

TABLE I  
DECARBOXYLATION OF PHENYLACETIC ACID

Acid specific activity	Carbon dioxide specific activity
IVa 830	66
IVb 360	350
IVc 820	11
IVd 830	6

**Hofmann Degradation of Phenylacetamide.**—The reaction was carried out with barium hypobromite rather than sodium hypobromite in order to eliminate the blank due to the carbonate that is always present in sodium hydroxide. A mixture of 135 mg. (0.001 mole) of phenylacetamide and 13.5 cc. of a solution containing 513 mg. (0.003 mole) of barium hydroxide and 324 mg. (0.002 mole) of bromine was placed in a heavy-walled Pyrex tube, the tube chilled in liquid nitrogen, evacuated and sealed. The contents were allowed to warm up to zero degrees and then shaken to dissolve the amide in the barium hypobromite solution. After complete solution the tube was placed in a steam-bath for two hours. After cooling, the tube was opened and the barium carbonate collected; yield 199 mg. (101%). The benzylamine was

isolated from the filtrate by the addition of solid potassium hydroxide and ether extraction. Benzylamine hydrochloride was obtained by adding the dried ethereal solution of the amine to a small volume of dry ether saturated with hydrogen chloride; yield 64 mg. (45%).

TABLE II  
HOFMANN DEGRADATION OF PHENYLACETAMIDE

Phenylacetamide specific activity	Benzylamine·HCl specific activity	Carbon dioxide specific activity
Va 830	825	1
Vb 360	0	360

### Summary

The Willgerodt reaction has been studied using acetophenone labeled in the carbonyl group with  $C^{14}$ . It has been shown that the major pathway of the reaction is to an amide by a non-rearrangement mechanism. The acidic portion, however, arises in part by a molecular rearrangement.

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[CONTRIBUTION FROM THE CHEMOTHERAPY DIVISION, STAMFORD RESEARCH LABORATORIES, AMERICAN CYANAMID COMPANY]

## Isolation and Structure of a Dihydroxyoctadecadienoic Acid from Tung Oil

BY SELBY B. DAVIS,\* EDWARD A. CONROY<sup>1</sup> AND NANCY E. SHAKESPEARE

In the course of a search for the reported hypotensive principle of tung oil,<sup>2</sup> an acidic fraction was separated by treatment of the oil with an anion-active ion exchange resin (Ionac A300) followed by elution of the resin with alkali, and extraction of the acidified eluate with carbon tetrachloride. Storage of the extract at 5° resulted in the separation of a partially crystalline precipitate which was further separated into crystalline Fraction I, m. p. 93–98°, and carbon tetrachloride-insoluble oil, Fraction II. Evaporation of the carbon tetrachloride filtrate left a soluble oil, Fraction III.<sup>3</sup>

Recrystallization of Fraction I yielded a microscopically homogeneous isolate consisting of colorless tabular crystals, m. p. 104–104.5°, devoid of optical activity. The results of quali-

tative and quantitative analysis, molecular weight determination and titration showed the substance to be an unsaturated, hydroxylated, monocarboxylic acid,  $C_{18}H_{32}O_4$ . The formation of an S-benzylthiuronium salt,  $C_{26}H_{42}N_2O_4S$ , m. p. 133–134°, and methyl ester,  $C_{19}H_{34}O_4$ , m. p. 63–64°, in high yield attested the chemical homogeneity of the isolate, m. p. 104–104.5°, and confirmed the presence of one carboxyl group in the molecule.

Quantitative acetylation showed the presence of two hydroxyl groups, and quantitative oximation demonstrated the absence of aldehydic or ketonic carbonyl groups. On hydrogenation the substance absorbed two moles of hydrogen, indicating the presence of two double bonds, and yielded a saturated tetrahydro derivative,  $C_{18}H_{36}O_4$ , m. p. 102–104°.

Attempted oxidation of the tetrahydro derivative, m. p. 102–104°, with periodic acid resulted in complete recovery of the starting material, indicating that the hydroxyl groups were not situated on adjacent carbon atoms.<sup>4</sup>

Oxidation of the tetrahydro derivative with potassium permanganate yielded a diketoid,  $C_{18}H_{32}O_4$ , m. p. 95–96°, from which a dioxime,  $C_{18}H_{34}N_2O_4$ , m. p. 111–113°, was prepared. The diketoid, m. p. 95–96°, was found to be not identical with the 9,12-diketostearic acid, m. p.

