conversion to 70%. At 380–390°, 90% conversion was obtained and recyclization of the pyrolysate failed to increase this yield.

Treatment with 2,4-dinitrophenylhydrazine in methanol as above gave the deep red 2,4-dinitrophenylhydrazone which was recrystallized three times from methanol, m.p. 143–144°; λ_{max}^{EtOH} 381 mμ, ε 29,500.

Anal. Calcd. for $C_{16}H_{18}N_4O_4$: C, 58.20; H, 5.45. Found: C, 58.30; H, 5.29.

Deuterium Exchange of 1,4,4-Trimethylbicyclo(3.2.0)heptan-2-one (III) and 4,4,6-Trimethylbicyclo(3.2.0)heptan-2-one (VI).—Sodium (20 mg.) was added to 1 ml. of deuterioethanol followed by 0.5 ml. of deuterium oxide. 1,4,4-Trimethylbicyclo(3.2.0)heptan-2-one (60 mg.) was added and the solution refluxed under nitrogen for 10 min. and the product distilled *in vacuo*. The distillate was diluted with 2 ml. of deuterium oxide and extracted with three 5-ml. portions of petroleum ether and the extracts were dried over magnesium sulfate. Evaporation of the petroleum ether on a steam-bath followed by distillation of the residue in a micro Hickman still at 45 mm. gave a clear oil which had a mass spectrum indicating 81% of the dideuterioketone and 17.3% of the monodeuterioketone.

Treatment of 4,4,6-trimethylbicyclo(3.2.0)heptan-2-one in the same manner gave a mixture of 41% trideuterioketone, 35.2% dideuterioketone and 18.1% monodeuterioketone.

Interconversion of 4,4,6-Trimethylbicyclo(3.2.0)hept-6-en-2-one (V) and 1,4,4-Trimethylbicyclo(3.2.0)hept-6-en-2-one (II).—To a small quartz flask equipped with a reflux condenser and a nitrogen inlet was added 200 mg. of 4,4,6-trimethylbicyclo(3.2.0)hept-6-en-2-one, 2 drops of triethylamine and 5 ml. of *n*-hexane. The solution was agitated by a slow stream of nitrogen and illuminated by an external quartz mercury arc (Hanau) for 25 hr. Both the lamp and the flask were cooled by a circulating water-bath. The *n*-hexane was removed under reduced pressure and the residual oil chromatographed in the vapor phase over tricyanoethoxypropane at 150°. The two major components present in a ratio of *ca.* 1:5 were collected and comparison of their infrared spectra indicated the major component to be starting ketone and the minor component to be 1,4,4-trimethylbicyclo(3.2.0)hept-6-en-2-one. Irradiation of 1,4,-4-trimethylbicyclo(3.2.0)hept-6-en-2-one under the above conditions gave the same mixture in a ratio of 1:4.

Conversion of 3,3,5-Trimethylcycloheptadien-1-one (IV) to 4,4,6-Trimethylbicyclo(3.2.0)hept-6-en-2-one (V).—3,3,-5-Trimethylcycloheptadien-1-one (100 mg.) in 5 ml. of *n*-hexane contained in a small quartz flask was illuminated under nitrogen with a quartz mercury arc (Hanau) for 5 hr. After removal of the *n*-hexane under reduced pressure at room temperature, a small sample of the residual oil was chromatographed in the vapor phase over tricyanoethoxypropane at 150°. Collection followed by infrared spectra comparison of the two primary components indicated 72% of starting ketone and 25% of 4,4,6-trimethylbicyclo-(3.2.0)hept-6-en-2-one.

3,3,5 - Trimethylcycloheptanone - 1 (VII).—3,3,5 - Trimethylcycloheptadienone (70.0 mg., 0.466 millimole) was hydrogenated over 10 mg. of 20% palladized charcoal in 10 ml. of absolute ethanol at 28° and 1 atm. pressure. After 10 min., 2.3 equivalents of hydrogen had been consumed and uptake ceased. The mixture was filtered, the ethanol removed under reduced pressure at room temperature, the residue distilled in a micro Hickman still at 15 mm. to give 35 mg. (49.0%) of 3,3,5-trimethylcycloheptanone-1.

The semicarbazone after three recrystallizations from methanol and water had m.p. 186–186.5° (lit. 196–197°,[23] 189°[14]) pure and mixed with a synthetic sample described below. Both samples had identical infrared spectra in KBr.

In a three-necked flask equipped with a magnetic stirrer and thermometer was placed 5.35 g. (0.04 mole) of dihydroisophorone and 4.5 g. (0.08 mole) of potassium hydroxide in 100 ml. of methanol. N,N'-Dimethyl-N,N'-dinitrosoterphthalamide (du Pont EXR-101, 6.57 g., 0.4 mole) was washed three times with 50-ml. portions of *n*-hexane to remove the mineral oil stabilizer. Small portions of the nitroso compound were added to the dihydroisophorone solution maintained at 5–10° with external cooling. After one-third of the product had been added, the solution was allowed to warm to room temperature and the addition continued (3 hr.). After each addition the solution was allowed to decolorize. Excess diazomethane was destroyed by acidifications and the methanol was removed by distillation. Filtration of the residue followed by distillation through a Holtzman column at 20 mm. afforded 0.643 g. of a fraction, b.p. 107–110°. Chromatography of a small sample of this fraction in the vapor phase over nitromethylpimelonitrile at 100° indicated three components in the ratio of *ca.* 1:2:4 which were subsequently collected. The infrared spectrum of the major component was identical with that of dihydroisophorone (VIII).

