Catalytic hydrogenation of III. (a) *With platinum oxide in 0.2% acetic acid.* A solution of 0.5 g. of III in 25 ml. of ethyl acetate containing 0.05 ml. of acetic acid was hydrogenated at 3 atm. in presence of 0.5 g. of platinum oxide for 3 hr. After the usual workup the crude product was isolated. The infrared spectrum showed presence of hydroxyl (3600 cm.$^{-1}$); acetate (1735 cm.$^{-1}$); absence of 12-ketone and presence of the same three strong bands in the 1250–1165 cm.$^{-1}$ discussed under III.

(b) *With platinum oxide in the presence of 5% acetic acid.* A solution of 5.0 g. of III in 240 ml. of ethyl acetate containing 5% acetic acid was hydrogenated at 3 atm. for 18 hr. in the presence of 5.0 g. of platinum oxide. The solvent was evaporated and the glassy product was oxidized with chromium trioxide in acetic acid at room temperature in the usual manner. The product, weighing 4.77 g., was examined by infrared spectroscopy and showed absence of hydroxyl, a strong band at 1735 cm.$^{-1}$ and a considerably weaker band at 1710 cm.$^{-1}$ Only one strong band at 1245 cm.$^{-1}$ was present in the 1250–1165 region.

3β-Acetoxy-5α-pregnane, IV. The total crude product obtained by method (b) above (4.77 g.) was treated with Girard T reagent. The noncarbonyl fraction, 1.5 g., was crystallized from acetone to give 0.8 g. of IV, m.p. 114–116°, $[\alpha]_D^{25}$ +3.9° (lit.,[6a,b] gives m.p. 115–116°, $[\alpha]_D^{19}$ +6°), infrared spectrum shows 1735 cm.$^{-1}$ and 1245 cm.$^{-1}$ bands.

3β-Acetoxy-5α-pregnan-12-one, V. The carbonyl fraction from the Girard T separation (3.0 g.) was deacetylated by hydrolysis with refluxing 5% potassium hydroxide in methanol. The residue after standard work-up was dissolved in benzene and chromatographed on Florisil. Elution with 20% methylene chloride in benzene and 100% methylene chloride gave 1.2 g. of a monohydroxy product. Acetylation of this compound followed by crystallization from ethanol-water gave V, m.p. 139–140°, $[\alpha]_D^{25}$ +95°; infrared spectrum shows two strong bands at 1735 and 1706 cm.$^{-1}$, one band at 1243 cm.$^{-1}$

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.84; H, 10.33.

Conversion of V *to* IV. Wolff-Kishner reduction of 0.3 g. of V by the Huang-Minlon procedure[6] yielded, after workup and acetylation, 0.15 g. IV, m.p. 113–115°, infrared spectrum identical with that of IV isolated from hydrogenation of III.

3β,20α-Diacetoxy-5α-pregnan-12-one, VI. After removal of the monohydroxy fraction described under V, elution with 5% ethanol in benzene gave 1.3 g. of a dihydroxy compound. Acetylation yielded 0.9 g. of VI, m.p. 181–183°, $[\alpha]_D^{25}$ +69°; infrared spectrum shows strong broad band at 1735–1730 cm.$^{-1}$ and a strong but less broad band at 1706 cm.$^{-1}$, and one strong broad band at 1250–1240 cm.$^{-1}$

Anal. Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.54; H, 9.04.

3β,20α-Diacetoxy-5α-pregnane, VII. A 0.36-g. sample of the 12-ketone VI was reduced by the Huang-Minlon modification[6] of the Wolff-Kishner procedure. After acetylation, 0.2 g. of VII was obtained, m.p. 163–165° (lit.,[11] gives m.p. 165–167°), with an infrared spectrum showing one strong band at 1735 cm.$^{-1}$ and one broad band at 1250–1240 cm.$^{-1}$ The entire infrared spectrum was identical with that of VII given in reference 12.

PHILADELPHIA 18, PA.

[CONTRIBUTION FROM THE UNIT OF NATURAL PRODUCTS, NATIONAL RESEARCH CENTRE]

Natural Coumarins. I. Marmesin and Marmesinin, Further Products from the Fruits of *Ammi majus* L.

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The isolation of marmesinin and its synthesis are described. Several reactions with marmesin and its derivatives establish that bromination and nitration occur at the six position and the same is suggested to happen with nodakenetin and analogous dihydrofurocoumarins. A correlation has been made between marmesin and products derived from peucedanin.

In a preliminary communication,[1] we reported the isolation of marmesin[2] (I, R = H), in 0.25% yield, from the alcoholic extract of defatted *A. majus* fruits, after mineral acid hydrolysis, and its presence in the fruits as a glycoside has been alluded to. In a more recent publication[3] the isolation of this glycoside, in fact a glucoside, from the same source has been described and the name "ammajin" was given to it. With the unfortunate[4] names ammoidin, ammidin, and majudin given,[5] on the basis of the botanical name of the source, to the constituents of *Ammi majus* L. before they were realized[6] to be the already well known xanthotoxin, imperatorin, and bergapten respectively having led to nomenclatural confusion—the choice of "ammajin" to denote the natural glycoside of marmesin is in our view an unjustifiable carry on of an erroneous system of names for the products of one plant source. The apparently relevant "marmesinin" would conform more closely to the conventional system of generic derivation of aglycone-glycoside names. The name is therefore proposed by the present authors to denote the natural marmesin glucoside.

