gave 1.1 g. (29%) of a pale yellow oily acid which could not be crystallized.

The amide was prepared by the procedure given for the amide of the acid obtained from the diolefin. A 0.250-g. sample of the acid gave 0.140 g. of impure amide of m.p. 87–92°. On two recrystallizations from aqueous ethanol the silky needles melted at 97–98°. Analysis was correct for ω-(2,3-dimethoxyphenyl)-caprylamide.

Anal. Calcd. for $C_{16}H_{25}O_3N$: C, 68.78; H, 9.01. Found: C, 68.71; H, 8.94.

Ultraviolet Absorption Spectra.—The ultraviolet spectra of the saturated, diolefinic and triolefinic components of dimethyl "urushiol" were determined using a Cary recording photoelectric spectrophotometer with 0.00010 *M* solutions in 95% ethanol. Very similar spectra for the corresponding components of methylcardanol have been presented elsewhere.[13]

Acknowledgment.—The authors are indebted to the Lederle Laboratories Division of the American Cyanamid Company for a grant to Columbia University for support of this investigation.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Terpenes. I. Structure and Synthesis of the $C_{17}H_{20}$ Hydrocarbon Obtained by Dehydrogenation of Agathic Acid

BY G. BÜCHI AND JAMES J. PAPPAS

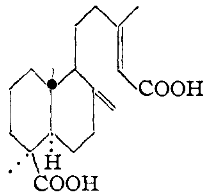
RECEIVED OCTOBER 17, 1953

1,1,4,7-Tetramethylphenalan has been synthesized and shown to be identical with the hydrocarbon $C_{17}H_{20}$ obtained by dehydrogenation of agathic acid.

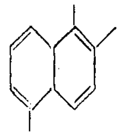
The structure of agathic acid (I) has been established through the researches of Ruzicka and his co-workers.[1] The carbon skeleton of this compound was determined from the structures of the aromatic hydrocarbons formed in the dehydrogenation of agathic acid. The detailed structure was deduced from results obtained in a study of oxidative degradation. The *trans*-locking of the two rings was demonstrated by conversion of agathic acid (I) to a degradation product of manoöl[2] which in turn had been related to abietic acid,[3] the structure of which is known in all details.[4]

Dehydrogenation of agathic acid with either sulfur or selenium gave agathalene (1,2,5-trimethylnaphthalene) (II), pimanthrene (1,7-dimethylphenanthrene) (III) and a hydrocarbon $C_{17}H_{20}$ (IV).[1a] When tetrahydroagathic acid was dehydrogenated, agathalene and the $C_{17}H_{20}$ hydrocarbon (IV) were isolated but pimanthrene (III) could not be detected.

The hydrocarbon $C_{17}H_{20}$ (IV) was resistant to further dehydrogenation and readily absorbed two equivalents of hydrogen when hydrogenated over Adams platinum catalyst. Exhaustive oxidation of IV with potassium ferricyanide in aqueous potassium hydroxide solution gave a ketodicarboxylic acid $C_{16}H_{12}O_5$ (V). The ultraviolet absorption spectrum of IV was similar to the spectrum of naphthalene and Ruzicka and Rey[5] assumed that IV was 3,6-dimethyl-1-isopropylacenaphthene (VI). When they synthesized VI they found it to be different from the hydrocarbon obtained from agathic acid. Fieser and Fieser[4] suggested 2,2,8-trimethyl-1,2,3,4-tetrahydrophenanthrene (VII) as an expression for the $C_{17}H_{20}$ hydrocarbon. However, this structure can be ruled out because it would not give a ketodicarboxylic acid ($C_{16}H_{12}O_5$) an oxidation with potassium ferricyanide, and in addition VII should give pimanthrene on further dehydrogenation. It is worthy of note that the structure of this important product of dehydrogenation, in which more carbon atoms of agathic acid are retained than in any other one, was, until the present investigation, still unknown. The knowledge of its structure would certainly have facilitated the efforts to arrive at a structural expression for agathic acid (I). In this paper we report work on the structure and a synthesis of the hydrocarbon $C_{17}H_{20}$ (IV).