\* Harvard University Ph.D. 1942.

(1) Present address: Calco Chemical Division, American Cyanamid Company, Bound Brook, New Jersey.

(2) Grollman, *J. Pharm. Exp. Ther.*, **84**, 128 (1945).

(3) We are indebted to Professor Arthur Grollman, Department of Experimental Medicine, The Southwestern Medical College, Dallas, Texas, for assays of the original tung oil, the whole carbon tetrachloride extract and the three fractions. These assays were carried out by oral administration to rats made hypertensive by ligation of the kidneys [Grollman, *Proc. Soc. Exp. Biol. Med.*, **67**, 102 (1944)]. The blood pressure of the warmed, unanesthetized rats was measured with a tail plethysmograph and pressure cuff [Williams, Harrison and Grollman, *J. Clin. Invest.*, **18**, 373 (1939)]. The original oil, whole extract and Fractions II and III were reported active. Later assays, using the above technique, were carried out in these laboratories by Dr. R. H. Hall. The presence of hypotensive activity in the oil, or in any fraction thereof, was not confirmed.

(4) Malaprade, *Bull. soc. chim.*, [5] **1**, 833 (1934).

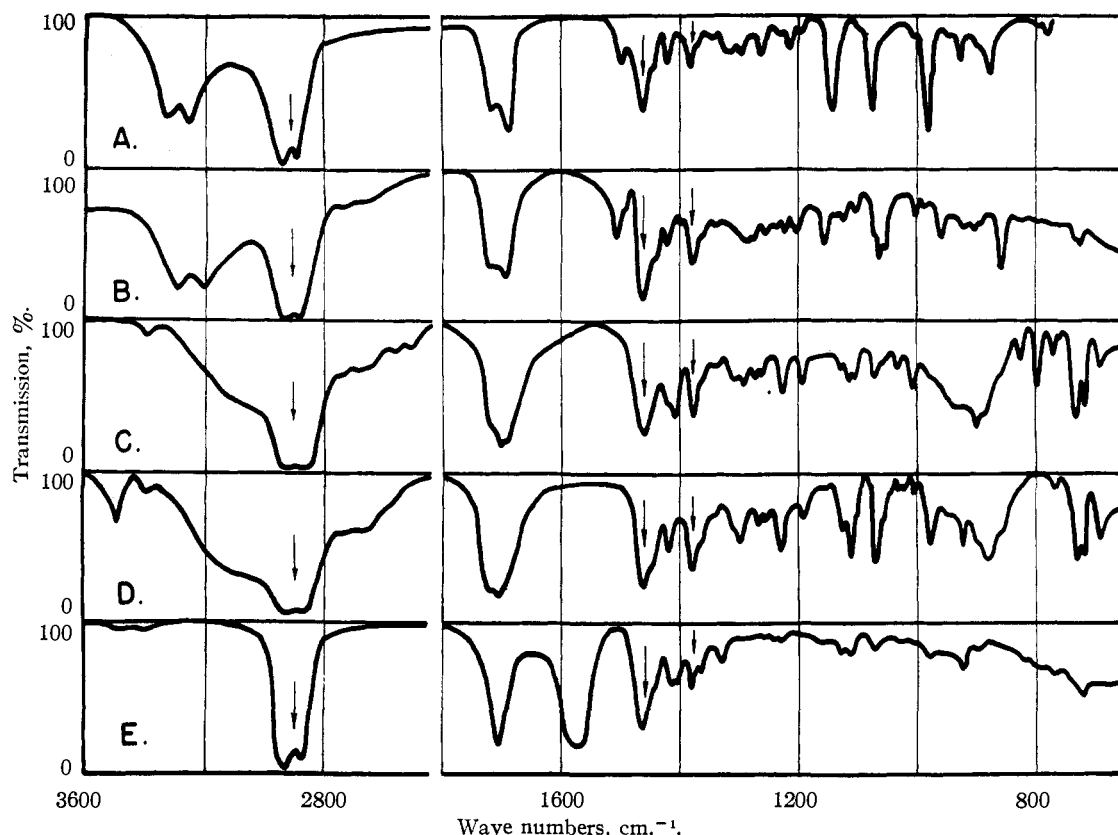


Fig. 1.—Infrared absorption spectra, arrows indicating absorption bands of Nujol in which the samples were mulled: curve A, 9,14-dihydroxy-10,12-octadecadienoic acid; B, 9,14-dihydroxystearic acid; C, 9,12-diketostearic acid; D, 9,14-diketostearic acid; E, sodium 9,14-diketostearate.