(1) E. A. Abu-Mustafa, N. Badran, M. B. E. Fayez, and N. A. Starkowsky, *Nature*, **182**, 54 (1958).

(2) A. Chatterjee and S. S. Mitra, *J. Am. Chem. Soc.*, **71**, 606 (1949).

(3) N. A. Starkowsky and N. Badran, *J. Org. Chem.*, **23**, 1818 (1958).

(4) T. B. Fitzpatrick and M. A. Pathak, *J. Invest. Dermat.*, **32**, 229 (1959).

(5) I. R. Fahmy, H. Abu-Shady, A. Schönberg, and A. Sina, *Nature*, **160**, 468 (1947); I. R. Fahmy and H. Abu-Shady, *Quart. J. Pharm. and Pharmacol.*, **20**, 281 (1947).

(6) A. Schönberg and A. Sina, *Nature*, **161**, 481 (1948); A. Schönberg and A. Sina, *J. Am. Chem. Soc.*, **72**, 4826 (1950); I. R. Fahmy and H. Abu-Shady, *Quart. J. Pharm. and Pharmacol.*, **21**, 499 (1948).

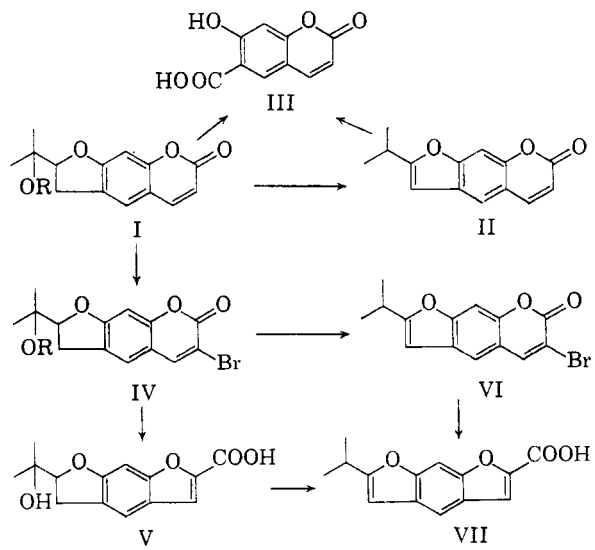
Marmesinin has been isolated in a pure crystalline state by chromatography of the acetylated glycosidic fraction of the alcoholic extract. The synthesis of marmesinin (I, R = $C_6H_{11}O_5$) has been accomplished in good yield (61%) (*cf.* ref. 3) by treating marmesin with α-acetobromoglucose in benzene solution in presence of silver carbonate under azeotropic distillation conditions. The synthesis, incidentally, precludes the possibility that the sugar moiety is attached to the phenolic hydroxyl group of the open coumarinic acid which is known[7,8] to occur with some furocoumarins.

Our work with marmesin leads us to support its constitution, as 2-(β-hydroxyisopropyl)-2′,3′-dihydro-6,7-furanocoumarin (I, R = H), proposed by Chatterjee and Mitra.[2] The presence, suspected[9] at one time, of a 2,2-dimethyl-3,4-unsaturated pyran in place of the isopropylfuran in anhydromarmesin (II) was disproved[7] by treatment with a 20% sodium hydroxide solution[10] whereby no acetone was produced and the anhydromarmesin was essentially unchanged. In addition, anhydromarmesin, like marmesin[2,3] gave unbelliferone-6-carboxylic acid (III) upon oxidation with potassium dichromate.

The optical relation between marmesin and its epimer, nodakenetin,[11,12] evident from their equal but opposite rotations,[2] has been more fully demonstrated by a comparison of their optical rotatory dispersion curves.[13] The ultraviolet absorption curve of marmesin (see Table I) was also found to be almost identical with that determined for nodakenetin. The apparent similarity of the chemical properties of these epimers has induced us to examine marmesin with the hope that its reactions might explain those described[11] for nodakenetin which remained hitherto unexplained. Our experiments with marmesin, a typical natural dihydrofurocoumarin, would also serve as examples of some general reactions in the dihydrofurocoumarin field which, as will be apparent in the sequel, are different from those known for furocoumarins.

