cooling, the hydrated sulfate was recovered as long colorless needles in virtually quantitative yield. A five-times recrystallized sample, dried at 100°, 0.02 mm. pressure for 6 hours showed no loss in biological activity. *Anal.* Calcd. for $C_{32}H_{49}N_{18}O_4 \cdot 2H_2SO_4$: C, 40.66; H, 5.55; N, 26.69; SO_4, 20.34. Found: C, 40.70; H, 5.57; N, 25.90; SO_4, 20.05. The molecular weight was determined ebullioscopically in water. Calcd. for $C_{32}H_{48}N_{18}O_4 \cdot 2H_2SO_4$: mol. wt., 945 (315 assuming dissociation to three ions in solution). Found: mol. wt., 360 ± 60.

This salt melts at 224–225°, when placed in a bath at 220°, with the temperature rising 2° per minute. It has a solubility of about 30 mg./ml. in water at 80°, less than 0.5 mg./ml. at 25°. It is quite insoluble in the common organic solvents.

Netropsin picrate crystallizes from water, in which it is very slightly soluble, as sheaves of yellow needles. This salt melts at 234° (dec.) when placed in a bath at 225°, with the temperature rising at 2° per minute. The analysis of the picrate dried at room temperature *in vacuo* most nearly conforms to that of a hydrated picrate. *Anal.* Calcd. for $C_{32}H_{48}N_{18}O_4 \cdot 4C_6H_3N_3O_7 \cdot H_2O$: C, 39.92; H, 3.71; N, 24.95. Found: C, 39.94; H, 3.91; N, 23.64.

Hydrogenation of Netropsin.—Hydrogenation of the hydrochloride over Adams platinum catalyst in aqueous acetic acid solutions at atmospheric pressure results in the absorption of 1.6% of hydrogen in 24 hours. The hygroscopic amorphous product is devoid of biological activity.

Alkaline Degradation Products of Netropsin.—One gram of netropsin hydrochloride was suspended in 30 ml. of water and 20 ml. of 0.20 *N* NaOH was added. The resulting solution slowly turned from pale yellow to a deep red color, ammonia was evolved and a colorless crystalline product precipitated. After standing overnight, 0.56 g. of colorless needles was removed by filtration. This material, I, was purified by dissolving in a minimum quantity (7.5 ml.) of 0.20 *N* HCl, warming with Darco G-60 charcoal, and precipitation with an equivalent quantity of sodium hydroxide. The purified product softens at 238°, melts at 245–249° (dec.). *Anal.* Calcd. for $C_{15}H_{20}N_6O_3$: C, 54.20; H, 6.07; N, 25.29. Found: C, 54.20; H, 6.17; N, 25.45.

I is monobasic, forming a sulfate which is very soluble in water. It gives a negative Sakaguchi test, and is readily oxidized by air or ferric chloride to a deep red substance in neutral or acid aqueous solution.

The mother liquor from the basic hydrolysis yielded 60 mg. of a more soluble fraction, II, which crystallizes from water, as a colorless solid, readily soluble in acids, but relatively insoluble in the common organic solvents. *Anal.* Calcd. for $C_3H_5N_3O$: C, 36.36; H, 5.09; N, 42.68. Found: C, 36.84; H, 5.20; N, 42.92. This product decomposes without melting when heated above 300°. It gives a positive Sakaguchi test.

A sample of a sulfate salt of II was analyzed. *Anal.* Calcd. for $C_3H_5N_3O \cdot {}^1/_2H_2SO_4 \cdot H_2O$: $SO_4^=$, 29.40; N, 25.31. Found: $SO_4^=$, 28.42; N, 25.72.

Barium Hydroxide Hydrolysis of Netropsin.—One gram (1.05 mmole) of netropsin hydrochloride was dissolved in 25 ml. of 0.5 *N* barium hydroxide, and heated under reflux for 8 hours. The volatile bases evolved were collected in a known volume of standard hydrochloric acid. This netropsin solution was distilled to a volume of 10 ml., water was added and the concentration repeated to liberate all volatile base. Five millimoles (27% of the total nitrogen) of base was evolved. It was identified as ammonia by analysis of the chloride. The reaction flask contained 0.25 g. (1.24 mmole) of barium carbonate, which was separated by filtration. The excess barium was precipitated by addition of carbon dioxide, and the aqueous phase evaporated to dryness. The amorphous product still contained barium, which could not be precipitated by sulfate ion. This acidic product was not isolated.