The semicarbazones of the two minor components were prepared in the usual manner and after three recrystallizations from methanol and water both had m.p. 185–186° (lit. for 3,3,5-trimethylcycloheptanone, m.p. 196–197°[23] and m.p. 189°[14]; for 3,5,5-trimethylcycloheptanone, m.p. 192–193°[23] and m.p. 194°[14]). The semicarbazones of the reduction product of IV gave no melting point depression when mixed with the corresponding derivative of 3,3,5-trimethylcycloheptanone but, on admixture of the derivative of 3,5,5-trimethylcycloheptanone, the melting point was depressed to 175°.

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[23] B. Tchoubar, *Bull. soc. chim. France*, 164 (1949).

CAMBRIDGE, MASS.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

Terpenoids. XLIV.[1] Synthetic Confirmation of the Structure and Absolute Configuration of Petasin[2]

BY DAVID HERBST[3] AND CARL DJERASSI

RECEIVED JANUARY 11, 1960

The total synthesis of (−)-*trans*-1,9-dimethyldecalin-2,6-dione (VIII) from an intermediate of known absolute configuration is described. The same diketone could also be obtained from the sesquiterpene petasin (I), thus confirming the earlier structural and absolute configurational assignments.

Petasin,[4,5] the angelate ester of petasol (II),[6] has recently been assigned[5] structure I (without any stereochemical implications). The main arguments in the structure proof[5] of petasin (I) have already been reviewed[7] and it was pointed out that

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[1] Paper XLIII, E. J. Eisenbraun, T. George, B. Riniker and C. Djerassi, THIS JOURNAL, **82**, 3648 (1960).

[2] Supported by the Division of Research Grants (grant No. RG-6840) of the National Institutes of Health, U. S. Public Health Service.

[3] From part II of the Ph.D. dissertation of David Herbst.

[4] A. Aebi, J. Büchi, T. Waaler, E. Eichenberger and J. Schmutz, *Pharm. Acta Helv.*, **30**, 277 (1955); A. Stoll, R. Morf, A. Rheiner and J. Renz, *Experientia*, **12**, 360 (1956).

[5] A. Aebi and T. Waaler, "Über die Inhaltstoffe von *Petasites hybridus* (L.) Fl. Wett," Verlag Helbing und Lichtenhahn, Basel, 1958. A preliminary note of these studies has been published by A. Aebi, T. Waaler and J. Büchi, *Pharm. Weekblad*, **93**, 397 (1958).

[6] Petasol (II) itself has never been isolated, because during the saponification of the angelate ester the double bond of the isopropenyl group migrates into conjugation to afford directly isopetasol (III).

[7] A. Aebi and C. Djerassi, *Helv. Chim. Acta*, **42**, 1785 (1959).

des-isopropylidenepetasol (IV) represented a promising intermediate for further studies. The carbon skeleton of petasin was established[5] by dehydrogenation to eudalin and the disposition of the substituents between carbon atoms 7 to 10[8] followed from the alkali treatment of isopetasol (III), which was accompanied by retroaldolization with formation of acetone and des-isopropylidenepetasol (IV). The rotatory dispersion curve[7] of IV was of the usual Δ^4-3-keto steroid type,[9] a result which not only confirmed the correctness of the earlier structure assignment[5] of des-isopropylidenepetasol (IV), but also settled the absolute configuration[10] of this substance insofar as the carbon atom bearing the angular methyl group is concerned. The only possible factor which could have affected the correctness of these conclusions was the location and configuration of the hydroxyl group. Its equatorial orientation was indicated[5] by the ease of saponification of petasin (I) as well as by the rate of oxidation and acetylation of the free hydroxyl group in des-isopropylidenepetasol (IV). Its location at C-3 (see I) was suggested[5] by the observation that the hydroxyl group was not eliminated by treatment with base, as would be expected for a vinylogous β-hydroxy ketone (location at C-2), and that the derived diketone, des-isopropylidenepetasone (V), possessed an isolated carbonyl group (thus excluding C-1) in addition to the original α,β-unsaturated ketone moiety.

Petasin (I) is thus a member of the rare class of eremophilone (VI) sesquiterpenes,[11] which do not follow the isoprene rule and whose relative[12] and absolute[13] configuration has recently been established. In view of the great interest in this type of sesquiterpene—notably from a biogenetic viewpoint[14]—it appeared desirable to subject the above structural and absolute configurational deductions to confirmation by total synthesis. For this purpose, we selected an approach which had been employed successfully by us[13] in the proof of absolute configuration of eremophilone (VI) and its congeners.