Arima[11] reported that bromination of nodakenetin gave a monobromo derivative which upon treatment with hot alcoholic potassium hydroxide gave a "coumaric" acid containing no bromine. A similar treatment of marmesin, using two moles of bromine and also using *N*-bromosuccinimide, gave us a monobromo derivative[14] which was resistant to treatment with organic base, thus precluding the possibility of presence of the bromine atom in the dihydrofuran ring. The hydroxyl group was also not involved, as a bromoacetate derivative was obtained upon acetylation. The compound, however, was converted to marmesin by treatment with activated zinc dust in ethanol or by hydrogenation on platinum. The compound, which resisted all attempts to nitration, very readily gave, upon treatment with aqueous or alcoholic alkali, a product containing no bromine and shown to be an acid which gave a methyl ester; marmesin is unaffected by diazomethane or methyl iodide. The same acid was also obtained by alkaline hydrolysis of the bromoacetate mentioned before.

It appears therefore that the behavior of marmesin towards bromination is analogous to that of unsubstituted coumarin[15] and 6,7-disubstituted coumarins[16] in that the first bromine atom enters at the 3-position (of the coumarin nucleus) and that a coumarilic acid results from alkali treatment of a 3-bromo derivative. The marmesin bromo compound is, therefore, represented by (IV, R = H) and the product of alkali fission must be 2′-(β-hydroxyisopropyl)-2′,3′-dihydro-5,6-furanocoumarilic acid (V), or "marmesilic" acid. While sufficient nodakenetin was not available to us—the only known natural source, *Peucedanum decursivum*, is unknown in Egypt—to repeat Arima's[11] experiments, we feel that the bromination product and the acid resulting therefrom are (IV, R = H)



Scheme 1

(7) F. M. Dean, *Fortschr. Chem. org. Naturstoffe*, 9, 228 (1952).

(8) A. Stoll, A. Pereira, and J. Renz, *Helv. Chim. Acta*, **33**, 1637 (1960); H. N. Khastgir, P. C. Duttagupta, and P. Sengupta, *Indian J. Appl. Chem.*, **22**, 82 (1959).

(9) From the related *A. visnaga* was isolated a 2,2-dimethylchromeno α-pyrone, provismine: N. Badran and N. A. Starkowsky, *Proc. Pharm. Soc. Egypt* (*Sci. Ed.*), **38**, 93 (1956).

(10) J. C. Bell and A. Robertson, *J. Chem. Soc.*, 1828 (1936).

(11) J. Arima, *Bull. Chem. Soc. Japan*, **4**, 113 (1929).

(12) E. Späth and P. Kainrath, *Ber.*, **69**, 2062 (1936).

(13) These have been determined for us through the courtesy of Professor G. Ourisson, Strasbourg University, to whom we are indebted. We also thank Dr. M. Pailer, Vienna, for a gift of nodakenetin.

(14) Also reported by N. A. Starkowsky and N. Badran (ref. 3), but no structure was assigned to it.

(15) W. H. Perkin, *Ann.*, **157**, 115 (1871).

(16) V. J. Dalvi and S. Sethna, *J. Indian Chem. Soc.*, **26**, 359 (1949).

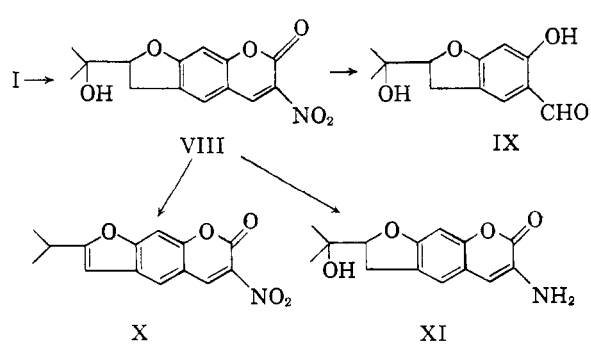
and (V) respectively but only different in the orientation of the side chain at C-2.

Additional experiments in this direction include the dehydration of 6-bromomarmesin (IV, R = H) with phosphorus pentoxide to 6-bromo-2-isopropylpsoralene (VI) which upon fission with alkali furnished an acid to be formulated as 2'-isopropyl-5,6-furanocoumarilic acid (VII). The latter compound was also obtained, in a different form with different melting point, by the direct dehydration of "marmesilic" acid (V) and by dehydration of the methyl ester of V followed by ester hydrolysis. The two forms of VII gave the same methyl ester. That the size of the isopropylfuran ring in the dehydration products (II, VI, and VII) remains the same was evident from the stability of anhydromarmesin (II) towards strong alkali. These reactions are outlined in Scheme 1.