Acknowledgment.—We are indebted to the members of the staff of Chas. Pfizer and Co., Inc., and especially to Dr. John B. Routien for isolating and identifying the culture, Dr. S. Y. P'an for determining toxicity, Dr. John A. Means for analytical determinations and absorption spectra, and Mr. K. B. Tate for running the bacterial spectrum and animal protection studies.

Summary

Netropsin is a new antibiotic obtained from culture filtrates of *Streptomyces netropsis*. Analysis of its crystalline salts indicate it to be a tetraacidic base with a formula approximating $C_{32}H_{48}N_{18}O_4$. The physical and biological characteristics of Netropsin are given. Two crystalline degradation products are described.

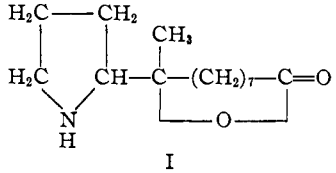
BROOKLYN 6, NEW YORK RECEIVED AUGUST 3, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, UNIVERSITY OF CALIFORNIA]

The Carbon Skeleton of Carpaine

BY HENRY RAPOPORT AND HENRY D. BALDRIDGE, JR.[1]

The alkaloid carpaine[2] was first isolated from the leaves[3] of the papaw tree, *Carica Papaya* L., by Greshoff.[4] Its formula was established as $C_{14}H_{25}NO_2$ by van Rijn[5] and structural investigations, initiated by Barger[6] and continued with Robinson and co-workers,[7,8] culminated in the proposal of I as the structure of carpaine. Although this structure was strongly supported by the reactions of the alkaloid, the only positively identified compounds derived from carpaine were suberic and azelaic acids, obtained by oxidation[7] with potassium permanganate and nitric acid, respectively.



I

A nitrogen-free, hydroxy acid of probable composition $C_{14}H_{28}O_3$, melting indefinitely from 20–25°, was isolated[8] from carpaine by a two-stage exhaustive methylation–Hofmann degradation procedure followed by hydrogenation and hydrolysis. However, this material, called "hydroxyisomyristic acid," was not further identified. This acid obviously provides the key to the carbon skeleton of

(1) U. S. Rubber Company Fellow, 1948–1949.

(2) For references to the pharmacological action of carpaine, see Henry, "The Plant Alkaloids," 4th ed., The Blakiston Company, Philadelphia, Pa., 1949, p. 600.

(3) An interesting account of the use of papaya leaves by natives in the Northern Celebes is found in Fairchild, "Garden Islands of the Great East," Charles Scribner's Sons, New York, N. Y., 1943, pp. 97–99.

(4) Greshoff, *Mededeel. uit's Lands. Plant., Buitenzorg*, **No. 7**, 5 (1890).

(5) van Rijn, *Arch. Pharm.*, **231**, 184 (1893); *ibid.*, **235**, 332 (1897).

(6) Barger, *J. Chem. Soc.*, **97**, 466 (1910).

(7) Barger, Girardet and Robinson, *Helv. Chim. Acta*, **16**, 90 (1933).

(8) Barger, Robinson and Work, *J. Chem. Soc.*, 711 (1937).

TABLE I

COMPARISON OF DEGRADATION ACID WITH 9-METHYLTRIDECANOIC, 12-METHYLTRIDECANOIC AND MYRISTIC ACID

Acid	Acid M. p.	Acid Mixed m. p.	2,4,6-Tribromoanilide M. p.	2,4,6-Tribromoanilide Mixed m. p.	*p*-Bromoanilide M. p.	*p*-Bromoanilide Mixed m. p.
Degradation	52.3–53.1		124.8–126.2		108–109	
9-Methyltridecanoic	B. p. 154 (2 mm.)		105.5–106	106.5–110	66.5–67	66–85
12-Methyltridecanoic	52.5–53.4	42–48.8	112.5–112.9	112–118.2		
Myristic	52.4–53.4	52.5–53.6	124.3–125.5	124.4–125.8	108.4–109.3	108–109.1

carpaine. It was the objective of the present work to present evidence either for or against the proposed structure I by degrading to the nitrogen-free, desoxy, fourteen-carbon acid and identifying the latter.