96.5°, of Goldsobel,<sup>5</sup> which likewise yields a dioxime, m. p. 112–113°. The mixed melting points of the acids and of the dioximes were depressed, and the infrared spectra (Fig. 1) were somewhat different.

The diketoacid, m. p. 95–96°, also failed to yield a pyrrole derivative when treated with ammonium acetate, indicating that the keto groups were not situated 1–4 to each other, whereas 9,12-diketostearic acid readily yielded the reported pyrrole derivative,<sup>5</sup> m. p. 73°, under identical conditions.

Reduction of the diketoacid, m. p. 95–96°, with hydrazine, however, yielded stearic acid (I), demonstrating the presence of an unbranched octadecanoic acid skeleton.

The position of the intense absorption band of the isolate, m. p. 104–104.5°, at 229  $\mu$  (Fig. 2) excludes the possibilities that the two double bonds present in the molecule are either isolated<sup>6</sup> or conjugated with the carboxylic carbonyl group.<sup>6</sup> Under these circumstances the double bonds must be conjugated with each other, and the diene system must be removed from the carboxyl group by at least one carbon atom.

The observed maximum agrees well with that calculated<sup>7</sup> for a normal, conjugated, disubstituted diene<sup>8</sup>: 227  $\mu$ .

Although the resistance of the tetrahydro derivative, m. p. 102–104°, to oxidation by periodic acid cannot be adduced to eliminate the possibility of a hydroxyl group situated alpha to the carboxyl,<sup>4</sup> the absorption maximum of the derived diketoacid, m. p. 95–96°, at 275  $\mu$ <sup>9</sup> (Fig. 2) effectively rules out this possibility.

The foregoing considerations serve to characterize the isolate, m. p. 104–104.5°, as a straight-chain dihydroxyoctadecadienoic acid in which (a) the hydroxyls are not vicinal, (b) no hydroxyl is located alpha to the carboxyl group, (c) the two double bonds are conjugated and (d) the diene system is not conjugated with the carboxyl group. There are 726 theoretically possible

(8) An attempt to confirm the conjugated diene structure chemically, by heating the isolate, m. p. 104–104.5°, with an excess of maleic anhydride, led to a complex mixture from which no homogeneous adduct was separated.

(9) This value lies in the region characteristic of normal, unconjugated ketones,<sup>6</sup> and is identical with that of the known 9,12-diketostearic acid (Fig. 2.) Conjugation of a keto group with the carboxylic carbonyl would necessarily result in an absorption maximum appreciably further toward the red. The absorption maximum of pyruvic acid, *e. g.*, occurs at 331  $\mu$  [Bielecki and Henri, *Compt. rend.*, **158**, 866 (1914)].

(5) Goldsobel, *J. Russ. Phys.-Chem. Soc.*, **38**, 900 (1906).

(6) Dimroth, *Angew. Chem.*, **52**, 545 (1939).

(7) Woodward, *THIS JOURNAL*, **64**, 72 (1942).

structures answering this description, exclusive of optically active forms.<sup>10</sup>

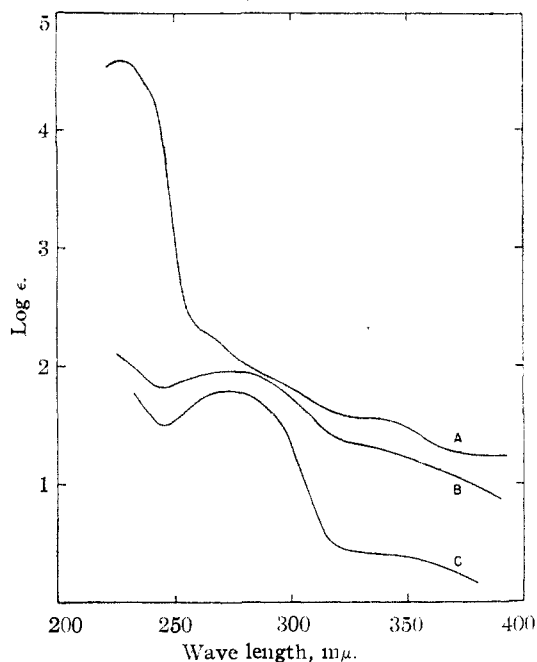
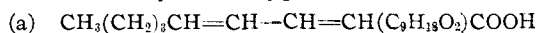
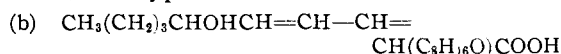


Fig. 2.—Ultraviolet absorption spectra: curve A, 9,14-dihydroxy-10,12-octadecadienoic acid; B, 9,14-diketostearic acid; C, 9,12-diketostearic acid.