I



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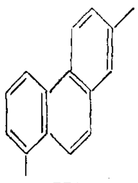

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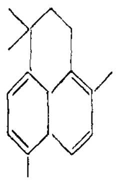
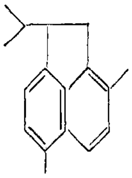
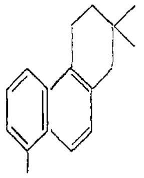


IV



VI



VII

We turn first to a discussion of a possible mecha-

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[1] (a) L. Ruzicka and J. R. Hosking, *Ann.*, **469**, 147 (1929); *Helv. Chim. Acta*, **13**, 1402 (1930); *ibid.*, **14**, 203 (1931); (b) L. Ruzicka, R. Steiger and H. Schinz, *ibid.*, **9**, 962 (1926); (c) L. Ruzicka and H. Jacobs, *Rec. trav. chim.*, **57**, 509 (1938); (d) L. Ruzicka, E. Bernold and A. Tallichet, *Helv. Chim. Acta*, **24**, 223 (1941); (e) L. Ruzicka and E. Bernold, *ibid.*, **24**, 931 (1941); *ibid.*, **24**, 1167 (1941).

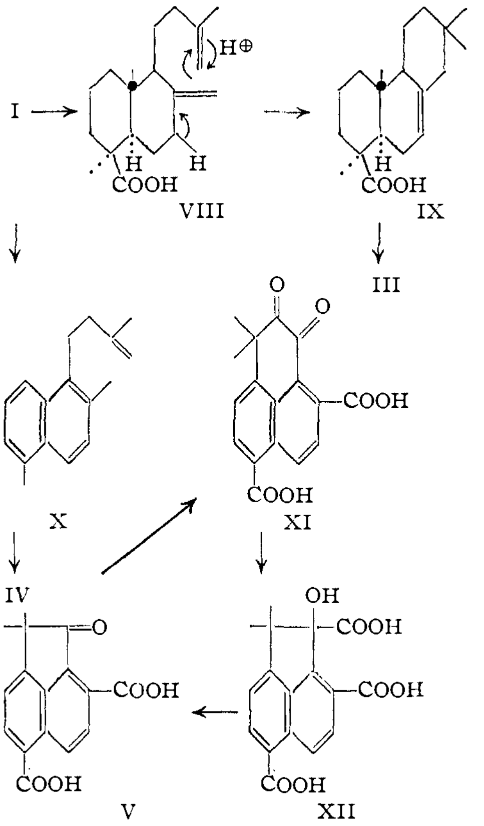
[2] L. Ruzicka, R. Zwicky and O. Jeger, *ibid.*, **31**, 2143 (1948).

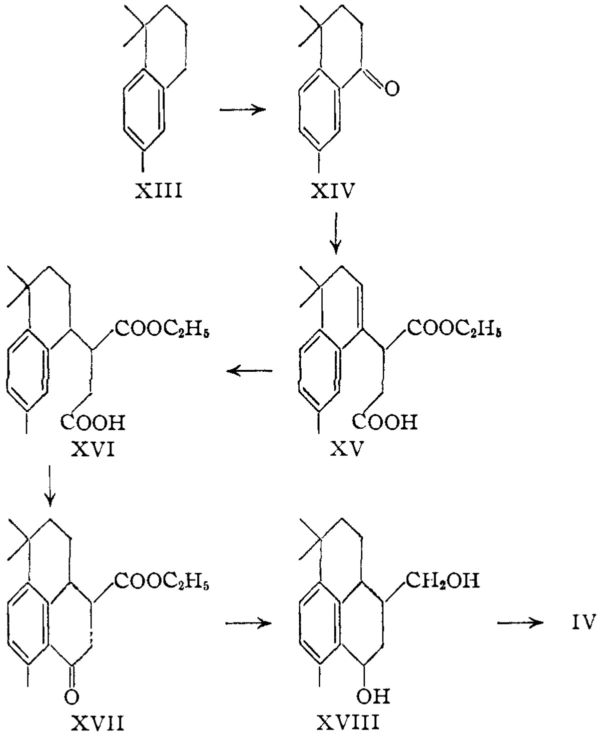
[3] O. Jeger, O. Dürst and G. Büchi, *ibid.*, **30**, 1853 (1947).