Isolation of carpaine from dried papaya leaves was accomplished by percolation of the ground leaves with ethanol containing 0.5% acetic acid. The percolate was then concentrated, basified and continuously extracted with ether. Evaporation of the ether and crystallization of the residue gave a 0.04% yield of pure carpaine. Previously reported[5,6,7,8] yields have varied from 0.01 to 0.07%. However, a yield of 0.25% has been claimed[4] from young leaves from old trees.

The exhaustive methylations and Hofmann degradations were carried out in a manner similar to that previously reported[8] except that the material was hydrogenated after each degradative step rather than at the end of the process. Quaternary methiodide was prepared from the secondary amine by heating with excess methyl iodide in methanol at 100° for twelve hours in a sealed tube. This was then converted to methocarbonate and dry-distilled. Although it has been well established that decomposition of a quaternary hydroxide results in much more of the desired olefin than is obtained from the quaternary carbonate,[9] the hydroxide could not be used in this case because of lactone hydrolysis which led to greatly reduced yields. With the methocarbonate, a high proportion of material reverts to tertiary amine, necessitating many repetitions of the process in order to remove the nitrogen. Also, the scale of the decomposition could not be advantageously increased above about four grams since the products were unstable at the high temperatures employed and had to be distilled as rapidly as possible. Because of these factors, the methylation–decomposition process had to be repeated a total of fourteen times to degrade 20.56 g. of carpaine to 1.66 g. of nitrogen-free, neutral material.

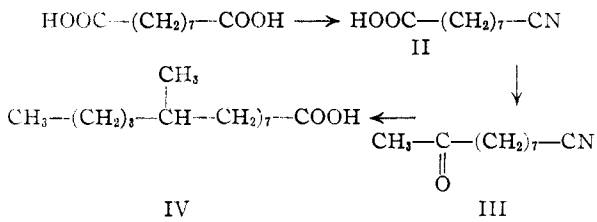
Saponification of the degradation product gave a crystalline acid (henceforth referred to as the degradation acid) melting at 52.3–53.1° for which the formula $C_{14}H_{28}O_2$ was established by neutralization equivalent and carbon and hydrogen analyses. The original degradation product unquestionably was an ester; however, it could not have been the expected lactone since on hydrolysis a saturated non-hydroxylic acid resulted. At some point (or points) in the methylation–decomposition–hydrogenation process the carbon–oxygen bond at the alcohol end of the lactone had been broken, the carbon saturated, and the carboxyl esterified. Thus the degradation, when carried out in this manner, led to a hydroxyl-free, saturated acid.

(9) Hanhart and Ingold, *J. Chem. Soc.*, 997 (1927); von Braun, Teuffert and Weissbach, *Ann.*, **472**, 121 (1929).

Recent work[10] has clearly demonstrated that for any group of isomeric fatty acids, the straight chain acid and the iso (branching methyl at the penultimate position) acid are the highest melting. Any other branching causes significant lowering of the melting point. Therefore, only myristic acid (m.p. 52.4–53.4°) and 12-methyltridecanoic acid (isomyristic) received serious consideration as the structure of the degradation acid. However, to remove any doubt, 9-methyltridecanoic acid (IV) was synthesized, since this would be the degradation acid if the proposed structure (I) for carpaine is correct. The three acids and the degradation acid were compared by mixed melting point determinations of the free acids, the tribromoanilides, and the *p*-bromoanilides. From the results compiled in Table I, there can be no doubt that the degradation acid is identical with myristic acid.

The isolation of myristic acid establishes the fact that the carbon skeleton of carpaine consists of a straight chain of fourteen atoms. In view of this, the Barger–Robinson formula (I) is untenable, and the structure of carpaine is being re-examined in detail.

The synthesis of 9-methyltridecanoic acid was effected by the path shown in the formula diagram.



To prepare the mononitrile of azelaic acid (II), a modification of the method of Biggs and Bishop[11] was used. It consisted in distilling a mixture of urea and azelaic acid and collecting the distillate in aqueous carbonate solution. Thus further equilibration among acid, acid nitrile and dinitrile was quenched and the yield of mononitrile was twice that obtained when the distillate was allowed to cool to room temperature. The mononitrile was readily converted to the acid chloride and thence to 9-ketodecanenitrile (III) with dimethylcadmium. Reaction of III with butylmagnesium bromide gave 9-methyl-9-hydroxytridecanenitrile which was hydrolyzed, dehydrated and hydrogenated to 9-methyltridecanoic acid (IV).