Ozonization of the isolate, m. p. 104–104.5°, followed by decomposition of the ozonide with hydrogen peroxide, yielded only two products: valeric acid (II) and azelaic acid (III). Of the 726 possible dihydroxyoctadecadienoic acids cited there are twenty-one of type



and seven of type

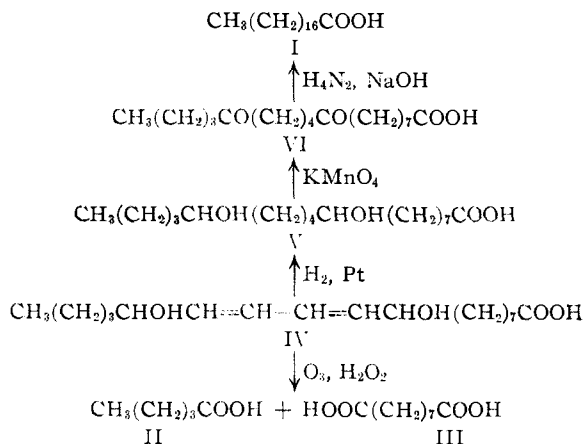


which could be expected to yield valeric acid<sup>11</sup> under the conditions of ozonization employed. Of the twenty-one structures of type (a) none could yield azelaic acid as a second ozonization product. Of the seven structures of type (b) only one (IV) could yield azelaic acid, thus establishing the structure of the isolate, m. p. 104–104.5°, as 9,14-dihydroxy-10,12-octadecadienoic acid.

The tetrahydro derivative, m. p. 102–104°, is hence characterized as 9,14-dihydroxystearic acid (V), and the derived diketo acid, m. p. 95–96°, as 9,14-diketostearic acid (VI).

(10) If the additional limitation that the hydroxyl groups cannot be situated 1–4 to each other is considered, this number is reduced to 636. The further elimination, however, is unnecessary to completion of the proof of structure.

(11)  $\alpha$ -Hydroxy acids, such as the  $\alpha$ -hydroxycaproic acid expected from the decomposition of ozonides from type (b), are readily oxidized by hydrogen peroxide yielding the acid of one less carbon atom [Dakin, *J. Biol. Chem.*, **4**, 91 (1908); Efront, *Compt. rend.*, **154**, 1296 (1912)].



It is possible that the isolated 9,14-dihydroxy-10,12-octadecadienoic acid is an artifact resulting from autoxidation of a 9,11,13-octadecatrienoic acid (eleostearic acid)<sup>12</sup> during production and storage of the oil, or in the course of the present fractionation.<sup>13</sup> The lack of optical activity of the isolate, m. p. 104–104.5°, which possesses two asymmetric carbon atoms, is consistent with this hypothesis.

#### Experimental<sup>14</sup>

**Separation of Crude Acid Fraction.**—A quantity of alkali-activated Ionac A 300<sup>15</sup> was washed with distilled water until the reaction of the washings approached neutrality (pH 8.6). A 250-g. portion of the undried resin was then stirred with 5 kg. of tung oil<sup>16</sup> for twenty-four hours. The resin was centrifuged, washed with three 250-ml. portions of light petroleum (Skellysolve F), and spread out to dry at 25°, relative humidity 50%, for six days. The dried resin was stirred for one hour with 250 ml. of 3% aqueous sodium hydroxide, and filtered. Two further elutions were carried out in the same manner. The combined eluate was acidified to pH 2 with concentrated hydrochloric acid and twice extracted with 425-ml. portions of carbon tetrachloride. On standing at 5° for several days the combined extracts yielded a semisolid precipitate which was filtered. Crystallization of the precipitate from ethyl acetate yielded 121 mg. (0.0024%) of Fraction I, pale yellow crystals, m. p. 93–98°. Evaporation of the mother liquor yielded 135 mg. (0.0027%) of Fraction II, a viscous, orange oil. Evaporation of the original carbon tetrachloride filtrate yielded 5.14 g. (0.103%) of Fraction III, a yellow oil.