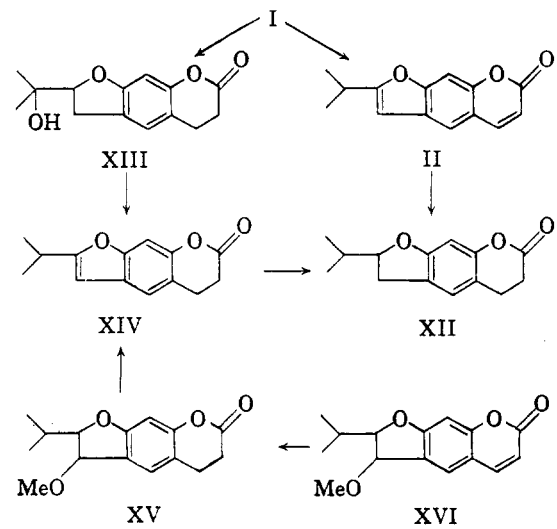
Nitration of marmesin gave a nitro derivative (VIII) in which the nitro group was shown to be attached to the 6-position by the action of mild alkali. This reaction led to an *o*-hydroxyaldehyde which is believed to be 5-formyl-6-hydroxy-2-(β-hydroxyisopropyl)-2,3-dihydrobenzofuran (IX) and from which a 2,4-dinitrophenylhydrazone derivative was prepared. It is known[17] that 3-nitrocoumarins undergo this type of reaction when warmed with aqueous alkali or concentrated ammonia solution and furnish salicylaldehydes. 6-Nitromarmesin (VIII), which was recovered unchanged after several attempts for bromination, gave an anhydro compound, 2-isopropyl-6-nitropsoralene (X), which behaved similarly towards the action of alkali. Reduction of VIII with activated zinc dust in ethanol or catalytically with hydrogen gave 6-aminomarmesin (XI); the reduction was not as effective using stannous chloride or tin and hydrochloric acid. It is noteworthy that the catalytic reduction did not affect the lactonic double bond as evidenced in the ultraviolet spectrum of the amino-compound in which the maximal absorption above 300 mμ (357 mμ) was retained (see Scheme 2).

It is known[18] that the lactone ring in a coumarin system can be opened with dimethyl sulfate to give a methoxy coumarinic acid, a reaction which was recently[19] successfully applied to xanthotoxin. Analogous to coumarins,[20] xanthotoxin[19] has also been reduced with lithium aluminum hydride to 6-hydroxy-7-methoxy-5-(3-hydroxy-1-propenyl)-benzofuran. Aluminum chloride in benzene cleaves[19,21] the furan ether–linkage in certain furocoumarins to yield 6-(1,2-diphenylethyl)-7-hydroxycoumarins. In our hands, however, the use of these reagents in similar fashion with marmesin led to no definite products.

The constitution of marmesin as 2-(β-hydroxyisopropyl)-2,3-dihydropsoralene suggests a close relationship to or even a possible common biogenetic origin[22] with some natural 2-isopropylfuracoumarins such as oreoselone and peucedanin.[23] Dehydration of dihydromarmesin (XIII), a hydrogenation product of marmesin,[2] gave a product to be formulated as 2-isopropyl-5,6-dihydropsoralene (XIV). A compound possessing the same constitution and believed to be identical with XIV has been previously prepared by Späth[23] by distillation of tetrahydropeucedanin (XV) resulting from the hydrogenation of peucedanin (XVI). The ultraviolet data, *vide infra*, seem also to support the proposed constitution. Catalytic hydrogenation of XIV gave desoxydihydrooreoselone (XII), previously prepared[2] by hydrogenation of anhydromarmesin (II) and by a similar sequence from nodakenetin[12] (Scheme 3).



Scheme 2



Scheme 3

(17) S. M. Sethna and N. M. Shah, *Chem. Revs.*, **36**, 27 (1945); A. Clayton, *J. Chem. Soc.*, 1397 (1910).

(18) H. Thoms, *Ber.*, **44**, 3325 (1911); N. M. Shah and R. C. Shah, *J. Univ. Bombay*, **7**, Pt. 3, 213 (1938); *Chem. Abstr.*, **33**, 3779 (1939).

(19) E. Brokke and B. E. Christensen, *J. Org. Chem.*, **23**, 589 (1958).

(20) P. Karrer and P. Banerjee, *Helv. Chim. Acta*, **32**, 1692 (1949).

(21) B. Krishnawaniy and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **16A**, 151 (1942).

(22) R. Aneja, S. K. Mukerjee, and T. R. Seshadri, *Tetrahedron*, **4**, 256 (1958).

(23) E. Späth, K. Klager, and C. Schlösser, *Ber.*, **64**, 2203 (1931).

TABLE I

ULTRAVIOLET ABSORPTION DATA OF MARMESIN AND ITS DERIVATIVES

Compound	Name	λ_{max} (log ϵ)			
I (R = H)	Marmesin	212[a] (3.89)	248[b] (3.50)	—	335 (4.09)
II	2-Isopropylpsoralene	211 (4.30)	251 (4.50)	294 (4.05)	334 (3.84)
IV (R = H)	Bromomarmesin	208 (4.49)	254[c] (3.71)	—	348 (4.31)
VI	6-Bromo-2-isopropylpsoralene	212 (4.32)	254 (4.34)	308 (4.07)	345 (3.87)
V	2′-(β-Hydroxyisopropyl)-2′,3′-dihydro-5,6-furocoumarilic acid	212 (4.29)	250 (3.85)	274[d] (4.04)	312[e] (4.19)
VII	2′-Isopropyl-5,6-furocoumarilic acid	—	242 (4.44)	285 (4.03)	312 (3.97)
VIII	Nitromarmesin	208 (4.20)	267 (3.82)	—	370 (4.10)
X	2′-Isopropyl-6-nitropsoralene	210 (4.38)	252 (4.32)	—	330 (3.92)
XIII	2-(β-Hydroxyisopropyl)-2,3,5,6-tetrahydropsoralene	210 (4.35)	—	292 (3.36)	—
XIV	2-Isopropyl-5,6-dihydropsoralene	211 (4.36)	255 (4.16)	288[f] (3.72)	—
XII	Desoxydihydro-oreoselone	208 (4.22)	—	294 (3.73)	—
IX[g]	5-Formyl-6-hydroxy-2-(β-hydroxy-isopropyl)-2,3-dihydrobenzofuran	214 (4.14)	242 (4.07)	284 (4.06)	329 (3.84)

