effect might explain the reaction of hydrogen chloride with methyl 9,10-epoxystearate. The experimental data reported in this paper are in agreement with this premise. However, in spite of this correlation, further experimental investigations appear necessary to determine whether other factors are involved.

Experimental[13]

Methyl 9,10-Epoxystearate.—Thirty grams (0.10 mole) of pure methyl oleate[14] was treated with 0.115 mole of peracetic acid in acetic acid at 20–25° in a similar manner as described by Swern, *et al.*[15]; m.p. 14–16°; yield 27 g. After four recrystallizations from acetone 16 g. (51% theoretical) of pure product was obtained, m.p. 17.1–17.8°.

Anal. Calcd. for $C_{19}H_{36}O_3$: oxiran O,[16] 5.12. Found: oxiran O, 5.02.

Methyl 9,10-(10,9)-Chlorohydroxystearate.—Methyl 9,10-epoxystearate (3.12 g., 0.01 mole) was allowed to react with hydrogen chloride in absolute diethyl ether at room temperature in a similar manner as described by Swern[8]; yield 3.30 g. (97%) of methyl 9,10-(10,9)-chlorohydroxystearate, m.p. 23–25.5°.

Anal. Calcd. for $C_{19}H_{37}O_3Cl$: Cl, 10.20. Found: Cl, 10.13.

Separation of the 9,10- and 10,9-Isomers of Methyl Chlorohydroxystearate.—In a three-necked round-bottom flask equipped with stirrer and low temperature thermometer, 15.7 g. of the mixed methyl chlorohydroxystearates were dissolved in 62 ml. of methanol. The solution was cooled (Dry Ice–acetone) slowly to −30 to −35° at which point a triangular fractional crystallization was carried out. Two distinct fractions were obtained: (1) 10.1 g. of isomer melting at 25–26°; recrystallization of this fraction from methanol yielded five crops of crystalline material, each melting at 25–26°; all of the starting material was recovered. (2) 3.3 g. of isomer melting at 36.5–37.5°; recrystallization of this fraction from methanol yielded three crops (total recovery 95%) of crystalline material; m.p. of each crop 36.5–37.5°. The final mother liquor still contained 0.6 g. of oily residue which was not purified.

Methyl Hydroxystearates.—Methyl chlorohydroxystearate (1.7 g., 5 mmoles) was dissolved in 100 ml. of glacial acetic acid and 5 g. of amalgamated zinc was added. The mixture was refluxed for six hours. The solution was cooled, filtered, diluted with water and extracted with diethyl ether. The extracts were washed and dried, and on removing the solvent 1.4 g. (90% yield) of crystalline solid was obtained. Analysis for chlorine indicated that all of the chlorine was removed.

Anal. Calcd. for $C_{19}H_{38}O_3$: sapn. equiv., 314. Found: sapn. equiv., 311.

Ketostearic Acids.—Methyl hydroxystearates (1 g., 3.2 mmoles) were oxidized with 25% excess of chromic oxide in glacial acetic acid at 30–35°, yield 0.8 g. Saponification of this intermediate with alcoholic potassium hydroxide followed by acidification and extraction with diethyl ether yielded the ketostearic acids.

The 9-ketostearic acid derived from methyl 10-chloro-9-hydroxystearate was obtained in 70% yield, m.p. 80° (reported m.p. 81.5°[10,17,18]).

Anal. Calcd. for $C_{18}H_{34}O_3$: neut. equiv., 298. Found: neut. equiv., 296.

The semicarbazone was prepared in the usual manner; m.p. 117–119° (reported m.p. 118–120°[10]).

Anal. Calcd. for $C_{19}H_{37}O_3N_3$: N, 11.83. Found: N, 11.80.

The 10-ketostearic acid derived from methyl 9-chloro-10-hydroxystearate was obtained in 75% yield; m.p. 72° (reported m.p. 72°[10,17,18]); a mixed melting point with the 9-keto compound was 66–69°.

Anal. Calcd. for $C_{18}H_{34}O_3$: neut. equiv., 298. Found: neut. equiv., 295.

The semicarbazone was prepared in the usual manner; m.p. 100.5–102° (reported m.p. 101–103[10]).

Anal. Calcd. for $C_{19}H_{37}O_3N_3$: N, 11.83. Found: N, 11.65.

Acknowledgment.—The authors wish to thank the Colgate–Palmolive–Peet Co. for use of their laboratory facilities.

(13) All melting points are uncorrected.

(14) D. Swern, H. B. Knight and T. W. Findley, *Oil and Soap*, **21**, 133 (1944).

