H), 4.76 (sex, J=12.0, 10.0, and 5.0 Hz, $W_{1/2}$=16 Hz, 3-H), 2.04 (s, 12-Me), 2.01 (s, AcO), 1.83 (s, 13-Me), 1.04 (s, 15-Me), 0.95 (d, J=6.0 Hz, 14-Me).

Found: C, 73.70; H, 8.79%. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75%.

Preparation of Petasitin (1). A stirred solution of isopetasin (**15**)[3] (1.0 g) and Rose Bengal (5 mg) in absolute methanol was irradiated with a circular fluorescent lamp (30 watt) for 36 h under the bubbling of air. The reaction mixture was then stirred with a solution of sodium sulfite (2.5 g) in water (15 ml) for 3 h. After the removal of the solvent, the residue was extracted with ether. The subsequent working-up in the usual manner gave a crude product, which was chromatographed over silica gel (20 g). Elution with benzene afforded petasitin (**1**) (430 mg), which was found to be identical with the natural specimen by a comparison of the spectral data (IR and NMR) and by GLC analysis under the conditions described above. The other products were not investigated further.

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