The following companion peaks with near extinction coefficients are also present: [a] 225; [b] 259; [c] 230, 264; [d] 266; [e] 307, 319; [f] 296 mμ. The following shoulders are also present: I (R = H), 302; V, 242, VII, 276, 306, 320; VIII, 226, 258. [g] The spectrum of this compound resembles that reported[26] for 2,4-dihydroxybenzaldehyde but with a general bathochromic shift.

In the hydrogenation products XII, XIII, and XIV, the saturation of the lactone double bond was evidenced in the ultraviolet spectra, *cf.* Table I, where no peaks above 300 mμ were present. It has recently[19] been pointed out by Brokke and Christensen that peaks above 300 mμ in the furocoumarins arise from the conjugation of the lactone carbonyl with the aromatic nucleus.[24] This important remark has been found to hold perfectly true with all our 2,3-dihydro compounds including marmesin. Moreover, the data presented in Table I indicate a remarkable association of the intense absorption in the 240–270 mμ region with the extension of the benzenoid conjugation to the furan ring in furocoumarins. The saturation of the furan ring results in a reduction of the intensity of absorption in this region or its disappearance. This observation, also evident from the spectral data given by Brokke and Christensen[19] for some psoralenes and 2,3-dihydropsoralenes and from those reported[25] for benzofuran and 2,3-dihydrobenzofuran, appears to be independent from the association of adsorption above 300 mμ with the continuity of conjugation in the coumarin portion of the molecule.

Professor A. C. Griffin of the M. D. Anderson Hospital and Tumor Institute, Houston, Tex., has kindly examined marmesin for us and reported that "as far as its photodynamic properties are concerned, it is only about one tenth as effective as xanthotoxin and is somewhat more effective following topical application rather than parential injections." Dr. M. A. Pathak, University of Oregon Medical School—through the courtesy of Professor T. B. Fitzpatrick—has also kindly examined products I (R = H), II, and V for photo-sensitizing activity on guinea pig's skin and found that II was most active although the three were considerably less so than psoralene or xanthotoxin.

(24) This observation has earlier [R. Goodwin and B. Pollock, *Arch. Biochem. Biophys.*, **49**, 1 (1954)] been made on a number of coumarin compounds.

(25) J. Jones and A. Lindsey, *J. Chem. Soc.*, 1836 (1950).

(26) H. W. Lemon, *J. Am. Chem. Soc.*, **69**, 2998 (1947).

EXPERIMENTAL[27]

Isolation of marmesinin (I, R = $C_6H_{11}O_6$). Exhaustive defatting of powdered *Ammi majus* L. fruits (300 g.) with benzene in a Soxhlet apparatus was followed by extraction with ethanol and the extract evaporated to dryness. The residue (80 g.) was taken up in hot water (1.5 l.) and after cooling it was extracted with chloroform. The aqueous layer was concentrated under vacuum to about 200 ml., excess acetone was added and the mixture left to stand overnight. The acetone layer was decanted leaving a dark brown gum (60 g.). This, after being repeatedly washed with acetone, was dried, then acetylated using pyridine and acetic anhydride. Three grams of the acetylated product were chromatographed on alumina. Prolonged benzene elution removed a small amount of an orange oil. Elution with 1% methanol in benzene gave a light orange gum which was crystallized from aqueous methanol. Pale creamish solid (30 mg.) resulted; m.p. 210–213° undepressed by a sample of marmesinin acetate prepared by the method of Starkowsky and Badran[3] who report m.p. 227°.

Synthesis of marmesinin. A solution of marmesin (0.5 g.) in benzene (dry, 75 ml.) was boiled with silver carbonate (freshly prepared, 1 g.) then treated with a solution of acetobromoglucose (dry, 2 g.) in dry benzene (75 ml.) added dropwise following exactly the rate of distillation of benzene during 1.5 hr. A further addition of dry benzene (75 ml.) was made in the same manner and the mixture then refluxed for 2 hr. Fresh silver carbonate (1 g.) was added followed by a solution of acetobromoglucose (2 g.) in benzene (75 ml.) while distilling benzene in the same way during 2 hr. The mixture was then refluxed for 0.5 hr. After cooling, the silver salts were filtered, washed with hot benzene, and the combined benzene solution evaporated on a steam bath under vacuum. Crystallization of the residue from chloroform-ethanol gave a mass of felted needles (710 mg.) which was recrystallized from ethanol to give a pure product;

(27) The melting points were taken on a Kofler block and are uncorrected, the optical rotations were measured in 1 dm. tube and the ultraviolet spectra were determined in ethanol.

m.p. 215–216° undepressed by the acetate of natural marmesinin, $[\alpha]_D$ −29° (chloroform).

