[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF ILLINOIS]

THE STRUCTURE OF CHAULMOOGRIC AND HYDNOCARPIC ACIDS. I

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The compounds present in chaulmoogra oil which are responsible for its curative action in the treatment of leprosy are chaulmoogric and hydnocarpic acids.[2] Although the earlier authentic reports on treatment with chaulmoogra oil date back to 1899, the specific therapeutic action of the chaulmoogric and hydnocarpic acids has been studied chiefly since 1916, when Hollman and Dean[3a] showed the excellent clinical results obtained by the use of the ethyl esters and Rogers[3b] published his results on the use of the sodium salts.

The pioneer work on the constituents of chaulmoogra oil and the chemistry of the fatty acids present in it was carried out in a series of brilliant researches by Frederick B. Power[4] and his associates from 1904–1907. After an extensive and very careful study of the chaulmoogric and hydnocarpic acids they showed that these acids are homologs and assigned formulas for each. Chaulmoogric acid was given Formula IX; that is to say, it was assumed to be an equilibrium mixture of Formulas VII and VIII. The only other work on the constitution has recently been published by Schmidt[5] who proposed Formula XVII for chaulmoogric acid; his structure will not explain many of the experimental facts and consequently need not be seriously considered.

The therapeutic importance of these acids leads us to a further study of their reactions and properties, particularly those which have a relation to their structures. This communication describes the results of these experiments from which the conclusion has been drawn that all facts may be explained by the simple formulas VII and XVIII for chaulmoogric and hydnocarpic acids, respectively, and that no equilibrium mixture exists

[1] This communication is an abstract of a portion of a thesis submitted by R. L. Shriner in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry in the Graduate School of the University of Illinois.

[2] Walker and Sweeney, *J. Infectious Diseases*, **26**, 238 (1920). Schöbl, *Phillipine J. Sci.*, **23**, 533 (1923). Muir, *Indian Med. Gaz.*, **54**, 130 (1919). Muir, *Indian J. Med. Research*, **11**, 543 (1923). McDonald and Dean, *Pub. Health Repts.*, **35**, 1959 (1920). For further bibliography see Warren, *J. Am. Pharm. Assoc.*, **10**, 510 (1920).

[3] (a) Hollman and Dean, *U. S. Pub. Health Bull.*, No. **75** (1916); *J. Cutaneous Diseases*, **37**, 367 (1919). See also Dean and Wrenshall, THIS JOURNAL, **42**, 2626 (1920). McDonald and Dean, *J. Am. Med. Assoc.*, **76**, 1470 (1921). Hashimoto, THIS JOURNAL, **47**, 2325 (1925). Wrenshall and Dean, *U. S. Pub. Health Bull.*, **141** (1924). (b) Rogers, *Lancet*, **190**, 288 (1916); **200**, 1178 (1921); **206**, 1297 (1924); *Brit. Med. J.*, **1919**, I, 147.

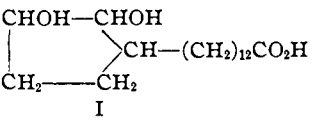
[4] (a) Power and Gornall, *J. Chem. Soc.*, **85**, 838, (b) 851 (1904). (c) Barrowcliff and Power, *ibid.*, **91**, 557 (1907).

[5] Schmidt, Ph.D. *Dissertation*, Hessischen-Ludwigs, Universität, Giessen, 1923.

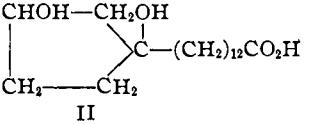
between these formulas and the corresponding bicyclopentane tautomers (see Formula VIII) as suggested by Power.

Power and his co-workers[4] showed that chaulmoogric acid possessed the formula $C_{18}H_{32}O_2$, was optically active ($[\alpha]_D = +62.1°$) absorbed two atoms of bromine or iodine and one of hydrogen bromide. The double bond was not reduced by sodium and alcohol, but chaulmoogryl alcohol, $C_{18}H_{33}OH$, and chaulmoogryl chaulmoograte were produced, while phosphorus and iodine produced some dihydrochaulmoogric acid and a hydrocarbon chaulmoogrene, $C_{18}H_{34}$. Reduction of the hydrogen bromide addition product with zinc and acid gave inactive dihydrochaulmoogric acid. Potassium permanganate solution was reduced in the cold with the production of various oxidation products depending on the amount of permanganate used. Since the determination of the structural formula of chaulmoogric acid depends to a considerable extent on these oxidation products, they are listed below with the formulas assigned to them by Power.

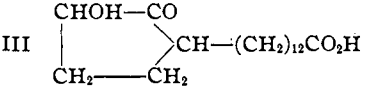
(1) Two dihydroxy-dihydrochaulmoogric acids, I ($[\alpha]_D = +11.6°$) and II, ($[\alpha]_D = -14.2°$); (2) hydroxyketo-dihydrochaulmoogric acid, III; (3) *n*-pentadecane-α,α',γ-tricarboxylic acid, IV; (4) *n*-pentadecane-γ-keto-α,α'-dicarboxylic acid, V; (5) *n*-dodecane-α,α'-dicarboxylic acid, $HO_2C(CH_2)_{12}CO_2H$; (6) *n*-undecane-α,α'-dicarboxylic acid, $HO_2C(CH_2)_{12}CO_2H$.