The resolution and absolute configuration of our starting material,[15] the (+)-antipode of the enol ether IX, had already been recorded earlier[16] and so had its transformation[13] into the hexalone X by means of methyllithium and acid hydrolysis. Oxidation with perbenzoic acid furnished the crystalline epoxide XI, whose anticipated α-configuration (rearward approach of the reagent) can be deduced from the subsequent reactions and from analogy to the related perbenzoic acid oxidation[13] of the corresponding olefin lacking the α,β-unsaturated carbonyl group of ring B. Reduction with lithium aluminum hydride afforded a diol (XII), which was not purified but subjected directly to oxidation with manganese dioxide, a reagent known[17] to oxidize allylic alcohols in preference to saturated ones. The resulting, crystalline (+)-*trans*-1,9-dimethyl-6-hydroxy-Δ^1-octalone-3 (XIII) exhibited the typical infrared and ultraviolet bands of the α,β-unsaturated carbonyl chromophore, while the stereochemistry of the C-6 hydroxyl group in XIII follows from the usual course[18] of axial opening of such epoxides. Of interest is the difference in the optical rotatory dispersion curves (Fig. 1) of the oxide XI and its derived keto alcohol XIII. The multiple Cotton effect curve of the oxido ketone XI is characterized by an abundance of fine structure, which has been noted[13] in its precursor X and which is characteristic[19] of this particular hexalone system. This feature appears to be associated with the strain caused by the double bond or oxide grouping in ring A of X and XI, since the rotatory dispersion curve (Fig. 1) of the keto alcohol XIII is substantially different and now resembles the anticipated mirror image curve of a Δ^1-3-keto steroid[20] or the corresponding octalone.[21]

(+)-*trans*-1,9-Dimethyl-6-hydroxy-Δ^1-octalone-3 (XIII) represented the key intermediate in our synthetic sequence, the α,β-unsaturated ketone moiety in ring B serving as the point of stereospecific entry for the oxygen function in ring B of petasin (I). The now unnecessary keto group of the octalone XIII was removed by Wolff–Kishner reduction to yield a hydrocarbon mixture. Microhydrogenation demonstrated that no more than 12% of that mixture could consist of a saturated hydrocarbon resulting from reduction of the double bond. The remaining 88% contained one double bond, which could be either in the Δ^1 (XV) or Δ^2 (XIV) position, since migration of a double bond during the Wolff–Kishner reduction of an α,β-unsaturated ketone has been reported several times.[22] Nuclear magnetic resonance measurements[23] demonstrated that 75% of the total mixture consisted of the migration product, *trans*-1,9-dimethyl-Δ^2-octalol-6 (XIV) with only 12% of the non-rearranged *trans*-1,9-dimethyl-Δ^1-octalol-6 (XV). For our purposes—introduction of an oxygen function at C-2—it was unnecessary to separate this mixture, since it was treated with hypobromous acid under

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(8) We are employing a numbering system (see I) for petasin which corresponds to that of its presumed eudalenoid biogenetic precursor.

(9) See C. Djerassi, R. Riniker and B. Riniker, THIS JOURNAL, **78**, 6362 (1956).

(10) C. Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, Chapter 10.

(11) See J. Simonsen and D. H. R. Barton, "The Terpenes," Cambridge University Press, 1952, Vol. III, pp. 212–224.

(12) C. Djerassi, R. Mauli and L. H. Zalkow, THIS JOURNAL, **81**, 3424 (1959); D. F. Grant and D. Rogers, *Chemistry & Industry*, 278 (1956).

(13) L. H. Zalkow, F. X. Markley and C. Djerassi, THIS JOURNAL, **81**, 2914 (1959).

(14) R. Robinson, "The Structural Relations of Natural Products," Oxford University Press, 1955, p. 12; see also J. B. Hendrickson, *Tetrahedron*, **7**, 82 (1959).

(15) We are greatly indebted to the Monsanto Chemical Co., St. Louis, Mo., for a generous gift of a precursor of IX.

(16) A. J. Speziale, J. A. Stephens and Q. E. Thompson, THIS JOURNAL, **76**, 5011 (1954).

(17) R. M. Evans, *Quart. Revs.*, **13**, 61 (1959).

(18) (a) A. Fürst and P. A. Plattner, *Helv. Chim. Acta*, **32**, 275 (1949); (b) D. H. R. Barton and R. C. Cookson, *Quart. Revs.*, **10**, 67 (1956).

(19) C. Djerassi, R. Riniker and B. Riniker, THIS JOURNAL, **78**, 6377 (1956).

(20) A. E. Lippman, E. W. Foltz and C. Djerassi, *ibid.*, **77**, 4364 (1955).

(21) C. Djerassi and D. Marshall, *ibid.*, **80**, 3986 (1958).

(22) (a) R. Fischer, G. Lardelli and O. Jeger, *Helv. Chim. Acta*, **34**, 1577 (1951), and earlier papers; (b) C. Djerassi and J. Fishman, THIS JOURNAL, **77**, 4291 (1955), have shown that such bond migration occurs also under Huang-Minlon's conditions (*ibid.*, **71**, 3301 (1949)).