[4] *Cf.* J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. III, Cambridge University Press, Cambridge, 1952; L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, N. Y., 1949.

[5] L. Ruzicka and E. Rey, *Helv. Chim. Acta*, **26**, 2136 (1943).

nism of ring closure during the dehydrogenation of agathic acid. The formation of pimanthrene involves the synthesis of a new carbocyclic ring, which must precede the aromatization of the bicyclic system. This change may go through the following stages: (a) decarboxylation of agathic acid to an intermediate VIII; (b) cyclization of VIII to a tricyclic species IX, a reaction which is probably catalyzed by either hydrogen selenide or hydrogen sulfide depending on the dehydrogenating agent used; and (c) dehydrogenation of IX to pimanthrene (III). This mechanism explains the absence of pimanthrene (III) in the products of the dehydrogenation of tetrahydroagathic acid.[1a] If the dehydrogenation precedes the formation of the third ring the production of a phenanthrene hydrocarbon becomes impossible, but instead substitution on the α-carbon atom of the naphthalene nucleus can occur in the intermediate X and the resulting product is 1,1,4,7-tetramethylphenalan ($C_{17}H_{20}$) IV. The formula IV explains all of the reported reactions of the hydrocarbon $C_{17}H_{20}$ thus: (a) phenalan and its homologs are resistant to further dehydrogenation[6]; (b) two out of the five double bonds present in such compounds can be hydrogenated over Adams platinum catalyst; (c) the ultraviolet spectrum is similar to the spectrum of naphthalene; and (d) the oxidation of IV with potassium ferricyanide in basic solution leads to a ketodicarboxylic acid V. Oxidation to carboxyl and ketone functions, respectively, would occur at the activated methyl and methylene groups to give intermediate XI. This α-diketone could undergo a benzilic acid rearrangement and the α-hydroxy acid XII would be oxidized further to $C_{16}H_{12}O_5$ (V) which would be resistant to further oxidation because it does not contain any activated hydrogen atoms. Consequently we were convinced that the $C_{17}H_{20}$ hydrocarbon has structure IV and decided to synthesize this compound.





Ionene (XIII) was oxidized with chromium trioxide in acetic acid solution,[7] and the neutral fraction separated into ketonic and non-ketonic fractions by extraction with Girard reagent "T." A ketone whose ultraviolet spectrum was similar to that of tetralone[8] was obtained in approximately 25% yield. The compound was identical with 4,4,7-trimethyl-3,4-dihydro-1(2H)-naphthalenone (XIV) which had previously been synthesized by another route.[9] The Stobbe condensation between diethyl succinate and XIV proceeded in excellent yield when potassium *t*-butoxide[10] was used as a condensing agent. The ultraviolet absorption spectrum indicated that the ester is β-carbethoxy-β-(4,4,7-trimethyl-3,4-dihydro-1-naphthyl)-propionic acid (XV) rather than the corresponding α,β-unsaturated ester. The hydrogenation of XV to β-carbethoxy-β-(4,4,7-trimethyl-1,2,3,4-tetrahydro-1-naphthyl)-propionic acid (XVI) was fastest in the presence of a mixed catalyst consisting of palladium on charcoal and Adams platinum catalyst. Conversion of XVI to XVII could not be brought about by anhydrous hydrogen fluoride. Cycliza-

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(6) (a) L. C. Craig, W. A. Jacobs and G. I. Lavin, *J. Biol. Chem.*, **139**, 277 (1941); (b) K. Fleischer and E. Retze, *Ber.*, **55**, 3280 (1922).