(15) D. Swern, T. W. Findley and J. T. Scanlan, THIS JOURNAL, **67**, 412 (1945).

(16) B. H. Nicolet and T. C. Poulter, *ibid.*, **52**, 1186 (1930).

(17) J. Baruch, *Ber.*, **27**, 172 (1894).

(18) G. M. Robinson and R. Robinson, *J. Chem. Soc.*, 2204 (1926).

BROOKLYN, NEW YORK

[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ILLINOIS]

Synthesis of *erythro*- and *threo*-α-Amino-β-hydroxystearic Acids[1]

BY H. E. CARTER, J. B. HARRISON[2] AND DAVID SHAPIRO[3]

RECEIVED MAY 2, 1953

The two DL-α-amino-β-hydroxystearic acids have been synthesized and characterized as the *threo* and *erythro* forms on the basis of physical and chemical properties.

Dihydrosphingosine has been characterized as one of the four 1,3-dihydroxy-2-aminoöctadecanes[4] and the amino carbon atom has been shown to have the D-configuration.[5] In order to complete the stereochemical characterization of dihydrosphingosine we have synthesized the two racemic forms by reduction of the corresponding *threo*- and *erythro*-DL-α-amino-β-hydroxystearic acids.[6] The preparation of the latter compounds is described in the present paper.

Attempts to prepare the α-amino-β-hydroxystearic acids from octadecanoic acid by procedures applicable to the synthesis of the threonines were not promising. Since Attenburrow, Elliott and Penny[7] had reported excellent results in the preparation of threonine and allothreonine by a procedure involving the condensation of acetic an-

(1) This investigation was supported in part by a research grant (RG 2031) from the National Institutes of Health, Public Health Service. Part of the material in this paper was taken from the thesis submitted by J. B. Harrison to the Graduate College of the University of Illinois in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry.

(2) AEC fellow in Chemistry, 1951–1952.

(3) On leave of absence from Weizmann Institute of Science, Rehovoth, Israel.

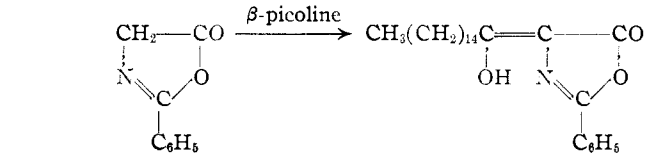
(4) H. E. Carter, F. J. Glick, W. P. Norris and G. E. Phillips, *J. Biol. Chem.*, **142**, 449 (1952).

(5) H. E. Carter and C. G. Humiston, *ibid.*, **191**, 727 (1951).

(6) A preliminary note describing this work was published recently (H. E. Carter, D. Shapiro and J. B. Harrison, THIS JOURNAL, **75**, 1007 (1953)).

(7) J. Attenburrow, D. F. Elliott and G. F. Penny, *J. Chem. Soc.*, 310 (1948).

hydride with 2-phenyloxazolone we attempted to apply this procedure to the synthesis of the amino-hydroxystearic acids. Palmitic anhydride did not condense readily with the oxazolone but palmitoyl chloride, under the proper conditions, gave satisfactory results.

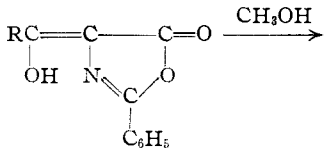


The first attempts to condense palmitoyl chloride with 2-phenyloxazolone gave a gross mixture of products melting at 60–100°. Extensive fractionation of this material gave a small amount of the desired 2-phenyl-4-(1-hydroxypalmitylidene)-oxazolone-5 (light yellow solid, m.p. 111–112°). This substance gave an absorption maximum at 340 mμ ($E^{1\%}_{1\ cm.}$ 486 in β-picoline) characteristic of unsaturated oxazolones, thus permitting the course of the reaction to be followed spectrophotometrically. It was then discovered that the absorption at 340 mμ reached a peak very rapidly and subsequently declined slowly but steadily. It also was observed that 2-phenyloxazolone condenses with itself in β-picoline to give a compound(s) absorbing at 340 mμ. However, this reaction is much slower than that with palmitoyl chloride.[8]

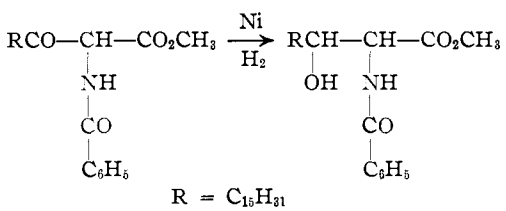
On the basis of these observations it was possible to obtain a 40–60% yield of 2-phenyl-4-(1-hydroxypalmitylidene)-oxazolone-5 by adding palmitoyl chloride to a freshly prepared solution of 2-phenyloxazolone in anhydrous β-picoline at room temperature (in larger runs the temperature must be controlled with a cooling bath) and working up the reaction mixture within 20–30 minutes after completion of the addition of palmitoyl chloride. The crude product thus obtained usually melted above 100° and could be purified without excessive loss by crystallization from acetonitrile or hexane (the former solvent removes the red impurities more efficiently). Products melting below 100°, however, were best purified by treatment with 0.1 *N* aqueous methanolic sodium hydroxide followed by crystallization from hexane.