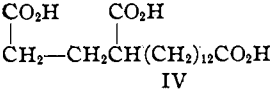
I



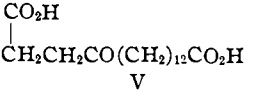
II



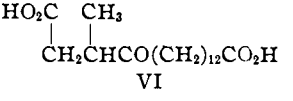
III



IV



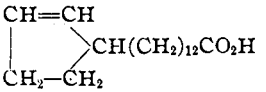
V



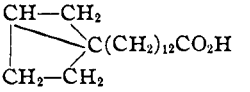
VI

By oxidation of the acids, produced by addition of hydrogen bromide to chaulmoogric acid, then elimination of hydrogen bromide by means of alcoholic potassium hydroxide, Power obtained a ketonic acid which he believed to be *n*-pentadecane-β-methyl-γ-keto-α,α'-dicarboxylic acid, VI.

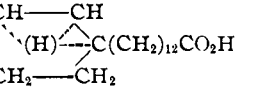
From a consideration of these reactions and the oxidation products, Power concluded that chaulmoogric acid could react either as a cyclopentene (VII) or bicyclopentane (VIII) derivative. Such a tautomeric state could be represented by a formula analogous to that assigned to glutaconic acid by Thorpe and hence the formula finally assigned to chaulmoogric acid[4c] was IX.



VII



VIII



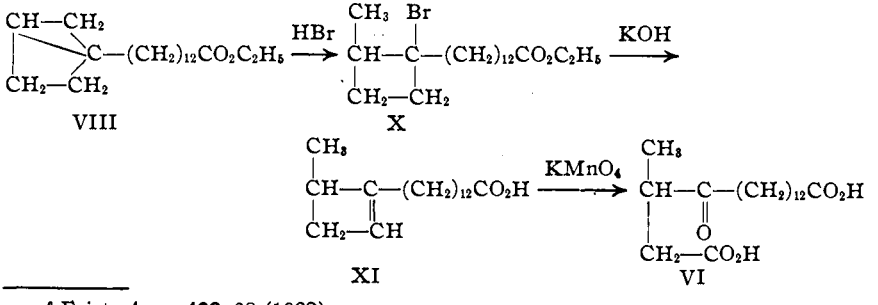
IX

The experimental evidence obtained in this investigation shows clearly that Formula VII is adequate in order to explain all the reactions of chaulmoogric acid and that the postulation of Forms VIII and IX is unwarranted. The evidence and explanation of the reactions of chaulmoogric acid which point conclusively to Formula VII may be reviewed.

Formula IX seems extremely unlikely for the following reasons. (1) Chaulmoogric acid is optically active; $[\alpha]_D$, $+62.1°$. In a condition where a molecule has a mobile hydrogen atom, optical activity would probably not exist or at least the compound might be expected to racemize very rapidly. Those compounds containing an asymmetric atom alpha to a carbonyl group racemize readily. The mobile nature of the hydrogen atom in such compounds is less pronounced than in glutaconic ester from which no optically active derivatives have ever been prepared, in spite of numerous attempts by Feist[6] and his collaborators. Chaulmoogric acid is not racemized when heated for two days at 250° or when heated with alkali, and may be distilled repeatedly with no change in optical activity. (2) Furthermore, glutaconic ester has a conjugated system and this is apparently necessary for this type of isomerism, since no examples of such isomerism are known in any other types of compounds. Chaulmoogric acid has no such conjugation.

Both Formulas VII and VIII were considered necessary in order to explain the acids obtained by oxidation, and this led Power to adopt a tautomeric formula (IX). A consideration of these oxidation products shows, however, that only two, (V) and (VI), are difficult to explain on the basis of Formula VII. Formula VIII was adopted, therefore, to explain their formation. The *n*-pentadecane-β-methyl-γ-keto-α,α'-dicarboxylic acid (VI) was considered by Power to be the result of the following series of reactions.

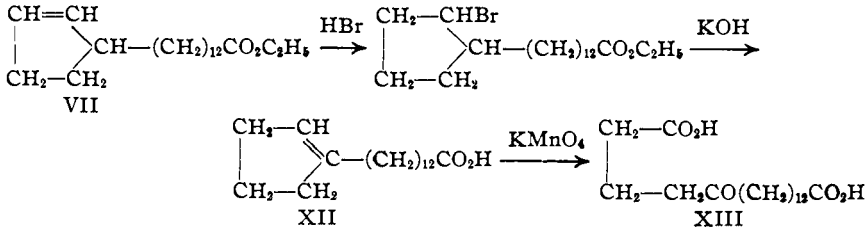
SERIES 1



[6] Feist, *Ann.*, **428**, 68 (1922).