(23) We are greatly indebted to Dr. James N. Shoolery of Varian Associates, Palo Alto, Calif., for the determination and interpretation of the nuclear magnetic resonance spectrum.

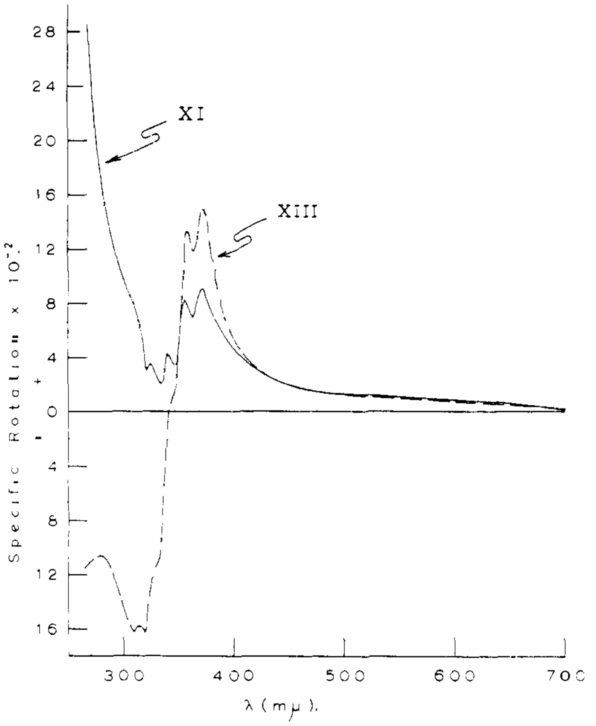

Fig. 1.—Optical rotatory dispersion curves (dioxane solution) of (+)-*trans*-1,9-dimethyl-6,7-oxido-Δ^1-octalone-3 (XI) and (+)-*trans*-1,9-dimethyl-6-hydroxy-Δ^1-octalone-3 (XIII).

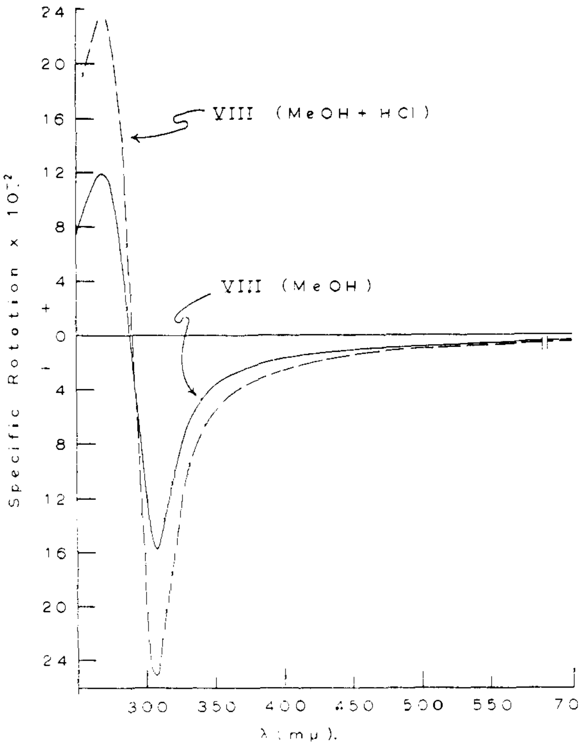

Fig. 2.—Optical rotatory dispersion curve of (−)-*trans*-1,9-dimethyldecalin-2,6-dione (VIII) in methanol and in methanol–hydrochloric acid solution.

conditions which in the case of Δ^1-[24] as well as Δ^2-[25] steroidal olefins (A/B *trans* ring juncture) yielded the expected[18b] diaxial bromohydrin. By analogy, the predominant product should be the bromohydrin XVII (from the Δ^2-octalol XIV) accompanied by a small amount of the isomer XVI. Since both bromohydrins should possess the newly introduced hydroxyl group in the identical position (C-2 of XVI and XVII), the mixture was oxidized to the isomeric bromo diketones XVIII and XIX and directly debrominated with chromous chloride[26] to the homogeneous, crystalline (−)-*trans*-1,9-dimethyldecalin-2,6-dione (VIII). Its structure was confirmed by its optical rotatory dispersion curve (Fig. 2), which was characterized by a negative Cotton effect. This type of Cotton effect was expected, since the 6-ketone should show a positive (by analogy to cholestan-3-one[27]) and the 2-keto group a negative (mirror image of cholestan-2-one[27]) Cotton effect. As the amplitude of the latter is considerably stronger,[27] it should govern the sign of the Cotton effect of the diketone VIII. Even more significant is the rotatory dispersion change (Fig. 2) attending the addition of a drop of hydrochloric acid to its methanol solution. As demonstrated earlier,[28] these conditions are sufficient to convert a 3-keto-5α-steroid (or its bicyclic analog in the decalone series) largely to its ketal, which does not any more show a Cotton effect curve. 2-Keto-5α-steroids, on the other hand, are not affected, because in the resulting ketal there would be set up a new 1,3-diaxial interaction with the angular methy group; furthermore, ketal formation is also inhibited[28] by the presence of adjacent alkyl groups. Both these factors should operate in the diketone VIII in such a manner that the 6-keto function with its dextrorotatory contribution (see Experimental for rotatory dispersion of VII) should be largely eliminated in the presence of hydrochloric acid *via* its ketal and that the resulting curve should now show an even stronger negative Cotton effect due to the sole contribution of the 2-keto function of VIII with its powerful negative Cotton effect. As shown in Fig. 2, this is precisely what happened experimentally.

