with b.p. 44–110° (0.3 mm.). Hexadecatriyne-5,8,11 (18.5 g., or 64% yield based on 1,4-dibromobutyne-2 used) was taken at 110–120° (mostly at 119–120°) (0.3 mm.). Redistillation permitted recovery of almost all of this hexadecatriyne-5,8,11 (b.p.'s 100–101° (0.1 mm.) and 114–115° (0.2–0.25 mm.)), which was collected and sealed without breaking the vacuum in several ampoules. The index of refraction was $n^{25}\text{D}$ 1.4818.

Anal. Calcd. for $C_{16}H_{22}$: C, 89.7; H, 10.3. Found: C, 89.46; H, 10.39.

Ultraviolet Absorption.—Ultraviolet absorption curves were determined using 10^{-3} *M* solutions of hexadecatriyne-5,8,11 in 95% alcohol. The product from nonadiyne-1,4 and 1-bromoheptyne-2 had λ_{max} 273 mμ (ϵ 480); the product from hexyne-1 and 1,4-dibromobutyne-2 has λ_{max} 272 mμ (ϵ 580). Both products had poorly defined maxima in the 220–228 mμ region (ϵ *ca.* 450). Actually, because of the presence of impurities, we are in no position to claim that the observed maxima are characteristic features of the skipped triyne system.

Hexadecane from Hexadecatriyne-5,8,11.—A sample of hexadecatriyne-5,8,11 (2.8356 g. or 0.01323 mole) prepared from nonadiyne-1,4 and 1-bromoheptyne-2 was transferred from a freshly opened ampoule to a flask containing 30 ml. of ethyl acetate (J. T. Baker analyzed reagent), and was hydrogenated at room temperature in the presence of 100 mg. of platinum oxide catalyst. Absorption of hydrogen ceased after ten hours at which time 94% of the theoretical six moles of hydrogen had been taken up. The mixture was filtered, and the catalyst rinsed on the funnel with 20 ml. of ethyl acetate. Solvent was removed from the filtrate with the help of a current of air at temperatures no higher than 100°. The dark amber residue was distilled in a Claisen flask to furnish 2.33 g. (78%) of water-white hexadecane, b.p. 105–105.5° (1 mm.) and $n^{22.5}\text{D}$ 1.4336. A few drops of forerun were rejected. The "Dreisbach–Dow Chemical Company Compilation of Physical Constants" gives b.p. 104.89° (1 mm.) for hexadecane; Egloff records $n^{22.5}\text{D}$ 1.4335.[12]

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[12] G. Egloff, "Physical Constants of Hydrocarbons," Vol. V (Revised Values), American Chemical Society Monograph No. 78, Reinhold Publishing Corp., New York, N. Y., 1953.

BOSTON, MASSACHUSETTS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BOSTON UNIVERSITY]

Configuration of 9,10-Dihydroxystearic Acid[1]

BY WALTER J. GENSLER AND HERBERT N. SCHLEIN

RECEIVED JULY 15, 1955

9,10-Dihydroxyoctadecanedioic acid, m.p. 121–122°, is shown to be the racemic form by resolution with brucine. The half-ester of this acid is reduced with sodium and alcohol to 9,10,18-trihydroxystearic acid. This acid is tosylated, the 18-tosyloxy derivative is converted to the 18-iodo compound, and the iodo group is removed with zinc to give *threo*-9,10-dihydroxystearic acid, m.p. 94.5–95°.