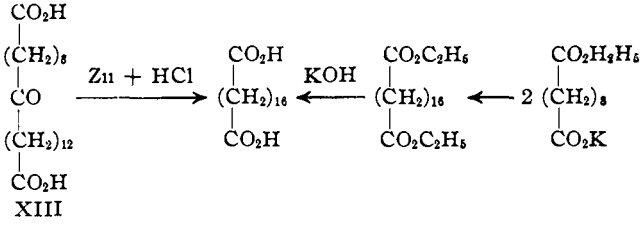
If the cyclopentene structure (VII) were correct the following series of reactions to give a ketonic acid of the proper empirical formula should occur.

SERIES 2



and the structure of the ketonic acid would be (XIII) instead of (VI). This possibility was considered by Power but discarded by him because further oxidation did not yield succinic acid but oxalic, acetic and formic acids; for this reason the ketonic acid was given Formula VI. However, conclusions as to structure based on the ultimate products of oxidation are not always reliable, especially since succinic acid can be further oxidized to oxalic acid by permanganate.[7]

A sample of this ketonic acid (VI) was prepared according to Power's directions[4c] and its structure proved to be that of Formula XIII. This was accomplished by reducing the ketonic acid to *n*-hexadecane-α,α'-dicarboxylic acid by means of a Clemmensen[8] reduction. The product obtained was shown to be identical with a sample of *n*-hexadecane-α,α'-dicarboxylic acid prepared by the electrolysis of potassium-ethyl sebacate and saponification of the resulting ester, as indicated by the following reactions.



Hence, the series of reactions leading to the formation of XIII are those given in Series 2.

The product obtained by the elimination of hydrogen bromide from ethyl-bromodihydro chaulmoograte was a mixture of chaulmoogric acid and its isomer (XII) which is optically inactive. Only 5.4% of the mixed acids is chaulmoogric acid as calculated from the rotation of the mixture. The fact that 94.6% of the product was an isomeric chaulmoogric acid shows that hydrogen bromide added in the manner indicated and that

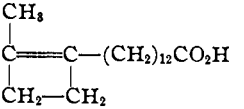
[7] Berthelot, *Ann. Spl.*, **6**, 186 (1867).

[8] Clemmensen, *Ber.*, **46**, 1837 (1913); **47**, 51 (1914).

on boiling with alcoholic potassium hydroxide the active tertiary hydrogen was the one that split out with the bromine, giving XII. The addition product of hydrogen bromide and chaulmoogric acid was optically inactive but by treatment with alcoholic potassium hydroxide the mixture of acids obtained was active; $[\alpha]_D$, $+13.8°$. This activity was due to the regeneration of chaulmoogric acid, since by fractional crystallization the optical activity gradually rose and finally, by conversion to the amides and recrystallization of these, chaulmoogramide, m. p. 103–104°, was obtained. The isomeric acid (XII) is much more soluble than chaulmoogric acid and is difficult to purify.

The formation of active chaulmoogric acid from the inactive bromodihydrochaulmoogric acid is rather remarkable. The final isolation of active chaulmoogric acid cannot be due to chaulmoogric acid which did not react with the hydrogen bromide in the initial reaction, for this would render the addition product active; moreover, the addition product was purified completely before it was decomposed with alcoholic potassium hydroxide. The inactivity of this hydrogen bromide addition compound must, hence, be ascribed to internal compensation of the two asymmetric carbon atoms. This is confirmed by the fact that a slight change in one of the groups (the free acid to ethyl ester) resulted in an ethyl bromodihydro chaulmoograte which was optically active[4c] but only slightly so; $[\alpha]_D$, $+7.1°$. Since the mixture of acids obtained by the elimination of hydrogen bromide from the bromodihydro ester gave a larger percentage of isochaulmoogric acid (XII) which by oxidation produces *n*-hexadecane-γ-keto-α,α'-dicarboxylic acid, the ester rather than the free acid was used to prepare the ketonic acid (XIII).

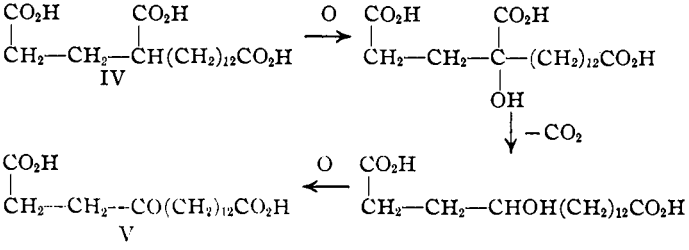
The fact that some chaulmoogric acid is regenerated by the treatment with alcoholic potassium hydroxide is not readily explained by equations in Series 1. The formation of the cyclobutene derivative XI from X, and the re-formation of chaulmoogric acid by splitting out of a hydrogen of the methyl group with the bromine to form a trimethylene ring, are both very unlikely since the adjacent carbon atom (carrying the methyl group) has a tertiary hydrogen atom which would be more reactive than any of the other hydrogen atoms. Hence, the loss of hydrogen bromide should give XIV and not XI or VIII. It is obviously impossible to obtain XIII from XIV by permanganate oxidation.