Marmesin (I, R = H). The finely powdered fruits of *Ammi majus* (750 g.) were first extracted with benzene in a Soxhlet apparatus then exhausted with ethanol, (5 l.). The alcoholic solution was then concentrated to a small volume and hydrolyzed by refluxing with concd. hydrochloric acid (23 ml.) for 2 hr. Excess water was added and the mixture extracted with chloroform. After working up in usual manner, the dark brown residue (23.5 g.) was crystallized from 95% ethanol to give 1.89 g. of crude marmesin. This was recrystallized from chloroform-ethanol to give colorless prisms, m.p. 189–190° undepressed by an authentic sample,[28] $[\alpha]_D$ +25° (chloroform); reported[2] m.p. 189.5°, $[\alpha]_D$ +26.8°. The infrared spectra[29] in Nujol, of the two samples were identical in every detail. Marmesin was also obtained by mineral acid hydrolysis of marmesinin acetate.

Anal. Calcd. for $C_{14}H_{14}O_4$: C, 68.26; H, 5.73. Found: C, 68.12; H, 5.75.

The acetate was prepared in the usual manner[2]; m.p. 130–132°, $[\alpha]_D$ +25° (chloroform); reported[2] m.p. 130°.

Anal. Calcd. for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.40; H, 5.54.

Alkaline hydrolysis of the acetate (100 mg.), using mild conditions, gave marmesin (70 mg.).

Umbelliferone-6-carboxylic acid (III). Anhydromarmesin (0.5 g.) was dissolved in acetic acid (stabilized, 15 ml.) and a solution of 1 g. of potassium dichromate in 10% sulfuric acid (10 ml.) was added dropwise while maintaining the temperature of the solution at 70–80°. The mixture was then left at room temperature for about 6 hr. A yellow crystalline substance deposited which was filtered and recrystallized from aqueous ethanol to give fine creamish needles, m.p. 253–257° dec. undepressed by the material prepared[2] by a similar oxidation of marmesin; reported m.p. 260°[2] and 258–262°.[3]

Bromomarmesin (IV, R = H). A. Marmesin (1 g.) was dissolved in chloroform (25 ml.), treated with a solution of bromine (2 moles) in chloroform (5 ml.) and the mixture was left at room temperature for 5 min. The solution was evaporated on a water bath and the residue, creamish fine needles, was repeatedly crystallized from chloroform-ethanol to give colorless plates (720 mg.); m.p. 231–233° dec., $[\alpha]_D$ +97° (chloroform); reported[3] m.p. 230–231°.

Anal. Calcd. for $C_{14}H_{13}O_4Br$: C, 51.38; H, 4.00; Br, 24.61. Found: C, 51.79; H, 4.07; Br, 24.84.

B. Marmesin (1.23 g.) and *N*-bromosuccinimide (0.9 g.) were refluxed in carbon tetrachloride (100 ml.) for 2 hr. Filtration of the hot solution to remove suspended matter and cooling gave colorless plates of bromomarmesin; yield 550 mg., m.p., 230–232° dec., was undepressed by product from the previous experiment.

Bromomarmesin acetate (IV, R = Ac) was prepared by refluxing a mixture of bromomarmesin (250 mg.) and anhydrous sodium acetate (500 mg.) in acetic anhydride (5 ml.) for 5 hr. Working up the product gave 260 mg. of a material which melted at 187–189° after crystallization from chloroform-ethanol.

Anal. Calcd. for $C_{16}H_{15}O_6Br$: C, 52.31; H, 4.08; Br, 21.80. Found: C, 52.50; H, 4.23; Br, 21.72.

Elimination of bromine from bromomarmesin. A. Bromomarmesin (250 mg.) was refluxed with zinc dust (2.5 g.), which had been previously treated with 8*N* hydrochloric acid, in ethanol (70 ml.) for 24 hr. After filtration, the solution was reduced to a small volume and treated with few drops of water. A crop of flat needles (0.12 g.), m.p. 232–235°, undepressed by bromomarmesin, was first obtained. From the mother liquor there was isolated another crop (40 mg.) which proved to be marmesin by mixed melting point.

B. Bromomarmesin (500 mg.) together with palladium-charcoal (10%, 250 mg.) in pyridine (15 ml.) were shaken for 3 hr. with hydrogen until about 1 mole was absorbed. After filtration, the solution was concentrated to a small volume then a few drops of water were added. Colorless needles (160 mg.) were obtained which, after crystallization from ethanol, melted at 178–180° alone or mixed with a sample of marmesin.