Various methods have been employed in assigning the *erythro* configuration to "high melting" 9,10-dihydroxystearic acid (m.p. 131–132°) and the *threo* configuration to "low-melting" 9,10-dihydroxystearic acid (m.p. 94–95°).[2] Yet among the methods reported, the most reliable of all, that is, relating the *erythro* form to a demonstrably *meso* derivative, or the *threo* form to a demonstrably *racemic* derivative, is not to be found. Böeseken and Belinfante[3] did attempt something on this order by relating the 9,10-dihydroxystearic acids to the 9,10-dihydroxyoctadecanes. However, difficulty with the resolution of racemic 9,10-dihydroxyoctadecane blocked completion of their plans. In the work described in the present paper, we have established the configuration of the 9,10-dihydroxyoctadecanedioic acids (I), and have converted the racemic form by steps not involving the groups at 9 and 10 to 9,10-dihydroxystearic acid, m.p. 94.5–95°. These relations provide independent and definitive proof that "low melting" 9,10-dihydroxystearic acid has the *threo* configuration.

Resolution of 9,10-dihydroxyoctadecanedioic acid (I) (phloionic acid), m.p. 121–122°,[4,5] with strychnine or with quinine failed. A crystalline brucine salt of acid I formed smoothly, but the usual fractional crystallization gave no sign of resolution. However when the brucine salt was repeatedly leached with alcohol, and the acid was recovered from the undissolved salt, a distinct rotation was observed. Optical activity persisted in the benzoyl derivative of the regenerated acid. The fact that the 121–122° acid I could be obtained with optical activity clearly establishes this form as the racemic modification.[6]

An attempt was made to apply an attractive alternate scheme—noteworthy in that resolution is not involved—in determining the configuration of the two 9,10-dihydroxyoctadecanedioic acids. The benzylidene derivative of the racemic dihydroxy diacid can exist in only *one* form, and was in fact obtained as a single material. *A priori*, the benzylidene derivative of the *meso*-dihydroxy diacid can exist in *two* forms, both *meso*. It follows that the dihydroxy diacid leading to *one* benzylidene derivative is the *dl*-form, and that the dihydroxy diacid leading to *two* derivatives is the *meso* form. Disappointingly, the latter two benzylidene derivatives were not obtained pure, so that the scheme, realized only in part, did not furnish clear-cut conclusions. In principle, the method is related to the work of Wislicenus[7] on the configuration of the two 2,5-dimethylcyclopentane-1,1-dicarboxylic acids.

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[1] Abstracted from the dissertation submitted by Herbert N. Schlein in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Boston University Graduate School.

[2] For pertinent work and for leading references see D. Swern, L. P. Witnauer and H. B. Knight, THIS JOURNAL, **74**, 1655 (1952). Also *cf.* T. P. Hilditch "The Chemical Constitution of Natural Fats," Second Edition (revised), Chapman and Hall, Ltd., London, 1947.

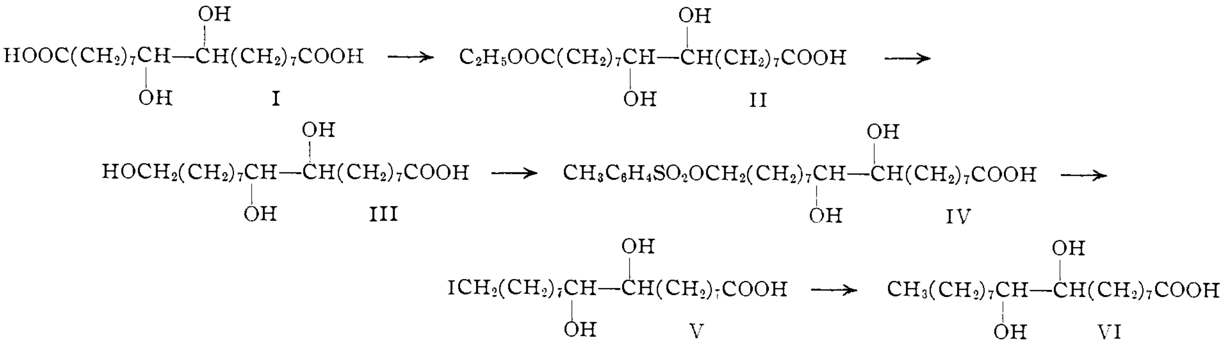
[3] J. Böeseken and A. H. Belinfante, *Rec. trav. chim.*, **45**, 914 (1926).