(7) The oxidation of ionene was reported previously by F. Tiemann and P. Krüger (*Ber.*, **26**, 2694 (1893)) but they did not investigate the neutral compounds formed in this reaction.

(8) Mme. P. Ramart-Lucas and M. J. Hoch, *Bull. soc. chim.*, **5**, 848 (1938).

(9) R. A. Barnes and G. R. Buchwalter, THIS JOURNAL, **73**, 3858 (1951).

(10) W. S. Johnson, H. C. E. Johnson and J. W. Petersen, *ibid.*, **67**, 1360 (1945).

tion of XVI in the presence of phosphorus pentoxide in benzene under reflux gave 3-carbethoxy-6,6,9-trimethyl-2,3,4,5,6,13-hexahydrophenalone (XVII) which crystallized after chromatography. Smooth reduction of XVII with lithium aluminum hydride formed 3-hydroxymethyl-6,6,9-trimethyl-1-hydroxy-2,3,4,5,6,13-hexahydrophenalan (XVIII). Dehydration of XVIII was effected by treatment with phosphorus pentoxide in boiling benzene. The hydrocarbon IV (1,1,4,7-tetramethylphenalan) was purified by chromatography. The infrared and ultraviolet absorption spectra of the synthetic hydrocarbon were identical with the corresponding spectra of IV obtained by dehydrogenation of agathic acid.[11] The picrate and styphnate of the synthetic hydrocarbon had melting points corresponding to the ones reported by Ruzicka, *et al.*,[1a] and an authentic sample of the picrate did not depress the melting point of our specimen.

Experimental[12]

Ionene (XIII).—Ionene was prepared from a mixture of commercial ionones by the method of Bogert and Fourman.[13] The yield was 36%; b.p. 108–110° (10 mm.), n^{25}D 1.5218.

4,4,7-Trimethyl-3,4-dihydro-1(2H)-naphthalenone (XIV).—In a 3-l. three-necked flask equipped with stirrer, dropping funnel and thermometer was placed 159 g. (0.914 mole) of XIII dissolved in 700 ml. of glacial acetic acid. A solution of 196 g. (1.96 moles) of chromic acid anhydride in 100 ml. water and 600 ml. glacial acetic acid was added dropwise at such a rate as to keep the reaction mixture at room temperature. The addition required 6 hours and the resultant solution was allowed to stand overnight. This solution was diluted eightfold with water and extracted with two 1-l. portions of ether. The combined ether extracts were washed thoroughly with saturated sodium bicarbonate solution and then with water. After drying over sodium sulfate the ether was distilled, yielding a residue of 113 g. of non-acidic material. The sodium bicarbonate extracts were acidified with dilute hydrochloric acid and the acids obtained amounted to 42 g.

The non-acids (113 g.) were dissolved in 900 ml. of absolute methanol and 54 g. of glacial acetic acid. This solution was added to 150 g. of Girard reagent "T" (betaine hydrazide hydrochloride), and the mixture was heated under reflux for 1 hour. After cooling, the solution was added to 45 g. of sodium carbonate in 900 g. of water and 900 g. of ice. The non-ketones were extracted with two 1-l. portions of ether. The ether extracts were washed with water, dried over sodium sulfate and distilled. The yield of non-ketones was 52 g. Dilute hydrochloric acid was added to the water solution until congo red paper turned blue. The solution was allowed to stand for 2 hours after which time an oil heavier than water separated. The oil was taken up in ether and the ether was washed with water, dried over sodium sulfate and distilled. The yield of ketones was 58 g. Distillation yielded 40.5 g. (24%) of XIV, b.p. 142–143° (8 mm.), n^{25}D 1.5469 (lit.[9] 1.5470).

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.90; H, 8.60.

The 2,4-dinitrophenylhydrazone of XIV was prepared in the usual way and recrystallized from 95% ethanol, m.p. 253–254° (lit.[9] 253–254°).

Anal. Calcd. for $C_{19}H_{20}O_4N_4$: C, 61.94; H, 5.47. Found: C, 62.00; H, 5.34.