XIV

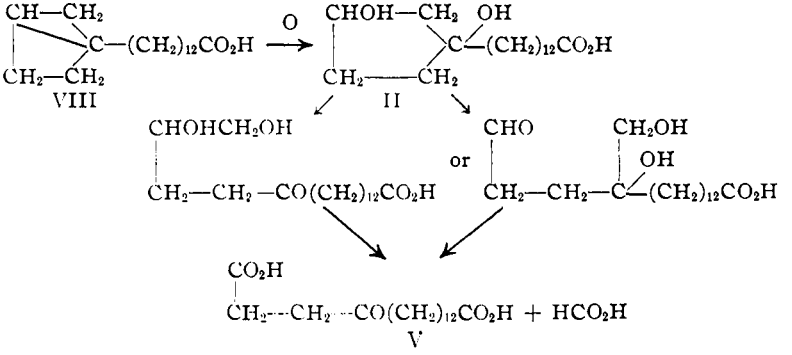
The only other oxidation product which was difficult for Power to explain from Formula VII was *n*-pentadecane-γ-keto-α,α'-dicarboxylic acid (V).

It might be expected that this product would result from the further oxidation of *n*-pentadecane-α,α',γ-tricarboxylic acid (IV) as follows.



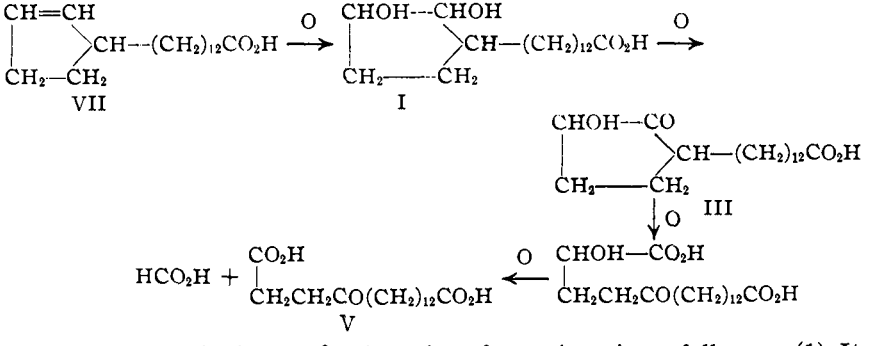
This, however, is not the case since the tricarboxylic acid is very stable to oxidizing agents. This fact was noted by Power in his work and has been confirmed during the present investigation.

In order to explain its formation Power makes use of Formula VIII and suggests the following series of reactions.



However, there is no evidence for this other than the isolation of formic acid as one of the products of oxidation.

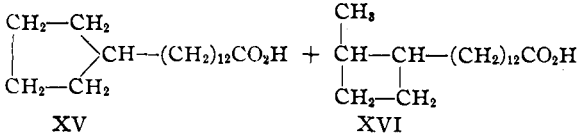
A much more probable explanation, based on Formula VII, is shown in the following series of reactions.



The evidence in favor of this series of reactions is as follows. (1) It is known that rings with a keto group adjacent to a side chain give ketonic

acids on oxidation; thus, 2-methyl-cyclopentanone[9a] and 2-methyl-cyclohexanone[9b] are oxidized by permanganate to γ-acetylbutyric and δ-acetyl-valerianic acids, respectively. (2) A methyl ketohydroxy-dihydrochaulmoograte (III) was isolated as one of the products of oxidation by Power.[4c] The direct oxidation of this acid would yield the *n*-pentadecane-γ-keto-α,α′-dicarboxylic acid by a reaction exactly analogous to the oxidation of 2-methyl-cyclopentanone, except that a loss of one carbon atom (which appears as formic acid) in the chain results, because of the additional hydroxyl group present.

Experimental confirmation of this view was impossible because of the difficulty in isolating the ketohydroxy acid (III) which is a rather unstable compound. Numerous attempts to obtain it all resulted in failure and it is probable that just the proper conditions, as were obviously obtained by Power, were not realized. (3) That the formula for the second dihydroxy-dihydrochaulmoogric acid (II) is correct seems very doubtful since permanganate oxidation of bicyclic rings does not result in such compounds. In fact, stability to permanganate is characteristic of saturated bicyclic rings. It will be noted that dihydroxy-dihydrochaulmoogric acid (I) has three asymmetric atoms; hence, it is much more probable that the two forms isolated are two diastereoisomers and not structural isomers as indicated by Power. Power and Gornall[4a] were unable to reduce chaulmoogric acid with sodium and alcohol but obtained dihydrochaulmoogric acid by reduction of the hydrogen bromide addition product with zinc and acid. Although it was optically inactive they regarded it as a mixture of α-carboxy-*n*-dodecyl-cyclopentane (XV) and 1-(α-carboxy-*n*-dodecyl)-2-(methyl)-cyclobutane (XVI).[4c]



XV XVI

The last-named compound contains two asymmetric atoms and should be optically active provided the reagents had not caused racemization. Since sodium and alcohol affect only conjugated systems, it is clear why this reagent did not reduce chaulmoogric acid.

Since catalytic reduction at room temperature does not produce racemization,[10] and since bridged rings are not split and reduced by platinum and hydrogen at low temperatures,[11] then the catalytic hydrogenation

[9] (a) Wallach, *Ann.*, **331**, 324 (1903); (b) **329**, 377 (1903).