[4] *Cf.* W. J. Gensler and H. N. Schlein, THIS JOURNAL, **77**, 4846 (1955).

[5] In the course of the present work, we have found that phloionic acid I, isolated from cork,[4] has no observable optical activity.

[6] Note ref. 4 as well as L. Ruzicka, Pl. A. Plattner and W. Widmer, *Helv. Chim. Acta*, **25**, 1086 (1942); H. Hunsdiecker, *Ber.*, **77**, 185 (1944); I. Ribas and E. Seoane, *Anales Real soc. españ. fis. y quim.* (series B), 963 (1954); G. Dupont, R. Dulou and J. Cohen, *Compt. rend.*, **240**, 875 (1955).

[7] J. Wislicenus, *Ber.*, **34**, 2565 (1901).



$$\mathrm{HOOC(CH_2)_7\underset{OH}{CH}-\overset{OH}{CH}(CH_2)_7COOH}\ \text{I} \longrightarrow \mathrm{C_2H_5OOC(CH_2)_7\underset{OH}{CH}-\overset{OH}{CH}(CH_2)_7COOH}\ \text{II} \longrightarrow$$

$$\mathrm{HOCH_2(CH_2)_7\underset{OH}{CH}-\overset{OH}{CH}(CH_2)_7COOH}\ \text{III} \longrightarrow \mathrm{CH_3C_6H_4SO_2OCH_2(CH_2)_7\underset{OH}{CH}-\overset{OH}{CH}(CH_2)_7COOH}\ \text{IV} \longrightarrow$$

$$\mathrm{ICH_2(CH_2)_7\underset{OH}{CH}-\overset{OH}{CH}(CH_2)_7COOH}\ \text{V} \longrightarrow \mathrm{CH_3(CH_2)_7\underset{OH}{CH}-\overset{OH}{CH}(CH_2)_7COOH}\ \text{VI}$$

Formulations I–VI describe the production of 9,10-dihydroxystearic acid by the transformation of one of the carboxyl groups of the 121–122° acid I to a methyl group. Preparation of the half-ester II of the 121–122° dihydroxy diacid by direct esterification with alcohol and hydrogen chloride resulted in a maximum conversion of 23%. Controlled saponification of the diester of I, in producing mainly unreacted diester and acid I, was again unsatisfactory. The desired half-ester II was obtained eventually in a practical manner by acid-catalyzed esterification of the diacid in ethyl acetate solvent containing some ethanol. Bouveault–Blanc reduction of the half-ester II gave 9,10,18-trihydroxystearic acid (III), m.p. 136–137°.[8] Tosylation with *p*-toluenesulfonyl chloride in pyridine occurred selectively on the primary hydroxy group[9] to furnish 9,10-dihydroxy-18-tosyloxystearic acid (IV). Treatment with sodium iodide yielded 9,10-dihydroxy-18-iodostearic acid (V), which was not purified but was reduced directly with zinc and acid. The product, which must still have the 9- and 10-hydroxy groups disposed as in *threo* (*i.e., racemic*) compound I, proved to be 9,10-dihydroxystearic acid, m.p. 94.5–95°. This "low melting" 9,10-dihydroxystearic acid accordingly is in the *threo* configuration.

The intermediate trihydroxystearic acid III is of some interest in connection with phloionolic acid, m.p. 104°, isolated from cork, and assigned the structure of 9,10,18-trihydroxystearic acid.[10] If a generalization based on comparing known *erythro* and *threo* forms of 9,10-dihydroxystearic acid (VI) and of compound I is valid, the *erythro-glycol* should melt *higher* than the corresponding *threo*-glycol. However, the melting point of phloionolic acid is *lower* than the melting point of compound III, which is *threo*, and therefore it appears unlikely that phloionolic acid is the *erythro* stereoisomer of III. Since the melting point of phloionolic acid has been confirmed at 104° (private communication from Dr. I. Ribas), the structure of this cork acid may not be that of 9,10,18-trihydroxystearic acid.[11]