Experimental[12]

Isolation of Carpaine.—Carpaine was isolated from the leaves of *Carica Papaya* L. by a modification of the method

(10) Cason, *J. Org. Chem.*, **13**, 227 (1948).

(11) Biggs and Bishop, "Organic Syntheses," Vol. 25, John Wiley and Sons, Inc., New York, N. Y., 1945, p. 95.

(12) All melting points are corrected. Microanalyses were performed by the Micro Chemical Laboratory, University of California.

of Greshoff.[4] The dried leaves were milled to 8 mesh and digested in a percolator for 48 hours with 95% ethanol containing 0.5% acetic acid. The digest thus obtained, using 60 pounds of solvent for 150 pounds of dried, powdered leaves, was filtered and concentrated to five gallons *in vacuo*.[13] This thick, green-black sirup was further concentrated by stirring and heating on the steam-bath in a current of air until its volume remained constant. A quantity of water approximately equal to one-half the volume of the residue was then added, the mixture was made distinctly acid with 1 *N* acetic acid, and this acid solution was extracted with ether in a 12-liter, round-bottomed flask type of continuous extractor.[14] Extraction was continued until the organic phase possessed only a very light green color. The aqueous phase was then basified with excess potassium carbonate, and the continuous extraction resumed with fresh ether until the returning solvent contained no alkaloidal material as determined with Mayer reagent. After drying over magnesium sulfate and filtering, the ether was evaporated to give 26.5 g. (0.04%) of crude carpaine. On crystallization first from 2-butanone and then from acetone, 24.1 g. of pure carpaine was obtained. A sample sublimed at 120° (0.05 mm.) melted at 119–120°; $[\alpha]^{21}D$ +24.7° (*c*, 1.07 in ethanol) [reported[5] m.p. 121°; $[\alpha]D$ +21.9° (ethanol)].

Degradation of Carpaine to a Nitrogen-free Acid.—A solution of 4.0 g. of carpaine in 5 ml. of methanol and 25 ml. of methyl iodide was heated in a sealed tube at 100° for 12 hours after which the volatile substances were evaporated on the steam-bath in a stream of air. The residue was dissolved in 200 ml. of water, silver carbonate (freshly prepared from 10 g. of silver nitrate and 50 ml. of 3 *N* potassium carbonate and washed until neutral with distilled water) was added, and the mixture was shaken for 2 hours. After the addition of filter-aid, the mixture was filtered and the insoluble material digested with three 50-ml. portions of ether. The combined digests were dried over magnesium sulfate, filtered and evaporated to give 1.45 g. of material that had not formed methocarbonate (*i.e.*, secondary and tertiary amines). This recovered material was recycled by adding it to the carpaine used in subsequent degradations. The aqueous filtrate from the silver carbonate treatment was concentrated at reduced pressure and a bath temperature of 50° to 50 ml. and then was evaporated to dryness by dropwise addition into a two-bulb short-path distillation apparatus maintained at 20–30° and 5 mm. pressure. Decomposition of the thoroughly dried methocarbonate was effected by heating under vacuum (liquid nitrogen trap) from room temperature to 150° over the course of an hour and then to 250° during the next 30 minutes. Between 140–160° most of the decomposition occurred and the pressure rose to 1 mm. It then gradually dropped to 0.2 mm. or less and most of the distillate was collected between 160–170°. The colorless, oily distillate was immediately hydrogenated in 10 ml. of absolute ethanol at room temperature and atmospheric pressure using 30 mg. of platinum oxide as catalyst. Hydrogenation ceased after the absorption of 3.0 millimoles of hydrogen, and the solution was filtered and evaporated to give 1.45 g. of oily residue.

Attempts to carry out this degradation on a larger scale resulted in considerably reduced yields. A total of 20.56 g. (86.0 millimoles) of carpaine was processed by repeating the above procedure six times, and 9.32 g. (35.8 millimoles, assuming 260 as the molecular weight) of distillate was collected which absorbed 20.8 millimoles of hydrogen.

The second stage of the degradation was carried out exactly as described above for the first stage. Decomposition occurred between 100–135°, and most of the product distilled from 135–180°. From the liquid nitrogen trap, trimethylamine was isolated and identified as its picrate, m.p. 220–221°. After hydrogenation, the distillate was separated into basic and non-basic fractions by extraction of its ether solution with 0.1 *N* HCl. Evaporation of the ether gave the nitrogen-free material; basification and ether extraction of the aqueous acid layer gave recovered basic material which was added to the first-stage degradation product and recycled.