[10] For example, *d*-limonene is reduced to *d*-carvomenthene [Vavon, *Bull. soc. chim.*, [4] **15**, 282 (1914)].

[11] The catalytic reduction of carene [*Ber.*, **47**, 384 (1914)] sabinene and thujene [*Compt. rend.*, **151**, 1058 (1910)] and pinene [Ref. 12 b] stops with the absorption of only two atoms of hydrogen and the reduced products still contain the bicyclic ring.

of chaulmoogric acid will lead to conclusions concerning a possible bicyclic form of chaulmoogric acid. If the latter form is present it will not be reduced, the theoretical amount of hydrogen will not be absorbed, and the resulting product should be optically active; if it should be reduced and a methyl-cyclobutane derivative is formed (as stated by Power in the reduction of X), then the resulting product must still be optically active.

By means of 0.1 g. of platinum-oxide platinum black,[12] 14 g. of chaulmoogric acid was reduced in one minute at 25° and at 2–3 atmospheres' pressure, and dihydrochaulmoogric acid was isolated in quantitative yield. Moreover, the calculated amount of hydrogen was absorbed and the product was optically inactive, m. p. 71–72°; and it was obviously identical with the product obtained by Power. This shows that formation of a bicyclopentane derivative is very unlikely and confirms Formula VII.

In a recent report Dean and Wrenshall[13] also describe the catalytic reduction of chaulmoogric acid using a mixture of colloidal platinum and palladium as catalyst. The reduction took place very much more slowly than was observed in this investigation and the product was reported as optically active $[\alpha]_D$, 5% $CHCl_3$, —0.12°; +0.57°. Since these values are so small, the individual readings would vary by as much as the observed rotations. The slight rotation reported may also have been due to a trace of chaulmoogric acid still present in the product and this is made more probable by the fact that a very small iodine number was found. No rotation was ever found for dihydrochaulmoogric acid obtained by reduction using platinum-oxide platinum black as described in the experimental part of this paper.

Another specific reagent for the double bond is ozone, and further evidence for Formula VII has been obtained by the ozonation of chaulmoogric acid and its ester. The ozonation of chaulmoogric acid is reported by S. Ghosh[14] but no description of the products obtained has been published.

The ozonide of chaulmoogric acid was split to the dialdehyde by means of zinc and acetic acid. The resulting compound was a glassy solid which could not be crystallized. It was identified by oxidation with the calculated amount of chromium trioxide to *n*-pentadecane-α,α',γ-tricarboxylic acid which was converted to the trimethyl ester. This ester was proved to be identical, by means of a mixed melting point, with that obtained by the direct oxidation of chaulmoogric acid with an excess of permanganate according to Power's directions.[4c]

Methyl chaulmoograte was also ozonized, split to the di-aldehyde, converted to the dioxime and the latter analyzed. These ozonation products again point to Formula VII as being correct, since bicyclic rings are not split by ozone.

Recently Schmidt[5] has assigned Structure XVII to chaulmoogric acid.

$$\begin{array}{l} CH_3(CH_2)_4CH{=}CH \\ \qquad\qquad\quad | \\ CH_3(CH_2)_6CH(CH_2)_2CO_2H \end{array}$$

XVII

The reasons assigned were: the analysis agrees with the formula $C_{18}H_{34}O_2$ just as well as $C_{18}H_{32}O_2$; the analysis of Power's tribasic acid corresponds

[12] (a) Adams and Shriner, THIS JOURNAL, **45**, 2171 (1923). (b) Kern and Shriner with Adams, *ibid.*, **47**, 1147 (1925).

[13] Dean and Wrenshall, *U. S. Pub. Health Bull.*, **141**, 25 (1924).

[14] Ghosh, *Indian J. Med. Research*, **8**, 211 (1920).

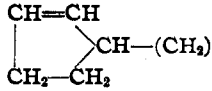
just as well to the dibasic acid $C_{12}H_{22}O_4$; Power did not determine nitrogen in his oxime of *n*-pentadecane-γ-keto-α,α′-dicarboxylic acid and Schmidt considers that the carbon and hydrogen analysis point just as well to a dihydroxy acid $C_{17}H_{32}O_6$; glutaric acid was isolated as an oxidation product; alkali fusion gave acetic and caproic acids.

The foregoing formula is undoubtedly incorrect and the criticism given is unwarranted. In the first place, Power proved that he had *n*-pentadecane-α,α′,γ-tricarboxylic acid, not only by analysis but also by molecular-weight determinations of the acid and its methyl and ethyl esters. The acid could not be $C_{12}H_{22}O_4$, because *n*-dodecane-α,α′-dicarboxylic acid, $C_{14}H_{26}O_4$, was isolated as an oxidation product. Its properties were totally different from those of the tricarboxylic acid and its structure proved definitely by comparison with a synthetic sample of the acid supplied to Power by Crum Brown who prepared it by electrolysis of potassium-ethyl suberate. The formula of Schmidt is absolutely incapable of explaining the formation of these acids by oxidation. The formation of glutaric acid is readily explained by the cyclopentene structure, and the existence of caproic acid as a product of alkali fusion is probably due to shifting of the double bond before splitting. It is well known that the compounds obtained by such a drastic reaction as alkali fusion cannot be used as arguments for the determination of structure. The above formula is also incapable of explaining the formation of the ketonic acid (XIII) and from this *n*-hexadecane-α,α′-dicarboxylic acid which was synthesized in the present research.