Experimental[12]

Brucine Salt (1:1) of Optically Active 9,10-Dihydroxyoctadecanedioic Acid (I).—A solution of 1.1 g. of brucine (0.0030 mole) and 0.5 g. (0.0015 mole) of 9,10-dihydroxyoctadecanedioic acid, m.p. 121–122°, in 50 ml. of absolute ethanol was boiled for one hour. Alcohol was removed by distillation until the volume was 15 ml., and the concentrated solution was held at 0° for three days. The small white cubic crystals were collected, washed on the funnel with a small volume of cold ethanol and air-dried. The salt weighed 1.15 g. and melted at 115–117°. Repeated crystallizations from ethanol–water as well as from ethanol did not change the melting point and did not give any sign of separation into two compounds. The following procedure did effect separation.

A mixture of 3.6 g. of the brucine salt, m.p. 115–117°, and 10 ml. of absolute ethanol was allowed to stand at room temperature for two days. The mixture was filtered, and the undissolved solids were treated in the same way with a fresh 10-ml. portion of absolute ethanol. After a total of eight successive exposures of the brucine salt to ethanol, 1.3 g. remained undissolved. Crystallization of this solid (m.p. 118–119°) from 8 ml. of ethanol afforded 0.92 g. of a white product, which was dried in vacuum at 78°.

Anal. Calcd. for $C_{41}H_{60}O_{10}N_2$: C, 66.5; H, 8.2. Found: C, 66.6; H, 8.4.

The rotation of the salt before the alcohol leaching was $[\alpha]^{26}\mathrm{D}$ −68° (0.108 g. in 10 ml. of alcohol solution), and after the leaching was $[\alpha]^{26}\mathrm{D}$ −65° (0.103 g. in 10 ml. of alcohol solution).

Optically Active 9,10-Dihydroxyoctadecanedioic Acid.—A mixture of 0.41 g. of brucine salt ($[\alpha]^{26}\mathrm{D}$ −65°) with 50 ml. of water and 1 ml. of concentrated hydrochloric acid was allowed to stand at room temperature. After addition of another 1 ml. of hydrochloric acid, the mixture was extracted with ether. The ether extract was washed with water until the washings were at *p*H 5, and the ether was dried over calcium chloride. Removal of drying agent and of solvent left 0.17 g. (88%) of 9,10-dihydroxyoctadecanedioic acid, m.p. 122–123°. Crystallization from ethyl acetate gave 0.15 g. of the acid with the same melting point, and with $[\alpha]^{26}\mathrm{D}$ 4.6 ± 0.4° (standard deviation) (0.112 g. in 5 ml. of ethanol).

Anal. Calcd. for $C_{18}H_{34}O_6$: C, 62.4; H, 9.9; N, 0.0. Found: C, 62.7; H, 10.0; N, 0.0.

Benzoyl Derivative of Optically Active 9,10-Dihydroxyoctadecanedioic Acid.—A mixture of 0.095 g. of the acid showing optical activity, 10 ml. of 10% aqueous sodium hydroxide and 1 ml. of benzoyl chloride was mechanically shaken for two hours. The mixture after acidification with concentrated hydrochloric acid (to *p*H 2) was extracted with ether. The ether extract was washed with several portions of water to remove all hydrochloric acid, and was dried

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[8] A 9,10,18-trihydroxystearic acid, m.p. 133°, of proved structure has been reported by I. Ribas and E. Seoane, *Anales Real soc. españ. fís. y quím.* (*series B*), 971 (1954). Presumably this acid is the same as our compound III.

[9] *Cf.* R. Stuart Tipson, *Adv. Carbohyd. Chem.*, **8**, 107 (1953).

[10] F. Zetsche and K. Weber, *J. prakt. Chem.*, **150**, 140 (1938).