A second run, identical with the foregoing except that the resin plus adsorbate was dried for only one and one-

(12) Distinct from the ketol-oxidoacid component,  $\text{CH}_3(\text{CH}_2)_8\text{CH}=\text{CH}-\text{CH}=\text{CH}-\text{CO}-\text{CHOH}(\text{CH}_2)_7\text{COOH}$ , of the autoxidized trioleostearin (oxyn) of Morrell, *et al.* [Morrell and Phillips, *J. Oil and Colour Chem. Assoc.*, **23**, 103 (1940)].

(13) Higher yields of crude isolate, m. p. 93–98°, (Fraction I) were consistently correlated with longer periods of drying of the resin prior to elution; *cf.* experimental section.

(14) (a) All melting points were determined on the Fisher-Johns block; (b) analyses were performed by the Microanalytical Laboratory, Technical Service Division, these laboratories, under the direction of Dr. J. A. Kuck, except as otherwise noted.

(15) An anion exchange resin produced by the American Cyanamid Company. We are indebted to Mr. H. M. Day of the Technical Service Division, these Laboratories, for samples of the resin and advice concerning its use.

(16) An imported product (Chinese) furnished by the Warners Division, American Cyanamid Company, Linden, New Jersey.

quarter hours, yielded 25.5 mg. (0.00051%) of Fraction I, 38 mg. (0.00076%) of Fraction II and 5.83 g. (0.117%) of Fraction III.

**Purification of Fraction I.**—A 4.0-g. portion of Fraction I, m. p. 93–98°, the product of a larger-scale run in which the resin was dried in an oven at 40° for three days, was thrice crystallized from ethyl acetate yielding 2.68 g. of colorless platelets of the pure isolate, m. p. 104–104.5°,  $[\alpha]_D^{20}$  0.0 ± 0.2° (absolute ethanol,  $c = 1.056$ ). Qualitative tests showed the absence of nitrogen, halogens and sulfur. The substance proved insoluble in water and 10% hydrochloric acid, but dissolved slowly in warm 5% sodium bicarbonate. It was relatively insoluble in petroleum ether, benzene and carbon tetrachloride; moderately soluble in chloroform, ether, ethyl acetate and acetone; readily soluble in ethanol and pyridine.

*Anal.* Calcd. for  $C_{18}H_{32}O_4$ : C, 69.19; H, 10.33; mol. wt. and equiv. wt., 312. Found: C, 69.11, 69.06, 69.28; H, 10.38, 10.34, 10.22; mol. wt. (Rast), 304, 301, 356; equiv. wt., 311, 312.

The ultraviolet absorption spectrum (Fig. 2) showed a maximum at 229  $m\mu$ ,  $\log \epsilon = 4.594$  (95% ethanol).<sup>17</sup> Bands in the infrared spectrum (Fig. 1) indicated the presence of hydroxyl (3325 and 3250  $cm^{-1}$ ) and carbonyl groups (1715 and 1685  $cm^{-1}$ ), and carbon-carbon double bond (980  $cm^{-1}$ ).<sup>18</sup> A chloroform solution of the substance rapidly absorbed bromine.

Quantitative acetylation<sup>19</sup> of the isolate, m. p. 104–104.5°, showed the presence of two (1.8) acetyltable hydroxyl groups. Quantitative oximation<sup>20</sup> showed the absence of aldehydic or ketonic carbonyl groups. On hydrogenation in absolute ethanol solution, using Adams catalyst, the acid absorbed two (2.11, 2.03, 2.25) moles of hydrogen per mole.

**S-Benzylthiuronium Salt.**—A methanolic solution of the isolate, m. p. 104–104.5°, was titrated to a pH meter-reading of 8.95 with 0.1*N* aqueous sodium hydroxide. The solution was evaporated and the residue was taken up in absolute methanol. After filtration, the sodium salt was precipitated as a colorless, crystalline solid, m. p. 185–187°, by the addition of ethyl acetate.

Treatment of the sodium salt, m. p. 185–187°, with an equivalent quantity of S-benzylthiuronium chloride in 50% ethanol yielded the S-benzylthiuronium salt (85%), m. p. 133–134°. Two recrystallizations from 50% ethanol gave an analytical sample of unchanged m. p.

*Anal.* Calcd. for  $C_{26}H_{42}N_2O_4S$ : N, 5.85; S, 6.70. Found: N, 5.66, 5.66; S, 6.83, 6.88.