Hydnocarpic Acid

This acid is the next lower homolog of chaulmoogric acid,[4c] possessing two less carbon atoms in the side chain. It is present in much smaller amount in the oil and its reactions are exactly analogous to those of chaulmoogric acid.

Our only experimental work on this acid was its reduction by platinum and hydrogen to dihydrohydnocarpic acid.

In less than one minute 12.6 g. was reduced by 0.1 g. of catalyst to dihydrohydnocarpic acid. This was isolated in quantitative yield with the absorption of the calculated amount of hydrogen and was optically inactive. The same arguments concerning the structure of this acid apply as already cited for chaulmoogric acid and it may hence be assigned Formula XVIII  (XVIII) in place of Power's tautomeric mixture of a substance of this formula and the corresponding bicyclopentane.

Experimental Data

Preparation of Chaulmoogric and Hydnocarpic Acids.—The oil used in this investigation was imported from India and shown to be the genuine chaulmoogra oil expressed from the seeds of *Taraktogenos kurzii* (King).

The physical constants were determined and are given in Table I, together with Power's values[4a] for comparison.[15]

TABLE I

CONSTANTS OF CHAULMOOGRA OIL

		Power and Gornall
M. p., °C.	20–25	22–23
D. (25°)	0.9461	0.951
Iodine no.	103.8	103.2
$[\alpha]_D(CHCl_3)$	50.8°	51–52°
$n_D^{40°}$	1.4731	1.476

A mixture of 8 kg. of chaulmoogra oil and 2 kg. of sodium hydroxide in 8 liters of water in a 60-liter autoclave was heated during stirring for three hours. About 30 liters of water was added and the solution boiled to dissolve the soap; the unsaponifiable resins were skimmed off and the solution was then acidified with hydrochloric acid. After being cooled, the solid cake was separated from the aqueous layer, heated in a vacuum to remove the water and then vacuum-distilled in an all-glass apparatus. The distillate was divided into three equal fractions according to the method of Dean and Wrenshall.[16]

Fraction 1.—This is rich in hydnocarpic acid and by recrystallization six times from ligroin (70–90°), pure white plates of hydnocarpic acid were obtained; m. p., 59–60°; $[\alpha]_D$, +68.3° (in chloroform); yield, 54 g. from 1800 g. of distillate.

Fraction 2.—This is a eutectic mixture and is returned to the distilling flask with the next batch.

Fraction 3.—This is rich in chaulmoogric acid and by two or three recrystallizations from 80% alcohol gave pure white plates; m. p., 67–68°; $[\alpha]_D$ in chloroform, +57.4°. On recrystallization again from ethyl acetate and removal of the solvent in a vacuum, a product, m. p. 68–68.5°, was obtained; $[\alpha]_D$, +62.4°; yield, 400 g. from 1800 g. of distillate.

Catalytic Reduction of Chaulmoogric Acid to Dihydrochaulmoogric Acid.—A solution of 14 g. (0.05 mole) of chaulmoogric acid in 200 cc. of 95% alcohol was reduced in one minute by 0.1 g. of platinum-oxide catalyst at 2–3 atmospheres with the absorption of 0.05 mole of hydrogen. After the catalyst had been filtered off, 14 g. of dihydrochaulmoogric acid, m. p. 71–72°, was obtained by crystallization from 80% alcohol. It was optically inactive and identical with the product obtained by Power[4c] by reduction of bromodihydrochaulmoogric acid with zinc and acetic acid.

Catalytic Reduction of Hydnocarpic Acid to Dihydrohydnocarpic Acid.—Upon reduction of 12.6 g. of hydnocarpic acid similarly to the chaulmoogric acid, the reaction was complete in half a minute. A quantitative yield of dihydrohydnocarpic acid resulted, m. p. 64–65°, after recrystallization from 70% alcohol. It was optically inactive. Dean and Wrenshall report a melting point of 63° after reduction with colloidal platinum-palladium and crystallization from glacial acetic acid.

Anal. Subs., 0.5200: 18.92 cc. of 0.1079 *N* NaOH. Calcd. for $C_{16}H_{30}O_2$: Neutr. equiv., 254.2. Found: 254.7.

Catalytic Reduction of Methyl Chaulmoograte to Methyl Dihydrochaulmoograte.—The reduction of 14.6 g. of methyl chaulmoograte, b. p. 198–199° (10 mm.), required one minute, and the optically inactive methyl dihydrochaulmoograte was isolated in quantitative yield; m. p., 27°; b. p., 204–205° (10 mm.); d_{25}^{30}, 0.9018; n_D^{30}, 1.4536.

Catalytic Reduction of Methyl Hydnocarpate to Methyl Dihydrohydnocarpate.—

[15] Compare also Warren, *J. Am. Pharm. Assoc.*, **10**, 513 (1920).