β-Carbethoxy-β-(4,4,7-trimethyl-3,4-dihydro-1-naphthyl)-propionic Acid (XV).—A mixture of 25.0 g. (0.133 mole) of XIV and 34.8 g. (0.200 mole) of diethyl succinate was added with 27 ml. of dry *t*-butyl alcohol (to aid in transfer) to a chilled solution of 5.7 g. (0.146 mole) of potassium in 110 ml. of dry *t*-butyl alcohol. The addition required 0.5 hour, but the solution was stirred for an additional period of 1.5 hours. The brownish-red solution was then heated under reflux for 40 minutes in a system which had been previously filled with nitrogen. After cooling, the mixture was acidified with dilute hydrochloric acid and the solvent was removed under reduced pressure. The oil which separated was taken up in ether, and the ether was washed with water and then thoroughly with saturated sodium bicarbonate solution. The sodium bicarbonate extracts were washed with ether and then acidified with dilute hydrochloric acid. The oil which separated was taken up in ether, and the ether was washed twice with water, dried with sodium sulfate and distilled. The yield of XV, which solidified on standing in the ice-box for a week, was 36.5 g. (87%). Crystallization from methanol–water gave an analytical sample with m.p. 81–83°.

Anal. Calcd. for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 71.99; H, 7.73.

β-Carbethoxy-β-(4,4,7-trimethyl-1,2,3,4-tetrahydro-1-naphthyl)-propionic Acid (XVI).—Hydrogenation of 36.0 g. of XV in 200 ml. of ethyl acetate in the presence of 2.00 g. of 10% palladium-on-charcoal and 0.21 g. of platinum oxide at atmospheric pressure and room temperature was complete in 5 hours. The calculated amount of one molar equivalent of hydrogen was absorbed. The catalyst was separated by filtration, and the ethyl acetate was distilled. Purification of the product by recrystallization from acetone–water yielded 34.1 g. (92%) of XVI, m.p. 121–122°.

Anal. Calcd. for $C_{19}H_{26}O_4$: C, 71.66; H, 8.23. Found: C, 71.57; H, 8.26.

3-Carbethoxy-6,6,9-trimethyl-2,3,4,5,6,13-hexahydrophenalone (XVII).—A solution of 28.7 g. of XVI in 350 ml. of benzene was added to 150 g. of powdered phosphorus pentoxide and the suspension was heated under gentle reflux for 2 hours. After cooling the mixture, the phosphorus pentoxide was neutralized with an excess of sodium bicarbonate solution. The mixture was diluted with 1 l. of water. The water layer was separated and extracted with two 500-ml. portions of ether. The benzene and ether layers were combined, extracted once more with sodium bicarbonate solution, and washed twice with water. After drying over sodium sulfate, the ether and benzene were distilled. The resultant, tarry-looking mass weighed 28.2 g. This product was dissolved in petroleum ether and passed through a chromatographic column packed with 100 g. of alumina. The column was eluted with a 10 to 1 solution of petroleum ether in benzene. Upon distillation of the petroleum ether and benzene 6.9 g. (25%) of a light yellow crystalline residue of crude XVII was obtained. An analytical sample was recrystallized from 95% ethanol and was obtained as a colorless solid, m.p. 93.0–93.5°.

Anal. Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.88; H, 8.30.

The 2,4-dinitrophenylhydrazone of XVII was prepared in the usual way and recrystallized from 95% ethanol, m.p. 196–197° dec.

Anal. Calcd. for $C_{25}H_{28}N_4O_4$: C, 62.48; H, 5.87. Found: C, 62.32; H, 5.92.