In most of the experiments a 1:1 molar ratio of palmitoyl chloride to 2-phenyloxazolone was employed. Increasing this ratio gave sharply reduced yields. Decreasing the ratio to 0.5 gave somewhat improved yields (calculated on palmitoyl chloride) but the results were not sufficiently better to warrant the expenditure of the extra oxazolone.

The conversion of 2-phenyl-4-(1-hydroxypalmitylidene)-oxazolone-5 to a mixture of the two methyl α-benzamido-β-hydroxystearates proceeded smoothly.



(8) However, certain of the highly-colored side products of the palmitoyl chloride reaction may well result from the self-condensation of 2-phenyloxazolone.



Fractionation of the mixture of methyl esters directly was only partially successful. However, the corresponding acids could be separated satisfactorily. Crystallization of the mixture of acids from methanol gave the less-soluble α-benzamido-β-hydroxystearic acid A melting at 174–176°. The more-soluble isomer B was obtained from the mother liquors by taking advantage of the observations of Carter and Risser[9] that in the case of the N-benzoyl derivatives of threonine and allothreonine (and several other similar isomeric pairs) the lower-melting more-soluble N-benzoyl derivative yielded the higher-melting less-soluble β-phenethylamine salt. This same behavior was exhibited by the α-benzamido-β-hydroxystearic acids. The higher-melting isomer A gave a β-phenylethylamine salt melting (with decomposition) at 138–150°. The mother liquors from isomer A yielded a less-soluble β-phenethylamine salt melting at 158–165°. The latter gave pure α-benzamido-β-hydroxystearic acid B melting at 93–95°. The N-benzoyl acids were readily converted to the corresponding methyl esters and to the O,N-dibenzoyl methyl esters. The latter compounds were especially satisfactory derivatives because of the ease with which they could be recrystallized.

Hydrolysis of the N-benzoyl acids to the amino-hydroxystearic acids presented a problem because of the insolubility of these substances in aqueous solvents. Thus, after refluxing 1.0 g. of N-benzoyl acid A for 24 hours with 3 *N* hydrochloric, 1.0 g. of unchanged material was recovered. However, the N-benzoyl acids were hydrolyzed smoothly by 1:1 glacial acetic–concentrated hydrochloric acid. On cooling the hydrolysis mixture, the amino acid hydrochlorides separated in crystalline form. These were readily converted to the amino acids. The α-amino-β-hydroxystearic acid B obtained in this way behaved as a homogeneous compound on recrystallization and on conversion to the methyl ester. The crude A isomer, however, melted over a wide range and gave a methyl ester which was obviously inhomogeneous. Preparation of the N-benzoyl derivative showed that this material contained a considerable amount of the B isomer. The fact that the N-benzoyl derivative of the B isomer is hydrolyzed with retention of configuration whereas the A isomer undergoes partial inversion is significant as regards the configuration of the two materials and will be discussed in a later section. No completely satisfactory method was discovered for hydrolyzing the N-benzoyl acid A; however, a fair yield of aminohydroxy acid A could be obtained if the hydrolysis was effected with alcoholic hydrochloric acid.

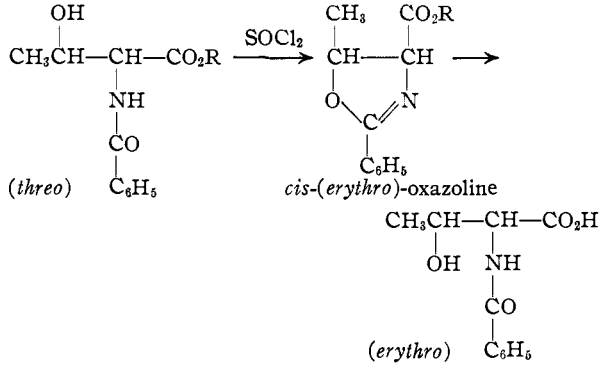
Configuration of α-Amino-β-hydroxystearic Acids A and B.—In assigning *threo* and *erythro* structures

(9) H. E. Carter and W. C. Risser, *J. Biol. Chem.*, **139**, 255 (1941).