By repeating the above process eight times, the 9.32 g. of material from the first-stage degradation yielded 1.66 g. of nitrogen-free product.

A 0.326-g. sample of the neutral, nitrogen-free material was hydrolyzed by heating under reflux overnight in 25 ml. of 3 *N* ethanolic potassium hydroxide. The ethanol was evaporated on the steam-bath and the residue was dissolved in water. After washing with ether, the aqueous solution was saturated with ammonium sulfate, acidified and extracted thoroughly with ether. From the ether extracts, after drying and evaporating the ether, was obtained 0.245 g. of crude acid. This material was distilled at 100–110° (0.1 mm.) onto a cold finger, crystallized twice from hexane and then redistilled to give pure **degradation acid**, m.p. 52.3–53.1°. *Anal.* Calcd. for $C_{14}H_{28}O_2$: C, 73.6; H, 12.4; eq. wt., 228. Found: C, 73.6; H, 12.2; eq. wt., 227.

The **2,4,6-tribromoanilide** was prepared by heating the acid chloride (prepared from the acid and thionyl chloride) with 95 mole % of 2,4,6-tribromoaniline for 2 hours in the steam-bath. Several crystallizations from 95% ethanol gave material of m.p. 124.8–126.2°.

The ***p*-bromoanilide** was prepared by heating under reflux a solution of the acid chloride in benzene with 250 mole % of *p*-bromoaniline. The reaction mixture was then dissolved in ether and the ether was washed with 1 *N* HCl and 1 *N* potassium carbonate. After drying and evaporating the ether, a residue was obtained which melted at 108–109° after several crystallizations from aqueous ethanol.

8-Cyanoöctanoic Acid.—A modification of the method used by Biggs and Bishop[11] for preparing 9-cyanononanoic acid was employed. A mixture of pure azelaic acid (188.2 g., 1 mole) and urea (75 g., 1.25 moles) was heated with stirring at 160° (internal temperature) for 4 hours and then heated rapidly to 220°. After being maintained at that temperature for about 5 minutes, the molten solution was allowed to cool, but before solidifying was transferred to a 500-ml. distilling flask fitted with a wide-bore side-arm. A three-necked flask equipped with a stirrer and condenser served as receiver. About 250 ml. of saturated potassium carbonate and a few drops of phenolphthalein were placed in the receiver flask which was cooled in an ice-bath and the distilling flask was heated in a salt-bath. Most of the distillation took place from 340–360° (bath temp.) and heating was discontinued at 380°. At intervals during the distillation solid potassium carbonate was added to the receiver in order to maintain an excess of alkali. The material in the receiver was separated into a basic aqueous phase and an oil layer, and the aqueous phase was then extracted with ether. The combined ether extracts and oil were washed with water, dried over magnesium sulfate and concentrated to give 65.7 g. (44%) of crude azelaonitrile. The aqueous phase and the water wash of the ether–oil solution were combined, acidified to congo red with hydrochloric acid, and extracted thoroughly with ether which was then washed with water, dried over magnesium sulfate, and evaporated, leaving 83.2 g. (49%) of crude 8-cyanoöctanoic acid. On standing at room temperature, the crude cyano acid (neut. equiv., 160) precipitated a white solid (about 5–10% of the total product) which was filtered after several days and had a neutralization equivalent of 115. The filtered oil now showed no further precipitation on standing and had a neutralization equivalent of 168 (theory for 8-cyanoöctanoic acid, 169).

8-Cyanoöctanoyl Chloride.—A solution of 110 g. (0.92 mole) of purified thionyl chloride in 50 ml. of dry benzene was added slowly with stirring to a refluxing solution of 78.4 g. (0.46 mole) of 8-cyanoöctanoic acid in 250 ml. of dry benzene. Refluxing was continued for 2 hours after the addition was complete and then the mixture was distilled to give 78.6 g. (91%) of 8-cyanoöctanoyl chloride, b.p. 144–148° (2–3 mm.).

The amide was prepared by adding the acid chloride to cold, concentrated aqueous ammonia, and the precipitated amide crystallized several times from water, m.p. 84–85°. *Anal.* Calcd. for $C_9H_{16}N_2O$: C, 64.3; H, 9.6; N, 16.7. Found: C, 64.2; H, 9.6; N, 16.5.