**Methyl Ester.**—The isolate, m. p. 104–104.5°, was treated with a slight excess of diazomethane in ether solution. Evaporation of the solvent left a mixture, m. p. 70–95°, which was separated by systematic fractional crystallization from ethyl acetate into recovered isolate (14%), m. p. and mixed m. p. 101–103°, and methyl ester (16%), m. p. 59–61°. Evaporation of the combined filtrates yielded further ester (70%), m. p. 58–60°, mixed m. p. 59–61°. Recrystallization of the combined ester fractions from absolute ethanol-petroleum ether gave the pure methyl ester, m. p. 63–64°.

*Anal.* Calcd. for  $C_{19}H_{34}O_4$ : C, 69.90; H, 10.50. Found: C, 70.06, 69.78; H, 10.25, 10.56.

**p-Phenylphenacyl Ester.**—A mixture of equivalent quantities of the sodium salt, m. p. 185–187°, and p-phenylphenacyl bromide, in 80% ethanol, was heated in a sealed tube at 80° for two hours. The product was crystallized twice from 80% ethanol, then three times from ethyl acetate, yielding the pure p-phenylphenacyl ester (40%), m. p. 103.5–104.5°. The mixed m. p. with the isolate, m. p. 104–104.5°, showed a depression (mixed m. p. 92–97°).

(17) We are indebted to Miss K. S. Howard of the Chemotherapy Division, these laboratories, for the ultraviolet absorption studies.

(18) We are grateful to Dr. R. C. Gore of the Physics Division, these laboratories, for the infrared absorption spectra, which were determined and interpreted under his direction.

(19) West, Hoagland and Curtis, *J. Biol. Chem.*, **104**, 627 (1934).

(20) Sabetay, *Bull. soc. chim.*, [5] **8**, 1419 (1938).

*Anal.* Calcd. for  $C_{27}H_{46}O_5$ : C, 75.85; H, 8.36. Found: C, 75.70, 75.74; H, 8.43, 8.15.

**Tetrahydro Derivative.**—The hydrogenation of 1.0 g. of the isolate, m. p. 104–104.5°, in 150 ml. of absolute ethanol, using 0.4 g. of Adams catalyst, was complete (2 moles absorbed) in one and one-half hours. Crystallization of the product from absolute ethanol yielded 645 mg. (63%) of the crystalline tetrahydro derivative, m. p. 102–104°. The mixed m. p. with the starting material, m. p. 104–104.5°, was depressed (mixed m. p. 90–95°). A chloroform solution of the substance absorbed no bromine. The infrared spectrum (Fig. 1), compared with that of the isolate, m. p. 104–104.5°, showed a slight shift of the hydroxyl bands to 3290 and 3200  $cm^{-1}$ , and lacked the carbon-carbon double bond absorption at 980  $cm^{-1}$ .

*Anal.* Calcd. for  $C_{18}H_{36}O_4$ : C, 68.31; H, 11.47. Found: C, 68.12, 68.16; H, 11.36, 11.29.

**Attempted Periodic Acid Oxidation of the Tetrahydro Derivative.**—To a solution of the tetrahydro derivative, m. p. 102–104° (50 mg.) in 3 ml. of dioxane there was added 40 mg. of periodic acid dihydrate in 0.5 ml. of water. The clear solution was allowed to stand at room temperature for fifteen hours. After the addition of a little glycerol to destroy the reagent, the solution was evaporated and the residue was washed with water, leaving 48 mg. of white solid, m. p. 99–102°. Recrystallization from ethyl acetate yielded 45 mg. of colorless crystals, m. p. 102–104°, identified as recovered tetrahydro derivative (mixed m. p. 102–104°).

**Permanganate Oxidation of the Tetrahydro-derivative.**—A solution of the tetrahydro derivative, m. p. 102–104° (100 mg.) in 8 ml. of acetone was kept at reflux temperature for six hours during the gradual addition of 200 mg. of solid potassium permanganate. The reaction mixture was acidified with 0.3 ml. of concentrated hydrochloric acid and filtered. The filter cake was washed with an additional 10 ml. of acetone and the combined acetone solution was evaporated. The residue was washed with water and twice crystallized from 50% acetone yielding 57 mg. of colorless platelets, m. p. 95–96°. The ultraviolet spectrum of the substance (Fig. 2) showed a maximum at 275  $m\mu$ ,  $\log \epsilon = 1.957$  (95% ethanol). The infrared spectrum (Fig. 1) showed poorly resolved carbonyl bands (centered at 1710  $cm^{-1}$ ) in the 6- $\mu$  region. The infrared spectrum of the sodium salt (Fig. 1), however, showed two distinct bands, indicating the presence of ketonic carbonyl (1705  $cm^{-1}$ ) as well as carboxylate carbonyl (1575  $cm^{-1}$ ).