2′-(β-Hydroxyisopropyl)-2′,3′-dihydro-5,6-furocoumarilic acid (V). Bromomarmesin (0.25 g.) was refluxed with 6*N* aqueous sodium hydroxide solution (12.5 ml.) for 30 min. The yellow solution was then acidified with 6*N* sulfuric acid solution. The flocculant precipitate (0.21 g.) formed was repeatedly crystallized from ethanol-water to give colorless plates; m.p. 215–217° dec., $[\alpha]_D$ +25.3°. The substance gave negative Beilstein reaction for halogen and readily dissolved in a solution of sodium bicarbonate with effervescence from which it was recovered upon acidification.

Anal. Calcd. for $C_{14}H_{14}O_5$: C, 64.11; H, 5.38. Found: C, 63.93; H, 5.34.

One-half gram of bromomarmesin acetate was treated as above to give 300 mg. of a material which proved to be identical with V.

The *methyl ester* of the coumarilic acid was prepared by refluxing a mixture of 200 mg. of V, 2 ml. of methyl iodide, and 3 g. of potassium carbonate in 50 ml. of acetone for 24 hr. Filtration of the solution while hot and evaporation to dryness gave a residue which yielded 180 mg. of the methyl ester, after crystallization from aqueous alcohol, in the form of shining plates; m.p. 135–136°.

Anal. Calcd. for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84. Found: C, 65.63; H, 5.83.

This substance was also prepared by treating a solution of V (250 mg.) in chloroform (20 ml.) with a solution of diazomethane in ether (8 ml.) and processed in the usual manner. The product was crystallized from aqueous ethanol to yield 230 mg. of the methyl ester; m.p. and mixed m.p. 133–134°.

In similar experiments, it was demonstrated that marmesin was unchanged by treatment with both of the above methylating agents.

6-Bromo-2-isopropylpsoralene (VI). A solution of bromomarmesin (0.25 g.) in dry benzene (40 ml.) was refluxed with phosphorus pentoxide (2.5 g.) for 5 hr. After decantation. the residue was repeatedly washed with hot benzene. The combined benzene solutions were evaporated nearly to dryness and alcohol added. Pale yellow needles (0.15 g.) deposited and were crystallized from aqueous ethanol to purity; m.p. 159–161° dec.

Anal. Calcd. for $C_{14}H_{11}O_3Br$: C, 54.72; H, 3.58; Br, 26.05. Found: C, 55.06; H, 3.90; Br, 26.31.

2′-Isopropyl-5,6-furocoumarilic acid (VII). A. A solution of 6-bromo-2-isopropylpsoralene (100 mg.) in hot ethanol (4 ml.) was treated with an alcoholic solution of potassium hydroxide (3 g. in 18 ml. ethanol) and the mixture refluxed for 0.5 hr. Excess water was added followed by dilute hydrochloric acid till slightly acidic; a flocculant precipitate was formed at once. Filtration and crystallization from aqueous acetone gave fine colorless needles (60 mg.) which have no definite melting point but sublime at 220–230°.

Anal. Calcd. for $C_{14}H_{12}O_4$: C, 68.84; H, 4.95. Found: C, 68.7; H, 5.13.

This substance, with acid properties was methylated as described under V, and the product was crystallized from aqueous acetone to give plates; m.p. 127–128°.

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 69.75; H, 5.46. Found: C, 69.46; H, 5.59.

B. 2′-(β-Hydroxyisopropyl)-2′,3′-dihydro-5,6-furocoumarilic acid (V) was dehydrated as described under VI and the product was crystallized from chloroform-methanol to give colorless felted needles; m.p. 232–233°. Methylation of this product (methyl iodide–potassium carbonate) gave

(28) We thank Dr. A. Chatterjee, Calcutta, for a sample of marmesin.

(29) We thank Dr. F. Johnson, The Dow Chemical Company, Framingham, Mass., for the infrared measurements.

the methyl ester as shining plates; m.p. 127–128°, was undepressed by a sample of the coumarilic acid methyl ester prepared under A.

C. The methyl ester of V (200 mg.) was dehydrated with phosphorus pentoxide as in the previous experiment. The product (140 mg.) was shown to be identical with the methyl ester of 2′-isopropyl-5,6-furocoumarilic acid obtained under A; m.p. and mixed m.p. 126–128°. A sample of this material (100 mg.) was treated with a mixture of concd. hydrochloric acid (3 ml.) and glacial acetic acid (13 ml.) under reflux for 2 hr. Water was added and the fluffy substance which deposited (85 mg.) was crystallized from aqueous ethanol to give colorless felted needles subliming at 220–230°. This was also obtained by alkaline hydrolysis of the methyl ester of 2′-isopropyl-5,6-furocoumarilic acid by refluxing 200 mg. of the substance in 6*N* aqueous sodium hydroxide solution (10 ml.) for 0.5 hr. After cooling, the mixture was acidified and the white substance which resulted (150 mg.) was crystallized from aqueous ethanol to sublime at 220–230° like 2′-isopropyl-5,6-furocoumarilic acid obtained under A.