The anilide was prepared by adding 1 ml. of 8-cyanooctanoyl chloride to a suspension of 1 g. of aniline in 30 ml. of cold water. After heating the mixture on the steam-bath for 15 minutes, enough ethanol was added to give a clear solution. The solid which separated was recrystallized from aqueous ethanol, m.p. 83.8–84°. *Anal.* Calcd. for

(13) We are greatly indebted to S. B. Penick and Company, New York, N. Y., from whom the leaves were purchased, for carrying out the extraction through this step.

(14) Cason and Rapoport, "Laboratory Text in Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1950, p. 206.

$C_{15}H_{20}N_2O$: C, 73.7; H, 8.3; N, 11.5. Found: C, 73.8; H, 8.2; N, 11.5.

9-Ketodecanenitrile.—Using the general procedure of Cason,[15] 43.7 g. (0.23 mole) of 8-cyanoöctanoyl chloride and dimethylcadmium [prepared from 0.5 mole of methylmagnesium bromide and 50 g. (0.27 mole) of cadmium chloride] were allowed to react and gave 27.0 g. of crude product, b.p. 130–135° (2 mm.). Fractionation through a one meter Podbielniak column separated this crude material into 2.5 g. of 2,10-hendecandione, b.p. 132–134° (4 mm.), and 23.5 g. (61%) of 9-ketodecanenitrile. After crystallization from methanol, the 2,10-hendecandione melted at 61.8–62.3° (reported[16] m.p. 65°) and formed a disemicarbazone melting at 183–184° (reported[16] m.p. 184°). The 9-ketodecanenitrile was refractionated and boiled at 161–162° (9–10 mm.); $n^{25}D$ 1.4430. *Anal.* Calcd. for $C_{10}H_{17}NO$: C, 71.8; H, 10.3; N, 8.4. Found: C, 72.0; H, 10.4; N, 8.3.

The semicarbazone was prepared in the usual manner and was crystallized from aqueous ethanol, m.p. 104.6–105.4°. *Anal.* Calcd. for $C_{11}H_{20}N_4O$: C, 58.9; H, 9.0; N, 25.0. Found: C, 58.8; H, 8.7; N, 25.0.

The 2,4-dinitrophenylhydrazone, prepared in the usual manner, was crystallized from 95% ethanol, m.p. 63–64° (dec.). *Anal.* Calcd. for $C_{16}H_{21}N_5O_4$: C, 55.3; H, 6.1; N, 20.2. Found: C, 55.2; H, 6.0; N, 19.8.

Hydrolysis of a sample of 9-ketodecanenitrile by warming with a mixture of equal volumes of glacial acetic acid and 6 *N* H_2SO_4 proceded overnight to give 9-ketodecanoic acid, m.p. 47.3–48.5° after crystallization from pentane containing a few drops of absolute ethanol (reported[17] m.p. 47.5–48.5°).

9-Methyl-9-hydroxytridecanenitrile.—To a solution of 6.61 g. (0.04 mole) of 9-ketodecanenitrile in 50 ml. of absolute ether, cooled in an ice-bath, was added over a one-hour period with rapid stirring 0.053 mole of *n*-butylmagnesium bromide in 150 ml. of ether. After addition was complete, the ice-bath was removed, rapid stirring was continued for one hour and the reaction mixture treated with ice and acidified with 3 *N* HCl. The layers were separated, the aqueous layer was washed with ether, and the combined ether solutions were dried and evaporated. Fractionation of the residue gave 2.76 g. of recovered keto nitrile, b.p. 124–126° (2 mm.), and 2.07 g. (40% yield based on keto nitrile consumed) of 9-methyl-9-hydroxytridecanenitrile, b.p. 156° (2 mm.); $n^{25}D$ 1.4550.

(15) Cason, THIS JOURNAL, **68**, 2078 (1946).

(16) von Braun, *Ber.*, **40**, 3943 (1907).

(17) Barger, Robinson and Smith, *J. Chem. Soc.*, 718 (1937).