All that was necessary now was to accomplish a tie-up between petasin (I) and the synthetic diketone VIII of established constitution and absolute configuration. For this purpose, des-isopropylidenepetasol (IV) was reduced with lithium in liquid ammonia, since such chemical reduction[29] is known to lead to the thermodynamically more stable A/B *trans* ring juncture. The resulting des-isopropylidenedihydropetasol (VII) was oxidized and yielded (−)-*trans*-1,9-dimethyldecalin-2,6-dione (VIII), which was identical in every respect with the above-

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[24] H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 4136 (1959). We are grateful to Prof. Henbest (Queens University, Belfast) for advance information on this subject.

[25] H. L. Slates and N. L. Wendler, THIS JOURNAL, **78**, 3749 (1956).

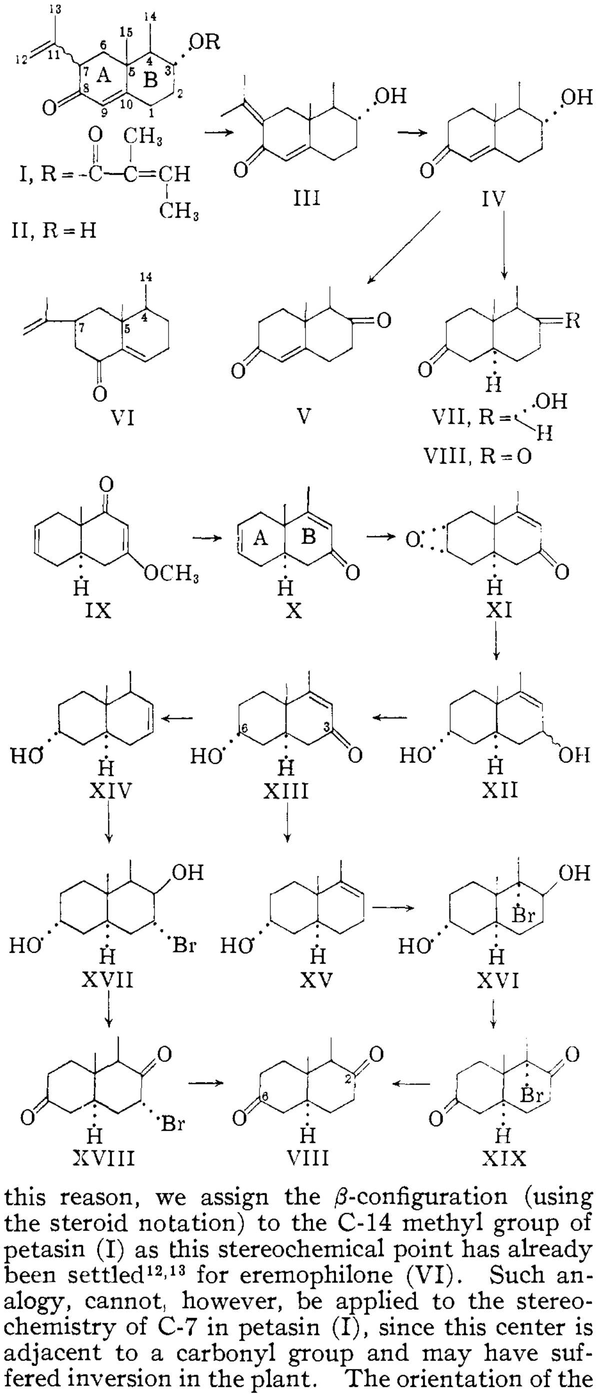
[26] (a) P. L. Julian, W. Cole, A. Magnani and E. W. Meyer, *ibid.*, **67**, 1728 (1945); (b) G. Rosenkranz, O. Mancera, J. Gatica and C. Djerassi, *ibid.*, **72**, 4077 (1950).

[27] C. Djerassi, W. Closson and A. E. Lippman, *ibid.*, **78**, 3163 (1956); see also Chapter 4 in ref. 10.

[28] C. Djerassi, L. A. Mitscher and B. J. Mitscher, *ibid.*, **81**, 947 (1959); see also Chapter 11 in ref. 10.