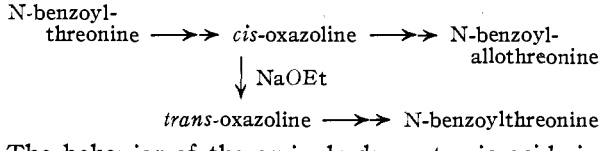
to the aminohydroxystearic acids three types of evidence were considered—physical properties, chemical reactions and infrared spectra. In each case the data obtained on various derivatives were consistent and the results of each of the three approaches support the assignment of the *erythro* structure to the A series and the *threo* structure to the B series.

In so far as physical properties are concerned the differences in melting point and solubility of the aminohydroxy acids A and B are similar to those between allothreonine and threonine, respectively.[10] Thus amino acid A, N-benzoyl A and N-benzoyl A methyl ester melt higher and are less soluble than the corresponding compounds of the B series. Furthermore, the lower-melting N-benzoyl B, like N-benzoylthreonine, gives the higher-melting β-phenethylamine salt. Finally in going from the N-benzoyl methyl ester to the O,N-dibenzoyl ester the melting point decreases in the *erythro* series (allothreonine, A) and increases in the *threo* series (threonine, B).

As regards the chemical properties of the aminohydroxystearic acids, their behavior toward oxazoline interconversion was of particular interest. Several workers[11] have noted that inversion of configuration occurs when the N-benzoyl ester of threonine or allothreonine is converted to the oxazoline. Hydrolysis of the oxazolines with dilute acid does not affect the configuration so that the over-all reaction results in the conversion of threonine to allothreonine (or *vice versa*).



Of greater interest, however, is the observation of Elliott[11b] that the oxazolines are not stable toward alkalies. Sodium ethoxide catalyzes a reversible transformation of the *cis*- and *trans*-oxazolines which yields an equilibrium mixture containing 95% of the *trans*-(threonine)-oxazoline.



The behavior of the aminohydroxystearic acids in these reactions was clean-cut and definitive. The oxazoline from methyl α-benzamido-β-hydroxystearate A gave only N-benzoyl B whether by direct acid hydrolysis or by acid hydrolysis after treatment with sodium ethoxide. The oxazoline from isomer B, on the other hand, gave N-benzoyl A on direct acid hydrolysis, but yielded N-benzoyl B as the only detectable product on treatment with sodium ethoxide followed by acid hydrolysis. These data strongly support the *erythro* structure for the A series and the *threo* structure for the B series.[12] The behavior of the α-benzamido-β-hydroxystearic acids on acid hydrolysis also affords some support for this view. It has been observed that N-acyl derivatives of *pseudo*-ephedrine (*threo*) can be hydrolyzed by acids without inversion while N-acylephedrines (*erythro*) under the same conditions may suffer extensive inversion.[13] The analogous behavior of N-benzoyl acids B and A, respectively, has been noted earlier.

We have made an extensive comparison of the infrared spectra of derivatives of threonine and allothreonine with the corresponding derivatives of the C_{18} homologs. There are several differences between the *threo* and *erythro* isomers and these were observed consistently in both the C_4 and the C_{18} series. The details of this study will be reported in a subsequent paper.

Taken together these data clearly establish that α-amino-β-hydroxystearic acid A has the *erythro* configuration and that α-amino-β-hydroxystearic acid B has the *threo* configuration.

The preparation of dihydrosphingosine by reduction of methyl α-amino-β-hydroxystearate A will be described in detail shortly.

Experimental

2-Phenyloxazolone-5.—For the large scale preparation of 2-phenyloxazolone it was found expedient to modify the procedure described by Cornforth[14] by substituting *t*-butyl alcohol for light petroleum in converting the viscous hippuric acid–acetic anhydride reaction product to the crystalline oxazolone. In this way a 50–60% yield of crystalline oxazolone (m.p. 90–91°) was obtained from a 2-mole run of hippuric acid.