[11] The referee in calling our attention to an exception to the "rule" that the *erythro*-glycol-acid melts higher than the *threo* form [J. Myers, THIS JOURNAL, **73**, 2100 (1951)] has pointed up a limitation common to any analogical argument. Phloionolic acid could prove to be another exception to the rule. However, particularly pertinent is the fact that structurally related *erythro*-9,10,16-trihydroxypalmitic acid (m.p. 126°) has a higher melting point than the *threo* isomer, natural aleuritic acid (m.p. *ca.* 100°). It is interesting that the melting points of aleuritic acid and phloionolic acid are very close. The opportunity is taken to add to the list of *vic*-dihydroxy acids, the melting points of which support the generalization: 9,10-dihydroxypalmitic acid, 11,12-dihydroxystearic acid, 13,14-dihydroxybehenic acid and 15,16-dihydroxytetracosanoic acid. The two forms of 9,10-dihydroxyundecanoic acid melt at the same temperature.

[12] Analyses were performed by Carol K. Fitz, 115 Lexington Avenue, Needham Heights 94, Mass. All melting points are corrected.

over sodium sulfate. The ether solution was decanted from the drying agent, the ether was removed by evaporation and the residual solid crystallized from 10 ml. of ethyl acetate. The resulting product weighed 0.10 g. (86%), melted at 114–116°, and showed $[\alpha]^{26}\text{D}$ 8.6 ± 0.6° (standard deviation) (0.082 g. in 5 ml. of ethanol).

Anal. Calcd. for $C_{25}H_{38}O_7$: C, 66.6; H, 8.5. Found: C, 66.9; H, 8.6.

Optical Inactivity of Natural 9,10-Dihydroxyoctadecanedioic Acid (Phloionic Acid) from Cork.[4]—A concentrated solution (1.0 g. in 10 ml. of absolute ethanol) of phloionic acid, m.p. 121–122°, isolated from cork, showed no detectable rotation in a 1-dm. tube.

Benzylidene Derivative of 9,10-Dihydroxyoctadecanedioic Acid, m.p. 121–122°.—Benzaldehyde was freed of benzoic acid by extracting an ether solution with 5% sodium hydroxide solution. A mixture of dry, freshly distilled benzaldehyde (25 ml.), 0.5 g. (0.0015 mole) of 9,10-dihydroxyoctadecanedioic acid, m.p. 121–122°, and 1.5 g. of anhydrous copper sulfate was shaken mechanically and intermittently over a period of ten days. The mixture was filtered, and the solids rinsed with 25 ml. of ether, which was added to the benzaldehyde solution. After removal of ether, most of the benzaldehyde was vacuum distilled at a bath temperature of 120°. The residual light brown material was dissolved in 50 ml. of ether and was washed quickly with two 50-ml. portions of saturated sodium bisulfite solution followed by two 50-ml. portions of water. Acidic material was extracted from the ether with 5% sodium hydroxide solution. The combined alkaline extract was brought to *p*H 2, and the acid solution rapidly extracted with ether. The ether extract was washed twice with water, and was dried over sodium sulfate.

After removal of drying agent and ether, 0.58 g. of product, m.p. 80–84°, remained. Two crystallizations from ethyl acetate afforded 0.45 g. (71%) of pure benzylidene derivative, m.p. 87–88°. No special effort was made to obtain maximal recovery from the crystallizations. Two more crystallizations did not change the melting point.

Anal. Calcd. for $C_{25}H_{38}O_6$: C, 69.1; H, 8.8; neut. equiv., 217. Found: C, 69.3; H, 9.0; neut. equiv., 218.