[29] For review and leading references see A. J. Birch and H. Smith, *Quart. Revs.*, **12**, 17 (1958).

described synthetic specimen. This experimental connection of petasin (I) with the synthetic diketone VIII completely confirms Aebi's structure[5] of petasin as well as the absolute configuration deduced[7] by rotatory dispersion measurements on des-isopropylidenepetasol (IV). Biogenetically, there is little doubt that petasin arises by methyl migration from an eudalenoid precursor possessing the same absolute configuration as the corresponding precursor in the eremophilone (VI) series.[13] For this reason, we assign the β-configuration (using the steroid notation) to the C-14 methyl group of petasin (I) as this stereochemical point has already been settled[12,13] for eremophilone (VI). Such analogy, cannot, however, be applied to the stereochemistry of C-7 in petasin (I), since this center is adjacent to a carbonyl group and may have suffered inversion in the plant. The orientation of the isopropenyl group attached to C-7 thus remains the only unknown feature of this interesting sesquiterpene.



Experimental[30]

Des-isopropylidenepetasol (IV).[5]—A solution of 300 mg. of isopetasol (III),[31] 600 mg. of potassium hydroxide, 15 cc. of ethanol and 18 cc. of water was heated under reflux with stirring in a current of nitrogen for 48 hr. Most of the ethanol was removed under reduced pressure, 100 cc. of saturated salt solution was added and the product was isolated by extraction with chloroform. The washed and dried extract was evaporated to dryness and the solid residue (219 mg., m.p. 73–89°) in chloroform was chromatographed on 10 g. of alumina (Alcoa, grade F-20). Elution with chloroform and recrystallization from cyclohexane afforded 90 mg. of des-isopropylidenepetasol (IV), m.p. 96–100.5°, λ_{max}^{MeOH} 236.5 mμ (ϵ 16,510); $\lambda_{max}^{CHCl_3}$ 2.98, 5.99 and 6.13μ; lit.[5] m.p. 102–103°, λ_{max}^{MeOH} 238 mμ (ϵ 17,520).

Des-isopropylidenedihydropetasol (VII).—An ethereal solution (150 cc.) of 200 mg. of des-isopropylidenepetasol (IV) was added dropwise to a stirred solution of 200 mg. of lithium in 200 cc. of liquid ammonia over a period of 30 min. After stirring for an additional 45 min., 4.0 g. of ammonium chloride was added slowly and stirring was continued for 2 hr. as the reaction flask gradually warmed to room temperature and the ammonia evaporated. Water (30 cc.) was added, the ether phase was separated and the aqueous layer was re-extracted with ether. All ether fractions were combined, washed with water, dried and evaporated and the residual oil (199 mg.) was chromatographed in chloroform solution on 10 g. of alumina. Elution with chloroform–methanol (95:5) led to 124 mg. of solid (m.p. 65–87°) which was distilled for analysis at a bath temperature of 90–95° and 0.4 mm. The colorless solid, m.p. 77–87°, λ_{infl}^{MeOH} 281 mμ (ϵ 45), $\lambda_{max}^{CHCl_3}$ 2.91 and 5.79 μ, contained less than 3% of unreacted α,β-unsaturated ketone as judged by the extinction (ϵ 383) at 237 mμ; R.D. in methanol (*c* 0.09): $[\alpha]_{700}$ +2°, $[\alpha]_{589}$ +9°, $[\alpha]_{307.5}$ +458°, $[\alpha]_{267.5}$ −592°, $[\alpha]_{260}$ −509°.

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27; O, 16.30. Found: C, 72.91; H, 10.01; O, 16.62.

Des-isopropylidenedihydropetasone (VIII).—A standard[32] chromium trioxide–sulfuric acid–water solution (0.3 cc.) was added dropwise with stirring at room temperature to a mixture of 85 mg. of des-isopropylidenedihydropetasol (VII) and 100 mg. of anhydrous magnesium sulfate in 15 cc. of acetone. After 20 min., 0.5 cc. of isopropyl alcohol and 100 mg. of sodium bicarbonate were added, most of the acetone was removed *in vacuo* and the residue was taken up in chloroform. Distillation of the washed and dried chloroform extract left 78 mg. of solid, m.p. 83–96°, which was chromatographed in chloroform solution on 10 g. of alumina. The chloroform-benzene (1:1) eluates yielded 55 mg. of the desired diketone VIII, m.p. 98–100°. Recrystallization from cyclohexane afforded the analytical specimen, m.p. 100–100.5°, λ_{max}^{MeOH} 284 mμ (ϵ 39), $\lambda_{max}^{CHCl_3}$ 5.86 μ; R.D. in methanol (*c* 0.10): $[\alpha]_{700}$ −28°, $[\alpha]_{589}$ −36°, $[\alpha]_{307.5}$ −1490°, $[\alpha]_{267.5}$ +1216°, $[\alpha]_{255}$ +860°. Addition of 0.01 cc. of concd. hydrochloric acid and repetition of the dispersion curve now gave a trough at $[\alpha]_{307.5}$ −2368° and a peak at $[\alpha]_{267.5}$ +2269°.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34; O, 16.47. Found: C, 74.13; H, 9.30; O, 16.39.