2-Phenyl-4-(1-hydroxypalmitylidene)-oxazolone-5.—In a 2-liter three-necked flask equipped with a stirrer, dropping funnel and calcium chloride tube was placed 80.5 g. (0.5 mole) of 2-phenyloxazolone. Five hundred milliliters of anhydrous β-picoline (dried over barium oxide) was added and the stirrer was started. The temperature decreased as the solid dissolved, yielding a red solution. From the dropping funnel 137 g. of palmitoyl chloride was added with stirring and cooling (reaction temperature should not exceed 45°) over a period of 10 minutes. The dark red mixture was stirred for 20 minutes longer and was then poured into a mixture of cracked ice and 475 ml. of concentrated hydrochloric acid. The curdy brown precipitate which formed was extracted into 4 l. of chloroform giving a very dark red solution. This was washed with water until neutral (4–6 washings usually required). The chloroform solution was dried over sodium sulfate and concentrated in vacuum to a viscous red oil which partially solidified on cooling. This residue was dissolved in the minimum of hot hexane and the solution was cooled overnight at 6°. The red powder thus obtained (m.p. 104–108°) was recrystallized twice from acetonitrile giving 83 g. (42% yield) of 2-phenyl-4-(1-hydroxypalmitylidene)-oxazolone-5 as a light

(10) For the physical properties of threonine, allothreonine and their derivatives see (a) H. D. West and H. E. Carter, *J. Biol. Chem.*, **119**, 109 (1937); (b) H. E. Carter and C. L. Zirkle, *ibid.*, **178**, 709 (1949); (c) K. Pfister, *et al.*, THIS JOURNAL, **70**, 2297 (1948); (d) reference 9.

(11) (a) K. Pfister, C. A. Robinson, A. C. Shabica and M. Tishler, THIS JOURNAL, **71**, 1101 (1949); (b) D. F. Elliott, *J. Chem. Soc.*, 489 (1949); (c) D. F. Elliott, *ibid.*, 62 (1950).

(12) E. E. Hamel and E. P. Painter (THIS JOURNAL, **75**, 1362 (1953)) have recently applied similar techniques in characterizing the *threo* and *erythro* forms of α-amino-β,γ-dihydroxybutyric acid.

(13) L. H. Welsh, THIS JOURNAL, **71**, 3500 (1949).

(14) J. W. Cornforth in H. T. Clarke, J. R. Johnson and R. Robinson, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 778.

yellow powder melting at 111.5–112° ($E^{1\%}_{1\,cm.}$ (340 m.) *ca.* 486 (β-picoline)).

Anal. Calcd. for $C_{25}H_{37}O_3N$: C, 75.14; H, 9.34; N, 3.51. Found: C, 75.04; H, 9.50; N, 3.53.

The following procedure was used to purify less pure material. Eighty-eight grams of crude reaction product (m.p. 70–100°) was added to 5 liters of 0.1 *N* sodium hydroxide in 80% aqueous methanol saturated with hexane. The mixture was allowed to stand for 23 hours with occasional shaking. The red solution which resulted was filtered to remove a buff-colored solid (9.8 g.). The filtrate was cooled to −10° (filtered if necessary) and concentrated hydrochloric acid was added slowly with stirring until no further precipitate formed (about 40 ml. required). The precipitate was filtered, washed with 90% aqueous methanol and dried in vacuum over phosphorus pentoxide giving 33 g. of a buff-colored powder melting at 104–109°.

Methyl α-Benzamido-β-ketostearate.—2-Phenyl-4-(1-hydroxypalmitylidene)-oxazolone-5 (53.4 g., 0.134 mole) was suspended in 760 ml. of anhydrous methanol, and the mixture was heated on the steam-cone under reflux for 4 hours. The solution was cooled at 6° for 7 hours and the precipitate was filtered and dried giving 47.4 g. of a buff-colored product. An additional 8.0 g. was obtained from the mother liquors. The crude ester was dissolved in 700 ml. of hot, anhydrous methanol and decolorized with 4 g. of Nuchar-CN. The filtrate was cooled at 6° overnight giving 40 g. of white crystalline material. An additional 6.0 g. of purified ester was obtained from the mother liquor on concentration to 100 ml. Pure methyl α-benzamido-β-ketostearate, recrystallized from methanol, usually melts at about 59°, then recrystallizes in the form of fine needles which melt at 70–71°. This dimorphic behavior is not always observed in material crystallized from acetonitrile.

Anal. Calcd. for $C_{26}H_{41}O_4N$: C, 72.35; H, 9.58. Found: C, 72.23; H, 9.51.

Reduction of Methyl α-Benzamido-β-ketostearate.—The keto ester (10 g.) was suspended in methanol (500 ml.) and reduced with Raney nickel catalyst (1 g.) under 1500 pounds hydrogen pressure at 100° for 3 hours. The hydrogenation mixture was filtered and the filtrate was concentrated to a small volume. On standing for 2 days at 6° the solution deposited a white crystalline precipitate (8.3 g., 83% yield) melting at 74–90°. Repeated recrystallization of this product from methanol and hexane gave 2.1 g. of crude ester A melting at 98–100°. This product did not give a homogeneous acid on saponification and presumably still contained some of isomer B. The mother liquors from the 98–100° melting material could not be fractionated successfully.