*Anal.*<sup>21</sup> Calcd. for  $C_{18}H_{32}O_4$ : C, 69.19; H, 10.33. Found: C, 69.01, 69.10; H, 10.32, 10.25.

The substance yielded a dioxime, m. p. 111–113°.

*Anal.* Calcd. for  $C_{18}H_{34}N_2O_4$ : N, 8.18. Found: N, 8.07.

An attempt to convert the substance to a pyrrole derivative by treatment with ammonium acetate in acetic acid<sup>22</sup> was unsuccessful.

**Reduction of the Permanganate Oxidation Product to Stearic Acid.**—The diketooacid, m. p. 95–96° (30 mg.) was heated under reflux for one hour with 50 mg. of sodium hydroxide and 0.05 ml. of 85% hydrazine hydrate in 1 ml. of diethylene glycol, following the modified Wolff-Kishner procedure of Huang-Minlon.<sup>23</sup> The condenser was removed and the mixture was heated at 200° for an additional hour. Water (3 ml.) was added to the reaction mixture, the suspension was washed with ether, acidified, and the product was extracted with ether. Evaporation of the ether, followed by two recrystallizations of the residue from 50% ethanol, yielded 14 mg. (51%) of essentially pure stearic acid, m. p. 66–68°. The mixed m. p. with authentic stearic acid, m. p. 67–69° (69.62°),<sup>24</sup> was 66–68°, and the infrared spectra proved identical. The substance yielded an anilide, m. p. 92.5–93.5°.

(21) Huffman Microanalytical Laboratories, Denver, Colorado.

(22) Kehrer, *Ber.*, **34**, 1263 (1901).

(23) Huang-Minlon, *This Journal*, **68**, 2487 (1946).

(24) Guy and Smith, *J. Chem. Soc.*, 615 (1939).

*Anal.* Calcd. for  $C_{24}H_{41}NO$ : N, 3.90. Found: N, 3.85, 4.01, 3.92.

The anilide showed no depression of m. p. (mixed m. p. 92.5–93.5°) on admixture with authentic stearanilide, m. p. 92.5–93.5° (95.5°).<sup>24</sup>

**9,12-Diketostearic Acid.**—12-Hydroxy-9-octadecynoic acid (ricinostearic acid) was prepared from castor oil by the method of Mühle.<sup>25</sup> This substance was converted to 12-hydroxy-9-ketostearic acid by the procedure of Goldsobel.<sup>26</sup> The latter compound was oxidized to 9,12-diketostearic acid with potassium permanganate in acetone, following the method outlined above for oxidation of the tetrahydro derivative, m. p. 102–104°. Crystallization from 50% aqueous acetone, followed by recrystallization from ethyl acetate, gave pure 9,12-diketostearic acid, m. p. 97.5–98° (96.5°)<sup>5</sup> in a yield of 47%. The ultraviolet spectrum of the substance (Fig. 2) showed a maximum at 275  $m\mu$ ,  $\log \epsilon = 1.788$  (95% ethanol). The infrared spectrum (Fig. 1) resembled that of the diketoacid, m. p. 95–96°, but showed minor characteristic differences, particularly in the region 1000 to 700  $cm^{-1}$ . The substance yielded the reported dioxime, m. p. 111.5–112.5° (112–113°),<sup>5</sup> and pyrrole, m. p. 71–72.5° (73°).<sup>5</sup>

The melting point of 9,12-diketostearic acid was depressed on admixture with the diketoacid, m. p. 95–96° (mixed m. p. 87.5–91°). The mixture of the corresponding dioximes also showed a depression (mixed m. p. 95–108°).

**Ozonization.**—Ozonized oxygen (10 l./hr.) was passed through an ice-cold solution of the isolate, m. p. 104–104.5° (500 mg.) in 50 ml. of methylene chloride for one hour. Two volumes of water was added to the solution and nitrogen was bubbled through the mixture until the methylene chloride was evaporated. A 20-ml. portion of 30% hydrogen peroxide was added to the resulting suspension, the mixture was boiled for one hour, and the solution was extracted three times with 100-ml. portions of chloroform. Evaporation of the combined extract left 400 mg. of yellow oil with a strong, fatty-acid odor. Vacuum distillation of the oil yielded 36 mg. of a volatile

acid, b. p. 80–90° (15 mm.). Comparison of the infrared spectrum of the distillate with that of *n*-valeric acid showed the two to be identical. The distillate yielded an **S-benzylthiuronium salt**, m. p. 154–155°.