(+)-trans-1,9-Dimethyl-6,7-oxido-Δ^1-octalone-3 (XI).—A solution of 1.06 g. of (+)-*trans*-1,9-dimethyl-$\Delta^{1,6}$-hexalone-3 (X)[13] in 175 cc. of benzene was treated at 27° with 25 cc. of a 0.286 *N* perbenzoic acid in benzene solution, the flask being protected from direct light. The course of the reaction was followed iodometrically and after 15 hr. one molar equivalent of perbenzoic acid was consumed. The solution was washed with 5% aqueous potassium carbonate solution, water, dried and evaporated to yield 0.99

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[30] Melting points were determined on the Kofler block. We are indebted to Miss B. Bach for the infrared spectral measurements, to Mrs. T. Nakano for the optical rotatory dispersion determinations, and to Dr. J. M. Vandenbelt and associates, Parke, Davis and Co., Detroit, Mich .for certain ultraviolet absorption curves. The microanalyses are due to Dr. A. Bernhardt, Mülheim, Germany.

[31] We are indebted to Dr. J. Renz (Sandoz, Ltd., Basel) for a gift of isopetasol with the following constants: m.p. 122.5–125°, $[\alpha]_D$ +116.6° (*c*, 1.04 in chloroform), λ_{max}^{MeOH} 245 (ϵ 17,500) and 279 mμ (ϵ 9800); $\lambda_{max}^{CHCl_3}$ 2.77, 2.92, 6.02 and 6.15 μ.

[32] A. Bowers, T. G. Halsall, E. R. H. Jones and A. J. Lemin, *J. Chem. Soc.*, 2555 (1953).

g. of a yellowish oil which was dissolved in benzene and chromatographed on 50 g. of alumina. The combined benzene–chloroform and chloroform eluates provided 0.66 g. of crude epoxide, m.p. 51–58°, whose melting point was raised to 60–62° (0.49 g.) after one recrystallization from hexane. The analytical sample was obtained from cyclohexane as colorless crystals, m.p. 64.5–65.5°, $\lambda_{\max}^{\mathrm{MeOH}}$ 235.5 mμ (ϵ 14,100), $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.99 and 6.13 μ; R.D. (Fig. 1) in dioxane (c 0.088): $[\alpha]_{589}$ +77°, $[\alpha]_{370}$ +910°, $[\alpha]_{362.5}$ +695°, $[\alpha]_{355}$ +831°, $[\alpha]_{347.5}$ +341°, $[\alpha]_{340}$ +436°, $[\alpha]_{335}$ +200°, $[\alpha]_{325}$ +363°, $[\alpha]_{322.5}$ +309°, $[\alpha]_{265}$ +2840°.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39; O, 16.65. Found: C, 74.93; H, 8.67; O, 16.56.

(+)-*trans*-1,9-Dimethyl-6-hydroxy-Δ^1-octalone-3 (XIII).—To a stirred and refluxing suspension of 300 mg. of lithium aluminum hydride in 25 cc. of anhydrous ether was added dropwise in a current of nitrogen a solution of 192 mg. of the above oxide XI in 25 cc. of ether. After continued stirring under reflux for 7.5 hr., the mixture was cooled, 2 cc. of water was added and this was followed, after stirring for 15 min., by 5.0 g. of anhydrous sodium sulfate. The insoluble material was filtered, washed well with ether and the combined ether filtrate and washes were dried and evaporated. The residual oil was placed in chloroform solution on a column of 10 g. of alumina; elution with chloroform–methanol (8:2) produced 158 mg. of the diol XII, which did not exhibit any infrared carbonyl bands.

The above alcohol in 50 cc. of chloroform was stirred at room temperature for 6.5 hr. with 2.0 g. of manganese dioxide,[33] the inorganic material was then filtered and washed well with chloroform. Evaporation of the chloroform and chromatography of the residue (135 mg.) on 10 g. of alumina gave 115 mg. of colorless solid (m.p. 84–92°) in the chloroform eluted fractions. Four recrystallizations from cyclohexane led to 63 mg. of analytically pure *trans*-1,9-dimethyl-6-hydroxy-Δ^1-octalone-3 (XIII), m.p. 91–94.5°, $\lambda_{\max}^{\mathrm{MeOH}}$ 238 mμ (ϵ 13,360); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 3.00, 6.02 and 6.15 μ; R.D. (Fig. 1) in dioxane (c 0.105): $[\alpha]_{589}$ +72°, $[\alpha]_{372.5}$ +1487°, $[\alpha]_{362.5}$ +1190°, $[\alpha]_{357.5}$ +1327°, $[\alpha]_{320}$ −1620°, $[\alpha]_{315}$ −1578°, $[\alpha]_{310}$ −1620°, $[\alpha]_{277.5}$ −1057°, $[\alpha]_{265}$ −1151°.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34; O, 16.47. Found: C, 74.03; H, 9.46; O, 16.56.