α-Benzamido-β-hydroxystearic Acids A and B.—A 5.0-g. sample of keto ester was reduced as described above and the entire reduction product was saponified in 200 ml. of 0.1 *N* sodium hydroxide in 90% aqueous methanol at room temperature for 6 hours. The resulting solution was diluted with cold water and acidified. The white precipitate was filtered and dried (weight 4.2 g., 86% yield, m.p. 90–145°). Recrystallization of this product from 50 ml. of methanol gave 1.25 g. of a crystalline product (hexagonal plates) melting at 160–170°. One additional crystallization from methanol gave pure α-benzamido-β-hydroxystearic acid A melting at 175–177°.

Anal. Calcd. for $C_{25}H_{41}O_4N$: C, 71.56; H, 9.85; N, 3.34; neut. equiv., 419.3. Found: C, 71.90; H, 9.99; N, 3.31; neut. equiv., 422.

The β-phenethylamine salt of N-benzoyl acid A was prepared by adding 0.12 ml. of β-phenethylamine to a solution of 0.20 g. of the acid in 5 ml. of hot methanol. On cooling the solution the crystalline salt separated (m.p. 138–151°).

The methanolic mother liquors from N-benzoyl acid A were combined and concentrated to 50 ml. The solution was warmed and 2 ml. (*ca.* 100% excess) of β-phenethylamine was added. The solution was allowed to cool slowly to room temperature in a water-bath, giving 1.8 g. of crystalline material (large plates) melting at 158–165° (dec.). This material is the β-phenethylamine salt of N-benzoyl acid B. On acidification it gave 1.2 g. of material melting at 83–86°. Recrystallization of this material from ethyl acetate gave pure α-benzamido-β-hydroxystearic acid B melting at 93–95°.

Anal. Calcd. for $C_{25}H_{41}O_4N$: C, 71.56; H, 9.85; N, 3.34; neut. equiv., 419.3. Found: C, 71.61; H, 9.97; N, 3.57; neut. equiv., 421.

Methyl α-Benzamido-β-hydroxystearates A and B.—The N-benzoyl acids A and B were converted to the methyl esters with ethereal diazomethane. In each case the suspended acid dissolved as the reaction proceeded and the ester then separated as a crystalline solid. The crude esters were recrystallized from methanol giving pure methyl α-benzamido-β-hydroxystearate A and B melting, respectively, at 98–100° and 86–88°.

Anal. Calcd. for $C_{26}H_{43}O_4N$: C, 72.02; H, 10.00; N, 3.23. Found: (ester A) C, 72.21; H, 9.88; N, 3.18; (ester B) C, 72.45; H, 10.16; N, 3.31.

O,N-Dibenzoyl Derivatives.—To a cold solution of 0.36 g. of methyl α-benzamido-β-hydroxystearate A in 12 ml. of anhydrous pyridine (dried over barium oxide) was added 1.0 ml. of benzoyl chloride. The solution was allowed to stand 4 hours at room temperature. Then 1.0 ml. of water was added to decompose excess benzoyl chloride. After standing 10 minutes, the solution was poured into iced hydrochloric acid and the suspension was extracted with ether. The ether solution was washed with water, dried and evaporated. The residual oil crystallized on cooling. Recrystallization of this material from methanol gave pure methyl α-benzamido-β-benzoxystearate A melting at 88–90°. A mixture of the two substances melted at 73–77°.

Anal. Calcd. for $C_{33}H_{47}O_5N$: C, 73.71; H, 8.81; N, 2.61. Found: (dibenzoyl A) C, 73.81; H, 8.81; N, 2.57; (dibenzoyl B) C, 73.55; H, 8.78; N, 2.71.

The dibenzoyl derivatives of threonine and allothreonine methyl ester were prepared from N-benzoylthreonine methyl ester (m.p. 82–84°)[11a] and N-benzoylallothreonine methyl ester (m.p. 110–111°)[10c] by the above procedure. The crude products were recrystallized from methanol giving pure O,N-dibenzoylthreonine methyl ester and O,N-dibenzoylallothreonine methyl ester melting at 113–114° and 103–104°, respectively.

Anal. Calcd. for $C_{19}H_{19}O_5N$: C, 66.85; H, 5.61; N, 4.10. Found: (dibenzoylthreonine ester) C, 67.09; H, 5.67; N, 4.19; (dibenzoylallothreonine ester) C, 66.80; H, 5.33; N, 4.21.