9-Methyltridecanoic Acid.—A solution of 2.07 g. (9.2 millimoles) of 9-methyl-9-hydroxytridecanenitrile in 10 ml. of 2 *N* ethanolic potassium hydroxide was heated under reflux for 23 hours, at the end of which time 98% of the theoretical amount of ammonia had been evolved. After evaporating the ethanol, the residue was dissolved in water, acidified with hydrochloric acid to congo red and extracted with ether. The ether extracts were dried and evaporated, and the residue was heated with a few crystals of iodine at 190–200° for 2 hours and then distilled at 0.5 mm. The distillate, 1.9 g., dissolved in 10 ml. of absolute ethanol, absorbed 8.3 millimoles of hydrogen at room temperature using platinum oxide as the catalyst. Fractionation of the hydrogenated material gave 1.16 g. (55% yield based on nitrile) of 9-methyltridecanoic acid, b.p. 154° (2 mm.); $n^{25}D$ 1.4462. *Anal.* Calcd. for $C_{14}H_{28}O_2$: C, 73.6; H, 12.4; eq. wt., 228. Found: C, 73.8; H, 12.2; eq. wt., 228.

The 2,4,6-tribromoanilide was prepared as described above and crystallized from 95% ethanol, m.p. 105.5–106°. *Anal.* Calcd. for $C_{20}H_{30}Br_3NO$: C, 44.5; H, 5.6. Found: C, 44.5; H, 5.5.

The *p*-bromoanilide, prepared as described above, melted at 66.5–67°. *Anal.* Calcd. for $C_{20}H_{32}BrNO$: C, 62.8; H, 8.4. Found: C, 63.3; H, 8.5.

12-Methyltridecanoic Acid.—An authentic sample[18] of this acid melted at 52.5–53.4°.

The 2,4,6-tribromoanilide was prepared as described above and melted at 112.5–112.9°. *Anal.* Calcd. for $C_{20}H_{30}Br_3NO$: C, 44.5; H, 5.6. Found: C, 44.7; H, 5.6.

Myristic Acid.—A sample of pure myristic acid, kindly supplied by Dr. J. Cason, melted at 52.4–53.4°.

The 2,4,6-tribromoanilide and the ***p*-bromoanilide** were prepared as described above and melted at 124.3–125.5° and 108.4–109.3°, respectively (reported[19] m.p. 124° and 107°).

Summary

The carbon skeleton of carpaine has been shown to consist of a straight chain of fourteen atoms by degrading the alkaloid to myristic acid. This fact necessitates revision of the Barger–Robinson structure for carpaine.

9-Methyltridecanoic acid has been synthesized.

(18) Weitkamp, THIS JOURNAL, **67**, 447 (1945). We are indebted to Dr. Weitkamp for a sample of this material.

(19) Robertson, *J. Chem. Soc.*, **115**, 1210 (1919).

BERKELEY, CALIFORNIA RECEIVED JULY 28, 1950

[CONTRIBUTION FROM THE NORTHERN REGIONAL RESEARCH LABORATORY[1]]

The Acylation of Corn Starch, Amylose and Amylopectin

BY IVAN A. WOLFF, DAVID W. OLDS AND G. E. HILBERT

In comparison with the amount of work on cellulose esters the study of starch esters has been most inadequate. Many of the data on starch esters revealed in the literature were obtained on materials degraded because of drastic conditions used in either the esterification reaction or the pretreatment of the starch. Recent literature reviews include those of Mullen and Pacsu[2a] and of Whistler.[2b] Carson and Maclay[3] have reported the esterification of white potato starch under mild conditions, using formamide as a solubilizing agent.

All whole starch esters (other than those of waxy or glutinous, starches) are mixtures of esterified linear and branched-chain polysaccharides. Organic esters of amylose and amylopectin, other than the acetate and carbanilate[4] are unreported in the literature. This paper deals with the preparation of the triacetates, tripropionates, tributyrates, tricaproates, tripalmitates and tribenzoates of whole starch, amylose and amylopectin.

It was found that the pretreatment of the polysaccharides was most important, both in determining their reactivity and in its effect on the solubilities of the resulting esters. For example, both amylose and starch whose granules had been disrupted ("disintegrated" starch) were more easily esterified and gave esters more soluble in organic solvents than did starches pretreated in liquid

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(2) (a) Mullen and Pacsu, *Ind. Eng. Chem.*, **34**, 1209 (1942); (b) Whistler, in "Advances in Carbohydrate Chemistry," Vol. I, Pigman and Wolfrom, editors, Academic Press, New York, N. Y., 1945, pp. 279–307.

(3) Carson and Maclay, THIS JOURNAL, **68**, 1015 (1946).

(4) Wolff and Rist, *ibid.*, **70**, 2779 (1948).