Wolff–Kishner Reduction of (+)-*trans*-1,9-Dimethyl-6-hydroxy-Δ^1-octalone-3 (XIII).—A solution of 800 mg. of the hydroxyoctalone XIII (m.p. 83–92°) in 35 cc. of diethylene glycol was treated successively with 1 cc. of 95% anhydrous hydrazine and 500 mg. of pulverized potassium hydroxide. The mixture was heated under reflux with stirring for 2 hr. at 135° (internal temperature), the condenser was replaced by a Claisen distilling head and the internal temperature was raised over a period of 1 hr. to 180–190°. After maintaining the mixture at that temperature for 9 hr., the contents of the flask and the distillate (2 cc.) were combined, diluted with 200 cc. of water and extracted with chloroform. The dried chloroform solution was evaporated and the residue was chromatographed on 50 g. of alumina. The benzene and benzene–ether (9:1) eluates were combined to yield 555 mg. of pale yellow oil, which was distilled at a bath temperature of 70–75° and 0.3 mm. affording 505 mg. of a hydrocarbon fraction lacking carbonyl absorption in the infrared.

Anal. Calcd. for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.57; H, 11.07.

Hydrogenation of 8.49 mg. of the product at 20.2° in 6 cc. of absolute ethanol with 11 mg. of pre-reduced 5% palladized charcoal catalyst resulted in the uptake of 0.93 cc. of hydrogen within 21 min. This indicated an 88% content of olefins (calcd. 1.06 cc.) and the nuclear magnetic resonance spectrum[23] showed the presence of *ca.* 75% *trans*-1,9-dimethyl-Δ^2-octalol-6 (XIV) and approximately 12% each of *trans*-1,9-dimethyl-Δ^1-octalol-6 (XV) and *trans*-1,9-dimethyldecalol-6.

(−)-trans-1,9-Dimethyldecalin-2,6-dione (VIII).—A solution of 477 mg. of the above hydrocarbon mixture in 47.5 cc. of *t*-butyl alcohol and 2.5 cc. of water was treated at 0° with a suspension of 677 mg. of N-bromosuccinimide in 59.6 cc. of *t*-butyl alcohol and 0.9 cc. of water, followed by 5.4 cc. of 1 *N* perchloric acid.[24] Some insoluble solid remained which dissolved upon the addition of 23.7 cc. of *t*-butyl alcohol and 1.25 cc. of water. The mixture was maintained at 5° for 19 hr., concentrated *in vacuo* to a volume of 10 cc., diluted with 100 cc. of water and extracted with ether. Evaporation of the dried ether solution to dryness left 7–8 mg. of viscous oil representing the mixture of bromohydrins XVI and XVII. Partial oxidation of the hydroxyl groups appeared to have occurred judging by a medium strong infrared absorption band at 5.87 μ.

The total oil was dissolved in 75 cc. of acetone, 500 mg. of anhydrous magnesium sulfate was added followed by dropwise addition of 2.0 cc. of standard chromium trioxide solution.[32] After 20 minutes, the reaction mixture was processed exactly as described above for the oxidation of des-isopropylidenedihydropetasol (VII) yielding 582 mg. of brownish oil, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.84 μ.

No attempt was made to purify this mixture of bromo ketones XVIII and XIX, but rather the oil was dissolved in 100 cc. of acetone and to it was added in portions over a period of 20 minutes 35 cc. of a chromous chloride solution[26b]) while maintaining the mixture under an atmosphere of carbon dioxide. After stirring for a total of 1 hr., the solution was concentrated to a volume of 50 cc., diluted with water and extracted with chloroform. Evaporation of the dried chloroform solution furnished 407 mg. of semi-crystalline material which was chromatographed on 25 g. of alumina. Elution with benzene–chloroform (1:9) afforded 141 mg. of colorless solid, m.p. 80–94°, while several recrystallizations from cyclohexane led to 81 mg. of the analytical specimen of (−)-*trans*-1,9-dimethyldecalin-2,6-dione (VIII), m.p. 99–101.5°, $\lambda_{\max}^{\mathrm{MeOH}}$ 283.5 mμ (ϵ 36), $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.86 μ; R.D. (Fig. 2) in methanol (c 0.105): $[\alpha]_{700}$ −42°, $[\alpha]_{589}$ −53°, $[\alpha]_{307.5}$ −1570°, $[\alpha]_{267.5}$ +1188°, $[\alpha]_{250}$ +758°. After addition of 0.01 cc. of concd. hydrochloric acid, the trough was changed to $[\alpha]_{307.5}$ −2506° and the peak to $[\alpha]_{267.5}$ +2373°. Identity of this diketone and des-isopropylidenedihydropetasone (VIII) was established by mixture melting point determination and infrared comparison as well as by the similarity of the optical rotatory dispersion curves in methanol and their amplitude changes upon addition of hydrochloric acid.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34; O, 16.47. Found: C, 74.52; H, 9.12; O, 16.59.

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[33] Prepared by Dr. B. Berkoz in this Laboratory according to the procedure of O. Mancera G. Rosenkranz and F. Sondheimer, *J. Chem. Soc.*, 2189 (1953).