[16] Dean and Wrenshall, THIS JOURNAL, **42**, 2626 (1920).

The reduction of 13.3 g. of methyl hydnocarpate, b. p., 182–183° (10 mm.), required half a minute. Optically inactive methyl dihydrohydnocarpate was isolated; b. p., 187–188° (10 mm.); d_{25}^{25}, 0.9057; n_D^{30}, 1.4523.

Anal. Subs., 0.9931: 37.57 cc. of 0.1 *N* NaOH. Calcd. for $C_{17}H_{32}O_2$: Sap. no., 266. Found: 264.4.

Preparation of Bromodihydro-chaulmoogric Acid.—A mixture of 120 g. of chaulmoogric acid and 300 g. of 31% hydrogen bromide in glacial acetic acid was warmed on the steam cone for one hour. It was poured onto ice and the product filtered off and recrystallized from 80% methyl alcohol; m. p., 37–38°. It was optically inactive. This compound was prepared by Power but was not recrystallized by him and his results from analysis differed by 1% from those calculated.

Anal. Subs., 0.5010: 14.02 cc. of 0.09974 *N* $AgNO_3$. Calcd. for $C_{18}H_{33}O_2Br$: Br, 22.15. Found: 22.30.

By refluxing for one hour with 2.5 molecular equivalents of alcoholic potassium hydroxide, a mixture of acids was obtained after dilution with water and acidification; $[\alpha]_D$, +13.8° in chloroform. By fractional crystallization of the acids from 80% alcohol, conversion to the amide by treatment with thionyl chloride and concd. ammonium hydroxide, and crystallization of the amide from 90% alcohol, pure chaulmoogramide, m. p. 103–104°, was obtained. This shows that chaulmoogric acid was regenerated to the extent of 22% as calculated from the rotation, since the isochaulmoogric acid is optically inactive.

Preparation of Ethyl Bromodihydro-chaulmoograte.—Dry hydrogen bromide was passed into a solution of 100 g. of ethyl chaulmoograte in ligroin until the solution no longer decolorized bromine. The solvent was removed in a vacuum and the ethyl bromodihydro-chaulmoograte remained behind as a light yellow oil; $[\alpha]_D$, +7.1°. It was used without further purification.

Preparation and Oxidation of Isochaulmoogric Acid.—The oil described above was refluxed for two hours with 50 g. of potassium hydroxide in 500 cc. of alcohol. The potassium bromide was filtered off and the filtrate diluted with water, then acidified with hydrochloric acid; yield, 96 g.; m. p., 51–53°; $[\alpha]_D$, +3.4° in chloroform. The slight optical activity shows that 5.4% of this mixture was chaulmoogric acid.

The above acids were dissolved in 50 g. of potassium hydroxide and 5 liters of water and this solution was run into 200 g. of potassium permanganate in 11 liters of water, the temperature being kept at 18–20°. After three hours the solution was filtered, evaporated to 1 liter, acidified, the acids were extracted with ether, converted to their methyl esters and fractionally distilled. The fraction boiling at 220–250° (9 mm.) solidified and was recrystallized from methyl alcohol; m. p., 64–65° (Power, 64°). This was saponified with alcoholic potassium hydroxide and the acid recrystallized from ethyl acetate; m. p., 125–126° (Power, 126°); yield, 2 g.

Reduction of *n*-Pentadecane-γ-keto-α,α′-dicarboxylic Acid to *n*-Hexadecane-dicarboxylic Acid.—The ketonic acid above was reduced according to Clemmensen's[8] method by being heated with 50 g. of amalgamated zinc and 100 cc. of 10% hydrochloric acid for 18 hours. The insoluble acid was separated and after recrystallization from alcohol melted at 118°.

Anal. Subs., 0.1293: CO_2, 0.3241; H_2O, 0.1222. Calcd. for $C_{18}H_{34}O_4$: C, 68.79; H, 10.82. Found: C, 68.38; H, 10.57.

Synthesis of *n*-Hexadecane-α,α′-dicarboxylic Acid.—This acid was synthesized according to the method of Crum Brown and Walker[17] by electrolysis of potassium-ethyl sebacate; m. p., 117–118°. A mixture of this compound with that prepared from the

[17] Crum Brown and Walker, *Ann.*, **261**, 125 (1891).

keto acid melted at 117–118°, showing no depression and thus proving the identity of the compound obtained from chaulmoogric acid.

Ozonation of Chaulmoogric Acid. Preparation of Ammonium-*n*-pentadecane-α,γ-di-aldehydo-α'-carboxylate.—A solution of 28 g. of chaulmoogric acid in 500 cc. of glacial acetic acid was treated with ozone until the solution no longer decolorized bromine.

The ozonide was decomposed by dilution of the acetic acid solution[18] with 1 liter of ether, addition of 50 g. of zinc dust, and then the slow addition of 20 cc. of water during stirring. When the solution no longer gave a blue color with starch-iodide paper it was filtered, washed thoroughly with 5–6 portions of water to remove the acetic acid, dried with calcium chloride and the ether evaporated. A non-crystallizable, glassy solid was obtained weighing 26 g. A portion of this was dissolved in dry ether, and dry ammonia gas passed through. The ammonium salt is insoluble, precipitates and is filtered off immediately, dried and analyzed.