Half Ester II of *threo*-9,10-Dihydroxyoctadecanedioic Acid (I).—A solution of 1.73 g. (0.0050 mole) of *threo*-acid I, m.p. 121–122°, 40 ml. of ethyl acetate, 0.6 ml. of absolute alcohol, and two drops of concentrated sulfuric acid was boiled for two hours. Atmospheric moisture was excluded by a drying tube fitted to the reflux condenser. After the reflux period, most of the solvent was removed by blowing dry air over the hot solution. Ether (100 ml.) was added, and the ethereal solution was extracted with seven 30-ml. portions of saturated calcium hydroxide solution. The aqueous layers contained the precipitated calcium salt of the desired half ester II plus calcium sulfate. The solids were collected and air-dried.

The solids remaining after stirring with 100 ml. of 5% hydrochloric acid for three hours were collected by filtration, and were boiled with a large volume of petroleum ether, b.p. 60–90°. Filtration of the hot mixture removed insoluble inorganic material. Cooling the filtrate gave 0.75 g. of *threo*-9,10-dihydroxyoctadecanedioic monoethyl ester (II), m.p. 67–68°. Further crystallizations, once from petroleum ether and once from aqueous alcohol, did not change the melting point.

Anal. Calcd. for $C_{20}H_{38}O_6$: C, 64.1; H, 10.2; neut. equiv., 374.5. Found: C, 64.5; H, 10.0; neut. equiv., 370, 373.

Acidification of the calcium hydroxide solutions from which the calcium salt of the half ester had been removed afforded a precipitate, which on crystallization from ethyl acetate proved to be starting material (0.86 g., m.p. 121–122°). The yield of half ester II in several experiments was 50–52%; the recovery of pure unreacted acid I ranged from 40–50%.

Boiling a solution of 1.0 g. of the *threo*-acid I (0.0032 mole) in 100 ml. of absolute alcohol containing hydrogen chloride for three hours gave 1.08 g. (92%) of waxy sodium carbonate-insoluble diethyl ester, m.p. 45–49°, and no more than 0.07 g. of impure carbonate-soluble half ester. Similar experiments in which the reflux period was systematically varied showed that increasing the reaction time (a) increases the yield of diester, (b) decreases the amount of carbonate-soluble products and (c) lowers the melting point of the carbonate soluble products. The highest yield of half ester II (which in all cases was difficult to separate from unreacted starting material) obtained in this way was 23%.

Attempts at saponifying the diethyl ester to the monoethyl ester gave unsatisfactory results. The only products were diacid I, m.p. 119–131°, and unreacted diester.

9,10,18-Trihydroxystearic Acid (III) from Half Ester II.—To a solution of 1.0 g. (0.0027 mole) of half ester II in 50 ml. of absolute ethanol was added 0.46 g. (0.020 atom) of clean sodium in small pieces. The reaction flask, carrying a calcium chloride drying tube, was kept in a water-bath at 40°. The sodium required three minutes for the addition, and about 15 minutes for solution, after which time the bulk of the ethanol was removed by blowing a stream of pure dry nitrogen over the surface of the solution. The residual material was shaken with 75 ml. of ether and 100 ml. of 5% hydrochloric acid. The ether layer was extracted with three 25-ml. portions of 5% sodium hydroxide solution. Acidification of the combined alkaline extracts (to *p*H 2) furnished a white precipitate. After cooling the mixture overnight the precipitate was collected, washed with 5 ml. of cold water, and air-dried. This material (0.87 g., m.p. 131–136°) was crystallized by solution in 6 ml. of hot absolute alcohol, addition of water to the hot alcohol until a persistent turbidity developed, and cooling. Repetition of this crystallization procedure gave 0.70 g. (78%) of white crystalline 9,10,18-trihydroxystearic acid (III), m.p. 136–137°. A third crystallization did not change the melting point.

Anal. Calcd. for $C_{18}H_{36}O_5$: C, 65.0; H, 10.9; neut. equiv., 332.5. Found: C, 65.1; H, 11.0; neut. equiv., 331.

To show that the stereochemistry at the 9- and 10-positions did not change, 1 g. of *threo*-acid I was treated with a boiling solution of 0.6 g. of sodium in 50 ml. of absolute alcohol for one hour. From the resulting mixture there could be recovered 0.94 g. (94%) of material, melting alone or admixed with authentic *threo*-9,10-dihydroxyoctadecanedioic acid at 121–122°.