α-Amino-β-hydroxystearic Acids A and B.—The N-benzoyl acids A and B were hydrolyzed by refluxing for 15–20 hours with 70 volumes of a 1:1 mixture of concentrated hydrochloric acid and glacial acetic acid. The clear solutions which resulted were cooled giving nicely crystalline precipitates. These were extracted with ether to remove unhydrolyzed benzoyl derivative leading to essentially pure amino acid hydrochlorides. The hydrochlorides were converted to the free amino acids by treatment in glacial acetic acid with ammonia, and the amino acids which separated were recrystallized from hot glacial acetic acid. α-Amino-β-hydroxystearic acid B (m.p. 205–206°) was obtained in a pure state after one or two recrystallizations. The pure A isomer (m.p. 217–220°), however, was obtained only after repeated recrystallizations involving large losses. Hydrolysis of N-benzoyl acid A with 25% (w./v.) hydrogen chloride in 70% (v./v.) aqueous ethanol containing 20–25% (v./v.) dioxane (12 hours refluxing) gave essentially pure α-amino-β-hydroxystearic acid A but in only 53% yield.

Anal. Calcd. for $C_{18}H_{37}O_3N$: C, 68.52; H, 11.82; N, 4.44. Found: (A) C, 68.70; H, 11.88; N, 4.32; (B) C, 68.51; H, 11.75; N, 4.62.

The aminohydroxystearic acids are difficult to purify since they are highly water-insoluble and do not dissolve in dilute acids or alkalies. Hot glacial acetic acid was the only common solvent found from which they could be crystallized.

Methyl α-Amino-β-hydroxystearates A and B.—Crude α-amino-β-hydroxystearic acid hydrochloride B (7.67 g.) was suspended in 150 ml. of anhydrous methanol, and anhydrous hydrogen chloride was bubbled in while the solution was heated under reflux for 3 hours. The clear solution was evaporated to a paste which was treated with 200 ml. of cold 8% sodium carbonate solution. The aqueous suspension was extracted twice with ether and the ether extracts were washed and dried. The crude ester obtained on evaporating the ether was recrystallized from ether giving pure methyl α-amino-β-hydroxystearate B melting at 77–78°; yield 80%. The A ester was prepared in the same way from the hydrochloride of α-amino-β-hydroxystearic

acid A obtained by ethanolic hydrochloric acid hydrolysis of the N-benzoyl derivative. The crude ester was recrystallized from hexane giving pure methyl α-amino-β-hydroxystearate B melting at 71–73°.

Anal. Calcd. for $C_{19}H_{39}O_3N$: C, 69.25; H, 11.93; N, 4.25. Found: (A) C, 69.03; H, 11.65; N, 4.21; (B) C, 69.53; H, 12.03; N, 4.06.

Attempts to prepare ester A from the unfractionated hydrochloride obtained by glacial acetic acid–hydrochloric acid hydrolysis of N-benzoyl acid A gave products melting at 50–55°. Such preparations appeared to be a mixture of the two esters.

Oxazoline Interconversions.—Methyl α-benzamido-β-hydroxystearates A and B were converted to the corresponding oxazolines with thionyl chloride as described by Elliott.[11b,c] The crude oxazolines were obtained as oily residues on concentration of the chloroform solutions. The crude oxazolines without further purification were hydrolyzed directly or after sodium ethoxide treatment as follows:

(a) **Direct Acid Hydrolysis of Oxazoline.**—The oxazoline from 1.0 g. of N-benzoyl A methyl ester was dissolved in 42 ml. of methanol, and 4 ml. of 3 *N* hydrochloric acid was added. The solution was allowed to stand for 18 hours at room temperature to convert the oxazoline to the O-benzoyl derivative. The resulting solution was neutralized with 5% sodium hydroxide; 10 ml. of 10% sodium hydroxide was added and the solution was refluxed for 35 minutes. The solution was acidified with 5 ml. of concentrated hydrochloric acid and the precipitate was filtered and dried (yield 0.86 g., 88%, m.p. 83–90°). Recrystallization of the crude product from a mixture of 3 ml. of ethyl acetate and 5 ml. of hexane gave 0.62 g. of pure N-benzoyl acid B melting at 91–92°.

Treatment of the oxazoline from 0.40 g. of the N-benzoyl ester B under the above conditions gave 0.32 g. of N-benzoyl acid A melting at 165–173°.