3-Hydroxymethyl-6,6,9-trimethyl-1-hydroxy-2,3,4,5,6,13-hexahydrophenalan (XVIII).—A dry 500-ml. three-necked flask was fitted with a mercury-sealed mechanical stirrer, a dropping funnel and a reflux condenser. A solution of 5.0 g. (0.132 mole) of lithium aluminum hydride in 200 ml. of ether was transferred to the reaction flask. A solution of 5.6 g. (0.0215 mole) of XVII in 125 ml. of ether was added dropwise from the dropping funnel at such a rate that the capacity of the reflux condenser was not exceeded. The addition required 15 minutes. The mixture was allowed to stand with continued stirring for 3 hours after the addition had been completed. Water was then placed in the dropping funnel, and, with an ice-bath surrounding the reaction vessel, was added cautiously, one drop at a time, until there was no further evidence of hydrogen gas evolution. This was followed by 200 ml. of 10% sulfuric acid, which caused the precipitated alumina to dissolve. The contents of the flasks were then transferred to a separatory funnel, and the aqueous phase was extracted twice with 1-l. portions of ether. The combined ether solutions were dried over so-

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(11) We should like to express our appreciation to Dr. O. Jeger, Eidg. Techn. Hochschule, Zürich, for sending us samples of the hydrocarbon and its derivatives for comparison purposes.

(12) All melting points are corrected and boiling points are uncorrected. We are indebted to Dr. S. M. Nagy and his associates for analyses.

(13) M. T. Bogert and V. G. Fourman, This Journal, **55**, 4670 (1933).

dium sulfate and distilled. Crystallization of the product from ether yielded 4.6 g. (95%) of XVIII, m.p. 158–160°. An analytical sample, recrystallized from ether, melted with decomposition at 160–162°.

Anal. Calcd. for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.18; H, 9.23.

1,1,4,7-Tetramethylphenalan (IV).—A solution of 4.2 g. of XVIII in 110 ml. of benzene was added to 10 g. of powdered phosphorus pentoxide and the suspension was heated under gentle reflux for 3 hours. After cooling the mixture, the phosphorus pentoxide was neutralized with an excess of sodium hydroxide and the mixture was diluted with 200 ml. of water. The water layer was separated and extracted with two 100-ml. portions of ether. The benzene and ether layers were combined, extracted once more with sodium hydroxide and washed four times with water. After drying over sodium sulfate, the ether and benzene were distilled, leaving a tarry-looking residue of 3.6 g. This product was dissolved in petroleum ether and passed twice through a chromatographic column packed with 50 g. of alumina. Upon distillation of the petroleum ether 1.2 g. (33%) of a very light-colored semi-liquid, which solidified only upon standing in an ice-box for a week, was obtained. An analytical sample was obtained by distilling a portion of the product in high vacuum.

Anal. Calcd. for $C_{17}H_{20}$: C, 91.01; H, 8.99. Found: C, 90.97; H, 9.13.

The picrate of IV was prepared from stoichiometric amounts of IV and picric acid. When purified by recrystallization from 95% ethanol, this compound melted at 135.5–136.0° (lit.[1a] 138–139°). A mixed melting point with an authentic sample showed no melting point depression.

Anal. Calcd. for $C_{23}H_{23}N_3O_7$: C, 60.89; H, 5.12. Found: C, 60.83; H, 5.34.

The styphnate of IV was prepared from stoichiometric amounts of IV and styphnic acid. When purified by recrystallization from 95% ethanol, this compound melted at 151.6–152.4° (lit.[1a] 153–154°).

CAMBRIDGE, MASSACHUSETTS

[JOINT CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY AND THE INSTITUTO DE QUIMICA DE LA UNIVERSIDAD NACIONAL AUTONOMA DE MEXICO]

Terpenoids. V.[1] The Isolation of Iresin, a New Sesquiterpene Lactone[2]

BY CARL DJERASSI, PASUPATI SENGUPTA,[3] J. HERRAN AND F. WALLS

RECEIVED DECEMBER 9, 1953

From the Mexican plant *Iresine celosioides* there was isolated a new tricyclic sesquiterpene $C_{15}H_{22}O_4$, now named iresin. Two of the oxygen atoms are present as easily acylable hydroxyl groups while the other oxygen atoms are involved in an α,β-unsaturated five-membered lactone ring.