9,10-Dihydroxy-18-tosyloxystearic Acid (IV).—A solution of 0.50 g. (0.0015 mole) of 9,10,18-trihydroxystearic acid (III) and 0.30 g. (0.0016 mole) of pure *p*-toluenesulfonyl chloride, m.p. 68.5–69°, in 25 ml. of anhydrous pyridine was held at 0° for 18 hours. Pyridine was removed by blowing a stream of nitrogen over the solution at room temperature. An ethereal solution of the residue, after washing with three 25-ml. portions of water, was dried over anhydrous magnesium sulfate. Solvent was allowed to evaporate from the dried solution at room temperature. The resulting waxy solid, m.p. 48–57°, was dissolved in boiling ethanol, and ethyl acetate was added until the point of permanent cloudiness. Cooling afforded crystalline product. Three crystallizations in the same way furnished 0.55 g. (74%) of pure tosyl derivative IV, m.p. 67–68°. An additional crystallization did not change the melting point. The average yield in four similar tosylation experiments was 81%.

Anal. Calcd. for $C_{25}H_{42}O_7S$: C, 61.7; H, 8.7; neut. equiv., 486.6. Found: C, 61.9; H, 8.9; neut. equiv., 484.

9,10-Dihydroxy-18-iodostearic Acid (V).—Tosyl compound IV (0.50 g. or 0.0010 mole) dissolved in 40 ml. of acetone containing 1.5 g. (0.010 mole) of sodium iodide was allowed to stand at room temperature for three days. Solvent was removed at room temperature in a stream of dry nitrogen. The residue was taken up in ether, and the ethereal solution washed successively with 25-ml. portions of water, 5% sodium thiosulfate solution and water. After the ether solution was dried over sodium sulfate, solvent was removed in a stream of nitrogen. Exposing the residue at 45° to water-pump vacuum gave 0.45 g. of waxy iodo derivative V, which was used without further treatment.

***threo*-9,10-Dihydroxystearic Acid (VI), M.p. 94.5–95°, from the Iodo Derivative V.**—Glacial acetic acid (35 ml.), zinc dust (5 g.) and 5 ml. of concentrated hydrochloric acid were added to 0.45 g. of waxy 9,10-dihydroxy-18-iodostearic acid, and the mixture was stirred at steam-bath temperatures for two hours. Solids were removed by filtration, and were washed first with 25 ml. of water, which was added to the filtrate, and then with three small portions of ether, which was kept separate. More water (50 ml.) was added to the acid filtrate, and the resulting mixture extracted several times with ether. The combined ether extracts were washed twice with 25-ml. portions of water, and were dried over sodium sulfate. The dried ether solution was combined with the dried ether that had been used to wash the zinc, and the solvent was evaporated at room temperature. The residual solids, crystallized three times from ethyl acetate, furnished 0.15 g. (48%) of 9,10-dihydroxystearic acid, m.p. 94.5–95°. A fourth crystallization did not affect the melting point.

Anal. Calcd. for $C_{18}H_{36}O_4$: C, 68.3; H, 11.5; neut. equiv., 316.5. Found: C, 68.5; H, 11.4; neut. equiv., 318.

The melting point of this material admixed with authentic 9,10-dihydroxystearic acid (m.p. 94.5–95°) was 94.5–95°. Repetition of this preparation afforded the same product (m.p. 94–95°) in 65% yield from the tosyl compound.

When authentic *erythro*-9,10-dihydroxystearic acid, m.p. 131.5–132°, was carried through the entire procedure, unchanged starting material was obtained in over 90% recovery. *threo*-9,10-Dihydroxystearic acid, m.p. 94.5–95°, was likewise unchanged under the conditions of the experiment.

BOSTON, MASSACHUSETTS

[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT LABORATORIES OF THE COLGATE–PALMOLIVE CO.]