(b) **Sodium Ethoxide Treatment of Oxazoline.**—To the crude dry oxazoline from 1.0 g. of methyl α-benzamido-β-hydroxystearate A was added a solution of 1.7 g. of sodium ethoxide in 25 ml. of anhydrous ethanol. The solution became turbid and a precipitate formed. The suspension was allowed to stand for 10 minutes. Then 5 ml. of water was added and the solution was refluxed for 15 minutes. The white suspension was acidified with concentrated hydrochloric acid and allowed to stand for 4 hours at room temperature. The suspension was diluted with 50 ml. of methanol and made to alkaline (*p*H 11) with 10% sodium hydroxide. After 5 minutes the mixture was acidified with concentrated hydrochloric acid and water was added to cause complete precipitation of the N-benzoyl derivative. The crude product weighed 0.82 g. (84% yield) and melted at 84°. One recrystallization of this material from ethyl acetate–hexane gave pure N-benzoyl-α-amino-β-hydroxystearic acid B melting at 91–93°. There was no indication of the presence of the A isomer in the mother liquors.

The oxazoline from 0.40 g. of methyl N-benzoyl-α-amino-β-hydroxystearate B when treated as described above gave 0.37 g. of crude N-benzoyl acid B melting at 85–87°. Recrystallization from ethyl acetate–hexane gave 0.23 g. melting at 91–93°. No N-benzoyl A could be isolated from the mother liquors.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE WORCESTER FOUNDATION FOR EXPERIMENTAL BIOLOGY]

A New C_1-Ketone from Dehydroabietic Acid[1]

BY ROBERT P. JACOBSEN

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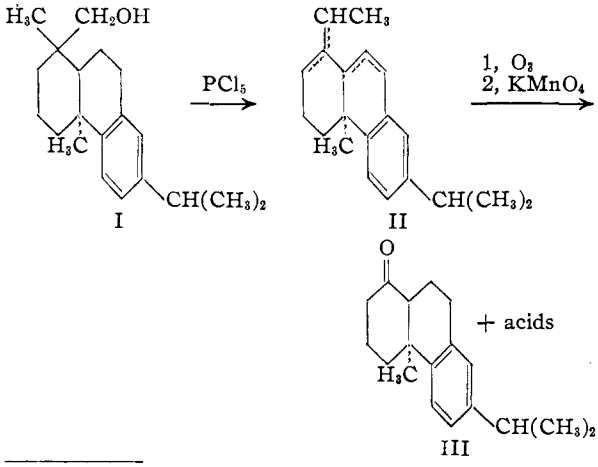
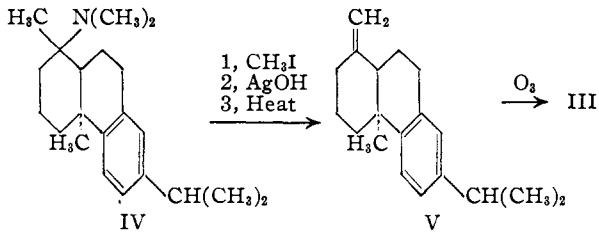
A report is made of the degradation of dehydroabietinol (I) and its 6-bromo derivative VII to the corresponding C_1-ketones, IIIa and VIII. The ketone IIIa, from the unsubstituted carbinol, isolated *via* its crystalline semicarbazone, was found to be different from that previously reported.

In their report[2] of the degradation of dehydroabietinol (I), Brossi, Gutmann and Jeger described the isolation and properties of the C_1-ketone III. In its formation the intermediate hydrocarbon mixture (II), obtained in the dehydration–rearrangement of I with phosphorus pentachloride, was subjected to ozonolysis followed by oxidation with potassium permanganate and isolation of the neutral ketonic fraction with Girard reagent T. Esterification of the accompanying acidic fraction followed by separation of the ketonic and non-ketonic esters provided compounds arising through cleavage of the tricyclic ring system at positions 1,2 or 10,10a and 9,10.



Recently Zeiss and Martin[3] have described another route for the degradation of dehydroabietic acid involving in its final stages the Hofmann degradation of nordehydroabietyldimethylamine (IV) to the hydrocarbon V. Ozonolysis of the latter afforded III whose structural identity with synthetic 1-oxo-4a-methyl-7-isopropyl-1,2,3,4,4a,9,10,-10a-octahydrophenanthrene[4] was demonstrated by a comparison of their infrared absorption spectra.



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(2) A. Brossi, H. Gutmann and O. Jeger, *Helv. Chim. Acta*, **33**, 1730 (1950).

(3) Presented before the 121st Meeting of the American Chemical Society at Buffalo, N. Y., March, 1952.

(4) G. Stork and A. Burgstahler, THIS JOURNAL, **73**, 3544 (1951).