Anal. Subs., 0.2000: 6.00 cc. of 0.1 *N* HCl. Calcd. for $C_{18}H_{25}O_4N$: N, 4.25. Found: 4.20.

Oxidation of *n*-Pentadecane-α,γ-dialdehydo-α'-carboxylic Acid.—The oxidation of 18 g. of the above ozonation product with the calculated amount of chromium trioxide was carried out in glacial acetic acid at room temperature. After one hour, the mixture was poured into water, the acids were extracted with ether, converted into the methyl esters and vacuum-distilled. The fraction boiling at 260–275° (15 mm.) solidified and after recrystallization from absolute methyl alcohol melted at 37–38°. This was shown to be identical with a sample of the trimethyl ester of *n*-pentadecane-α,α',γ-tricarboxylic acid obtained by the method of Power by oxidation of chaulmoogric acid.

Ozonation of Methyl Chaulmoograte. Preparation of the Dioxime of Methyl-*n*-pentadecane-α,γ-dialdehydo-α'-carboxylate.—A solution of 29.4 g. of methyl chaulmoograte in 300 cc. of glacial acetic acid was ozonized and the solution of the ozonide worked up in the same manner as the ozonized chaulmoogric acid. It was a non-crystallizable oil which decomposed when distillation was attempted. For identification it was converted into the dioxime by treatment of 5 g. of the oil in alcohol sufficient to dissolve it with 20 g. of hydroxylamine hydrochloride and 100 cc. of 10% sodium hydroxide. After 12 hours the solution was diluted with water and the precipitate filtered off. Considerable difficulty was experienced in purification of the compound but after six recrystallizations from methyl alcohol it melted constantly at 93–94°.

Anal. Subs., 0.2000: 10.99 cc. of 0.1 *N* HCl. Calcd. for $C_{19}H_{36}O_4N_2$: N, 7.86. Found: 7.69.

This dioxime is obviously only one of four possible isomers. Another sample obtained by heating the solution for a short time melted at 102–103°.

Summary

1. The ketonic acid produced by the oxidation of isochaulmoogric acid has been shown to be *n*-hexadecane-γ-keto-α,α'-dicarboxylic acid.

2. Catalytic reduction of chaulmoogric acid and hydnocarpic acid results in a quantitative yield of optically inactive dihydrochaulmoogric and dihydrohydnocarpic acids.

3. Chaulmoogric acid and its ester have been ozonized and the products identified.

[18] This method for decomposing ozonides is described by Helferich and Schäfer, [*Ber.*, **57**, 1913 (1924)].

4. An explanation is advanced for the formation of *n*-pentadecane-γ-keto-α,α′-dicarboxylic acid from chaulmoogric acid.

5. Power suggested that the formula of chaulmoogric acid was 1-(α-carboxy-*n*-dodecyl)-Δ^4-cyclopentene in equilibrium with a tautomeric bicyclopentane derivative. In view of the facts mentioned above it may be concluded that chaulmoogric acid does not exist in a tautomeric state and is merely 1-(α-carboxy-*n*-dodecyl)-Δ^4-cyclopentene.

6. By analogous reasoning, the structure of hydnocarpic acid is 1-(α-carboxy-*n*-decyl)Δ^4-cyclopentene.

URBANA, ILLINOIS

REACTIONS OF COMPOUNDS OF TRIPHENYLMETHYL AND TRIPHENYLSILICYL IN LIQUID AMMONIA

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While triphenylmethyl and other similar groups have been the subject of extensive investigation, our knowledge of the chemical properties of these groups is still very limited. The present investigation was undertaken for the purpose of securing further information regarding the chemistry of the triphenylmethyl and triphenylsilicyl groups.

Metallic Derivatives of Triphenylmethyl

Schlenk and Marcus[1] obtained a sodium derivative of triphenylmethyl by reduction of the chloride with sodium in the presence of mercury in ether. Kraus and Kawamura[2] have obtained the sodium and potassium compounds by the reduction of the halides with metals in liquid ammonia as well as by the direct action of the alkali metals on triphenylmethane in the same solvent.

Properties.—The alkali-metal derivatives of triphenylmethyl are true salts. They are readily hydrolyzable and oxidizable, readily soluble in liquid ammonia and appreciably, though much less, soluble in various organic solvents, such as toluene.

Schlenk and Marcus[3] have shown that solutions of sodium triphenylmethyl in ether conduct the electric current to some extent, the conductance increasing with increasing concentration.

In the present investigation, solutions of sodium and potassium triphenylmethyl for conductance measurements were prepared in liquid ammonia by the action of the free metals on triphenylmethane. For the sodium and potassium salts at 0.05 and 0.08 *N*, the equivalent con-

[1] Schlenk and Marcus, *Ber.*, **47**, 1664 (1914).

[2] Kraus and Kawamura, THIS JOURNAL, **45**, 2756 (1923).

[3] Ref. 1, p. 1678. For the equivalent conductance they found 4.8 × 10^{-2} at a dilution of 26.62 liters per mole.