The Preparation of Long Chain N-Acylamino Acids

BY E. JUNGERMANN, J. F. GERECHT AND I. J. KREMS

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A series of long chain acylamino acids were prepared by treating an acid chloride with the appropriate amino acids in an aqueous system. When the dicarboxylic amino acids were used and the acylation effected in an organic solvent, the N-acylamino acid anhydrides were obtained. Some of the physical properties of the long chain N-acylamino acids and their salts are reported.

The reported activity[1,2] of sodium N-lauroylsarcosine[3] as an effective anti-caries agent has prompted us to investigate a series of long chain acylamino acids. It is the purpose of this publication to present the syntheses and physical properties of the compounds prepared.

Most of the available literature on long-chain acylamino acids is concerned with the commercial grade of "Medialan" detergents[4,5] and only in a few instances are individual compounds described. Bondi[6] and Abderhalden[7] have reported the preparation of lauroyl and palmitoyl derivatives of glycine and alanine. Karrer, *et al.*,[8] and Miyamichi[9] studied the formation of ethoxyoxazoles from the ethyl esters of long-chain acylamino acids. Staudinger[10] was first to report the preparation and analysis of palmitoyl and stearoyl derivatives of sarcosine (N-methylglycine). Koebner[11] prepared palmitoyl and stearoyl derivatives of glycine, glycylglycine and diglycylglycine to investigate the surface films of the corresponding amides. Naudet[12,13] evaluated the detergent properties of some of the higher fatty acid derivatives of some polyfunctional amino acids. In a series of papers on microörganisms capable of hydrolyzing acylated amino acids, Kameda, *et al.*,[14–16] investigated a number of long chain acylamino acids. Neuberg, *et al.*,[17,18] reported the preparation of D- and L-amino acids by the enzymatic hydrolysis of DL-acylamino acids.

We synthesized the following two series of acylated amino acids: (I) the sarcosine derivatives, varying the length and nature of the acyl chain. (II) The lauroyl and/or palmitoyl derivatives of other amino acids.

In the preparation of all of the derivatives of monoaminomonocarboxylic acids, an acid chloride was treated with an excess of the sodium salt of the amino acid in aqueous medium while maintaining the *p*H in the range of 9–12.5. The amino acids containing an N-alkyl substituent were prepared by the reaction between the appropriate α-chloro acid and primary amine.

Kester[19] reported the acylation of glutamic acid in the presence of potassium hydroxide in sufficient proportion to maintain the *p*H at 7 or above, but we were unable to acylate aminopolycarboxylic acids such as glutamic and aspartic acids by this method or by the method employed by us for acylating the monoaminomonocarboxylic acids. We were able to accomplish this in low yield by refluxing a suspension of the amino acid with acid chloride in anhydrous ethyl acetate.[20] The intermediate acylated anhydrides were first isolated and then converted to the acylated dicarboxylic acids.

The melting points of the homologous series of acylated sarcosines show an alternation similar to that observed in other series of long chain compounds. When the alkyl group of the N-lauroyl-N-alkylglycines is increased from C_1 to C_4, a maximum is found for the N-ethyl derivative. The N-acyl-N-alkyl compounds in general melt at much lower temperatures than the corresponding derivatives of primary amino acids.

The sodium salts are usually white, crystalline, water-soluble materials, often with good foaming

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[1] W. J. King, U. S. Patent 2,689,170.

[2] L. S. Fosdick, J. C. Calandra, R. O. Blackwell and J. H. Burrill, *J. Dental Research*, **32**, 486 (1953).

[3] Colgate–Palmolive Co. Trade name: Gardol.

[4] W. Hentrich, H. Keppler and K. Hintzmann, German Patent 635,522.

[5] W. Hentrich, H. Keppler and K. Hintzmann, British Patents 459,039, 461,328.

[6] S. Bondi, *Z. Biochem.*, **17**, 543 (1909).

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