*Anal.*<sup>21</sup> Calcd. for  $C_{13}H_{20}N_2O_2S$ : N, 10.44. Found: N, 10.23, 10.20.

An authentic sample of the previously unreported **S-benzylthiuronium *n*-valerate**, m. p. 154–155°, was prepared for comparison.

*Anal.*<sup>21</sup> Calcd. for  $C_{13}H_{20}N_2O_2S$ : N, 10.44. Found: N, 10.11, 10.17.

The derivatives showed no depression of m. p. on admixture (mixed m. p. 154–155°).

The non-volatile still-residue was extracted with 3 ml. of hot water. The extract was decolorized with charcoal (Darco G-60), and filtered. On cooling, the solution deposited 40 mg. of crystalline solid, m. p. 96–99°. Recrystallization from water raised the m. p. to 101–103°. The infrared spectrum of the substance was found to be identical with that of azelaic acid. The mixed m. p. with an authentic sample of the latter, m. p. 103–105° (106°),<sup>27</sup> showed no depression (mixed m. p. 103–105°). Treatment of the substance with *p*-bromophenacyl bromide yielded a derivative, m. p. 129–130°.

*Anal.* Calcd. for  $C_{23}H_{26}Br_2O_6$ : Br, 27.45. Found: Br, 27.56, 27.64.

The mixed m. p. of the derivative with authentic di- (*p*-bromophenacyl) azelate, m. p. 130–131° (130.6°),<sup>28</sup> showed no depression (mixed m. p. 130–131°).

A search for other fragments in the mother liquor resulted only in the isolation of more azelaic acid.

### Summary

A crystalline substance, isolated in low yield from tung oil, has been shown to be 9,14-dihydroxy-10,12-octadecadienoic acid.

(27) Gantter and Hell, *Ber.*, **14**, 1545 (1881).

(28) Kelly and Kleff, *THIS JOURNAL*, **64**, 4444 (1932).

STAMFORD, CONNECTICUT

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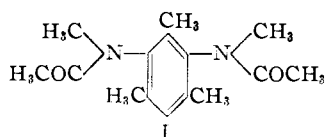
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

## Restricted Rotation in Aryl Amines. VIII. Ring Nitrogen Derivatives of Diaminomesitylene

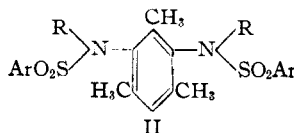
BY ROGER ADAMS\* AND JOHN B. CAMPBELL<sup>1</sup>

Stereoisomers of *N,N'*-dimethyl-*N,N'*-diacetyl-diaminomesitylene (I) could not be obtained.<sup>2</sup> However, *cis* and *trans* isomers due to restricted rotation of the groups about the carbon-nitrogen bond were prepared readily from compounds of the type shown in formula II.<sup>3</sup> When R is a carboxymethyl group, the *trans* isomer was resolved into its optical antipodes.

In the present investigation, a study was made of diaminomesitylene derivatives in which the two nitrogens were incorporated in five-membered ring systems. As a model experiment, disuc-



R = alkyl, benzyl,  
carboxymethyl  
Ar = phenyl or  
R = methyl  
Ar = phenyl, *p*-tolyl,  
*p*-bromophenyl



cinimidomesitylene was synthesized from *N,N'*-disuccinyl-diaminomesitylene by the action of acetic anhydride and sodium acetate. In a similar manner, diaminomesitylene and  $\alpha,\alpha$ -dimethylsuccinic anhydride were condensed to the *N,N'*-di-( $\alpha,\alpha$ -dimethylsuccinyl)-diaminomesitylene and the latter dehydrated to bis-( $\alpha,\alpha$ -

\* Harvard University Ph.D. 1912.

(1) An abstract of a thesis submitted by John B. Campbell to the Graduate College of the University of Illinois, 1949, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Adams and Chase, *THIS JOURNAL*, **70**, 4202 (1948).

(3) Adams and Tjepkema, *ibid.*, **70**, 4204 (1948); Adams and Rothstein, *ibid.*, **71**, 1620 (1949).