Nitromarmesin (VIII). One-half gram of marmesin was dissolved in glacial acetic acid (5 ml.), then treated with a solution of nitric acid (sp. gr. 1.4, 2 ml.) in acetic acid (5 ml.) and the mixture heated for 1.5 hr. on a boiling water bath. Water was added, whereby a voluminous bright yellow precipitate was formed which was filtered and crystallized from methanol to give 400 mg. of canary yellow needles; m.p. 202–204°, $[\alpha]_D$ +87° (chloroform).

Anal. Calcd. for $C_{14}H_{13}O_8N$: C, 57.73; H, 4.46; N, 4.81. Found: C, 57.98; H, 4.45; N, 4.91.

5-Formyl-6-hydroxy-2-(β-hydroxyisopropyl)-2,3-dihydrobenzofuran (IX). Nitromarmesin (100 mg.) was shaken with a 5% solution of potassium hydroxide (5 ml.) and left at room temperature for 15 min. A red color gradually developed and the solid dissolved. The solution was then acidified with dilute hydrochloric acid and chilled, whereby grayish platey needles were formed; yield 55 mg. Repeated crystallization of the product from water-ethanol gave lustrous plates; m.p. 83–85°.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.44; H, 6.27.

When the reaction was carried out as prescribed by Clayton[17] for 3-nitrocoumarins, where 1 g. of the nitro compound (VIII) was warmed with concentrated ammonia solution, a much lower yield (150 mg.) of the hydroxyaldehyde (IX) was obtained.

The 2,4-dinitrophenylhydrazone derivative, m.p. 242–244°, was prepared.

Anal. Calcd. for $C_{18}H_{18}O_7N_4$: N, 13.93. Found: N, 13.87.

2′-Isopropyl-6-nitropsoralene (X). One gram of 6-nitromarmesin was dehydrated with phosphorus pentoxide in benzene as described before and the product, orange prismatic needles (600 mg.), was crystallized from ethanol; m.p. 209–211°.

Anal. Calcd. for $C_{14}H_{11}O_5N$: C, 61.54; H, 4.06; N, 5.13. Found: C, 61.29; H, 4.03; N, 4.98.

6-Aminomarmesin (XI). A. A solution of 6-nitromarmesin (250 mg.) in ethyl alcohol (50 ml.) was refluxed for 25 hr. with zinc dust (1.5 g.) which was previously treated with 8*N* hydrochloric acid. The zinc deposit was then filtered off, and the filtrate concentrated to a small volume and treated with some water. The pale yellowish flat needles (0.1 g.) formed were recrystallized several times from aqueous ethanol; m.p. 248–250° dec.

Anal. Calcd. for $C_{14}H_{15}O_4N$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.17; H, 5.97; N, 5.43.

B. Nitromarmesin (250 mg.) was dissolved in glacial acetic acid (15 ml.) and 85 mg. of platinum oxide were added. The mixture was shaken for 1 hr. with hydrogen under atmospheric pressure. The catalyst was filtered off and the solution evaporated to dryness. The residue, after treatment with charcoal, was crystallized from aqueous ethanol to give 150 mg. of pale yellow plates; m.p. 248–250°, was undepressed by a sample of 6-aminomarmesin prepared in the previous experiment.

2-Isopropylpsoralene (II). Marmesin (1.0 g.) was refluxed with benzoyl chloride (10 ml.) for 2 hr. Water was added and the oil deposited was taken up in chloroform. The product, isolated in the usual manner, was crystallized from methanol to give colorless flat needles (0.4 g.); m.p. 135–136°, was undepressed by a sample of anhydromarmesin prepared as described in the literature[2,3]; reported m.p. 138–140°[2] and 138–138.5°.[3]

2-Isopropyl-5,6-dihydropsoralene (XIV). The starting material, 2-(β-hydroxyisopropyl)-2,3,5,6-tetrahydropsoralene or dihydromarmesin (XIII), was prepared as described by Chatterjee and Mitra[2] by hydrogenation of marmesin. This material (440 mg., m.p. 131°; reported[2] m.p. 135°) was dissolved in benzene (75 ml.) and refluxed with phosphorus pentoxide (4.5 g.) for 5 hr. The decanted benzene solution was then concentrated to a small volume and petroleum ether (b.p. 70–80°) was added until slightly turbid and left to cool. Colorless heavy prisms (280 mg.) were deposited; m.p. 134–135°. The substance was optically inactive. For the product from the distillation of tetrahydropeucedanin, reported[23] m.p. 126°.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13. Found: C, 73.19; H, 6.24.

Desoxydihydro-oreoselone (XII). A solution of 2-isopropyl-5,6-dihydropsoralene (185 mg.) in glacial acetic acid (15 ml.) was shaken with 10% palladium on charcoal (185 mg.) in the presence of hydrogen for 60 hr. The catalyst was removed and water added to the clear solution whereby colorless plates (90 mg.) deposited; m.p. 113–115°, undepressed by the material prepared[2] by a similar hydrogenation of 2-isopropylpsoralene (II), $[\alpha]_D$ +25.5°; reported m.p. 116–117°[2] and 115–117°.[12]

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.54; H, 7.08.

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