Iresine celosioides, a shrub occurring commonly in the Federal District of Mexico, belongs to the *Amarantacea* plant family, which from a chemical standpoint has hardly been investigated. It is known popularly as "tlatlancuaya"[4] and extracts of this plant and related *Iresine* species have been used by the natives for the treatment of various diseases including malaria and typhoid.[5] During the present chemical study, which confirmed the earlier reported[6] absence of alkaloids, there was isolated a new sesquiterpene, the preliminary characterization of which forms the subject of the present communication.

The alcoholic extract of *Iresine celosioides* upon dilution with water and addition of lead acetate produced a voluminous precipitate which was discarded. Repeated extraction of the filtrate with chloroform and subsequent evaporation of the solvent yielded a semi-crystalline residue which could be purified readily by chromatography. The pure, crystalline substance thus obtained exhibited m.p. 140–142°, $[\alpha]^{28}D$ +21°, $\lambda_{\max}^{\mathrm{EtOH}}$ 224 mμ (log ϵ 4.16) and pronounced infrared bands (*cf.* Fig. 1) at 2.95, 5.71 and 5.92 μ. The empirical formula $C_{15}H_{22}O_4$ indicates a sesquiterpenoid structure and we have named this new substance "iresin," the ending "-in" following that of the sesquiterpene lactones santonin and artemisin. With acetic anhydride at room temperature, iresin forms a diacetate, the infrared spectrum of which shows the absence of hydroxyl groups; in addition to the bands at 5.70 and 5.92 μ originally present in iresin, there were now also observed the characteristic acetate bands at 5.80 and 8.10 μ. Mild alkaline saponification at room temperature regenerated iresin, thus demonstrating that two of the oxygen atoms are present as hydroxyl groups. Since iresin is unaffected by lead tetraacetate, the hydroxyl functions cannot be vicinal.

A number of observations lead to the conclusion that the remaining two oxygen atoms form part of a lactone ring. Iresin is soluble in dilute sodium hydroxide solution and cannot be extracted from it with chloroform unless the solution is first acidified. The infrared absorption band at 5.71 μ is typical of an α,β-unsaturated five-membered lactone[7]; this was confirmed by several color reactions[8] given in the experimental portion of this paper and especially by the high intensity ultraviolet absorption maximum at 224 mμ. This is precisely the region in which ultraviolet absorption maxima[9] are exhib-

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(1) Paper IV, C. Djerassi, L. E. Geller and A. J. Lemin, *Chemistry and Industry*, 161 (1954).

(2) We are indebted to the Rockefeller Foundation for funds in support of the plant collections.

(3) Schenley Postdoctorate Research Fellow at Wayne University, 1952–1953.

(4) According to M. Martinez ("Catalogo de Nombres Vulgares y Cientificos de Plantas Mexicanas," Ediciones Botas, Mexico, D.F. 1937) the name "tlatlancuaya" refers to different *Iresine* species depending upon the locality. In the Federal District, it is the presently studied *I. celosioides*, in Puebla, *I. calea*, while in Morelos it applies to *I. interrupta*. We are indebted to Srta. Elizabeth Berlin and Prof. M. Martinez for the botanical identification of our material which was collected in the Federal District.

(5) *Cf.* M. Martinez, "Las Plantas Medicinales de Mexico," 3rd Edition, Ediciones Botas, Mexico, D.F., 1944, p. 285.

(6) F. Villasenor, *Anal. Inst. Medico Nacional (Mexico)*, **6**, 193 (1903).

(7) *Cf.* J. F. Grove and H. A. Willis, *J. Chem. Soc.*, **877** (1951).

(8) *Cf.* F. A. Kuehl, R. P. Linstead and B. A. Orkin, *ibid.*, 2213 (1950).

(9) *Inter al*, L. J. Haynes and E. R. H. Jones, *ibid.*, 954 (1946); D. D. E. Newman and L. N. Owen, *ibid.*, 4721 (1952); W. G. Dauben and P. D. Hance, THIS JOURNAL, **75**, 3352 (1953).