[Contribution from the Department of Chemistry of Douglass College, Rutgers University]

2-Hexadecenoic Acid and Related Compounds[1]

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α-Bromo-, α-iodo-, and α-hydroxy-palmitic acids and 2-hexadecenoic acid have been prepared and characterized. The infrared absorption spectra of these four acids have been determined.

In an attempt to prepare 2-hexadecenoic acid for use as an intermediate for a subsequent synthesis, discrepancies in properties of it and its precursors were found in the literature. This is apparent from Table I. Likewise there was little precise information on the preparation of these compounds, nor was it possible to prepare α-iodopalmitic acid in reasonable yield by Ponzio's method.[3] Thus it became desirable to develop the preparation of these compounds and to study them in more detail. It was felt that the inclusion of the absorption spectra of these compounds would be of value in showing the effect of varying substituted groups upon the long chain acid molecule.

TABLE I

Melting Points of Compounds Derived from Palmitic Acid

	Reference			
	Ponzio[3]	Jones[4]	Artamonov[5]	Authors[6]
Compound	C°	C°	C°	C°
α-Bromopalmitic acid	51–51.5			52.3–52.5
α-Bromopalmitamide	85			85
α-Iodopalmitic acid	57	60–61		59.5–59.9
α-Iodopalmitamide	108			109
2-Hexadecenoic acid	45		53.6	48.7–49.0
α-Hydroxypalmitic acid	83		86.5–87	81–82

The method of synthesis for the unsaturated acid was essentially that of Ponzio, which required the bromination of palmitic acid, the displacement of the bromine by the iodide ion and the removal of HI from the iodopalmitic acid to form 2-hexadecenoic and α-hydroxypalmitic acids.

α-Bromopalmitic acid was prepared by three methods: the usual Hell-Volhard-Zelinsky reaction with palmitic acid which gave a 94% yield of the crude product, the method of Schwenk and Papa[7] with a 98% yield of crude product, and by way of the malonic ester synthesis from diethyl tetradecylmalonate with direct bromination. As expected, the products from the three syntheses were identical.

Ethyl α-bromopalmitate was prepared directly from the bromopalmityl bromide secured in either of the first two syntheses above. The object in preparing this ester was to substitute iodine for bromine in the ester, to purify both esters by means of distillation and then to dehalogenate and saponify the ethyl α-iodopalmitate in a single operation. This method proved impracticable. Although the bromoester was readily distilled the iodo ester was too unstable to permit distillation even at 1 mm. pressure. Copious quantities of iodine were evolved and a tarry polymeric product resulted.

α-Iodopalmitic acid was finally prepared from α-bromopalmitic acid by reaction with sodium iodide in methyl ethyl ketone to give a 90% yield of crude product. Attempts to carry out the reaction in ethyl alcohol as directed by Ponzio led to negligible yields.

The action of alcoholic potassium hydroxide on α-iodopalmitic acid gave a mixture of 2-hexadecenoic acid and α-hydroxypalmitic acid in a ratio of about 2 to 1, and a combined yield of 90% of the crude product. The two acids were readily separated since the hydroxy acid was only slightly soluble in cold petroleum ether. Repeated treatments of the unsaturated acid with petroleum ether followed by recrystallization from ethyl alcohol gave a product having a sharp melting point and excellent acid value. The character of this product was confirmed by preparing the unsaturated acid by a Reformatsky reaction using myristic aldehyde and ethyl bromoacetate to form

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(3) Ponzio, *Gazz. chim. ital.*, **35**, II 132 (1905).

(4) Jones, *J. Am. Chem. Soc.*, **37**, 589 (1915).

(5) Artamonov, *Chem. Abstr.*, **47**, 8639 (1953).

(6) This paper.

(7) Schwenk and Papa, *J. Am. Chem. Soc.*, **70**, 3626 (1948).

ethyl β-hydroxypalmitate which was dehydrated and then saponified to the acid. A melting point of a mixture of the two acids showed no depression.

The unsaturated acid showed a lack of reactivity with bromine and potassium permanganate in the cold, characteristic of *alpha* unsaturated acids. On catalytic reduction over platinum the amount of hydrogen used was equal to that predicted by calculation. The reduction product, when mixed with an authentic sample of palmitic acid gave no depression of melting point.

α-Hydroxypalmitic acid was obtained as a by-product of the preparation of 2-hexadecenoic acid by the action of alcoholic potassium hydroxide upon α-iodopalmitic acid. It was also prepared by the action of alcoholic potassium hydroxide on α-bromopalmitic acid, in which case only negligible amounts of the unsaturated acid were obtained.

Discussion of absorption spectra.[8] As might be expected the ultraviolet absorption curves showed no characteristic absorption band. The curves for the infrared absorption spectra are shown in

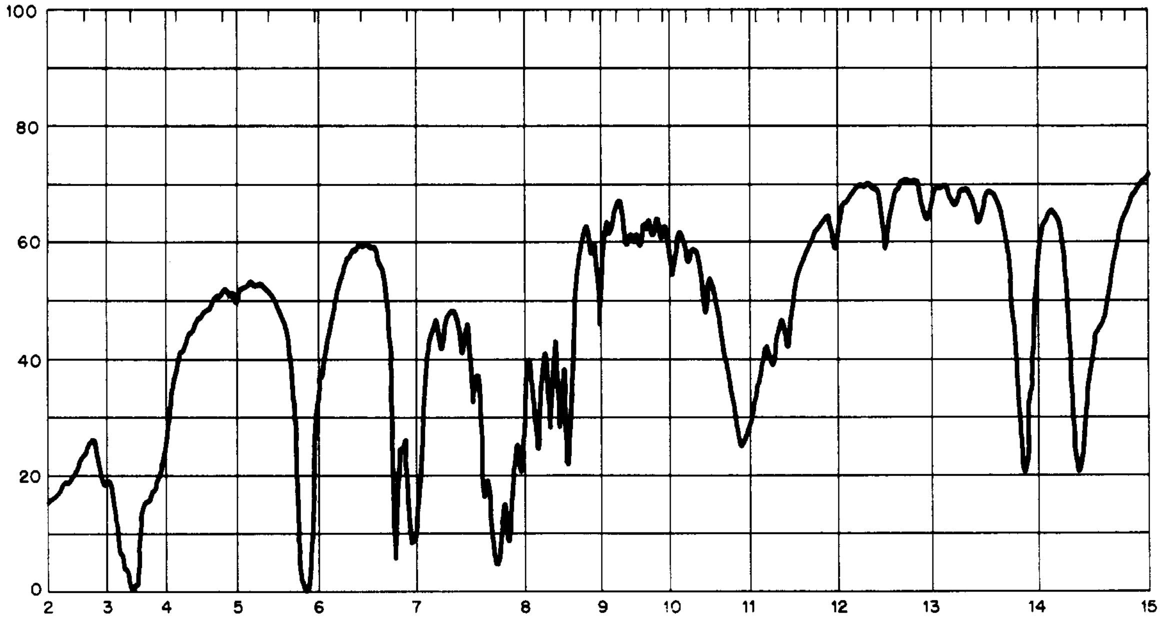

FIG. 1. INFRARED ABSORPTION SPECTRA OF α-BROMOPALMITIC ACID.

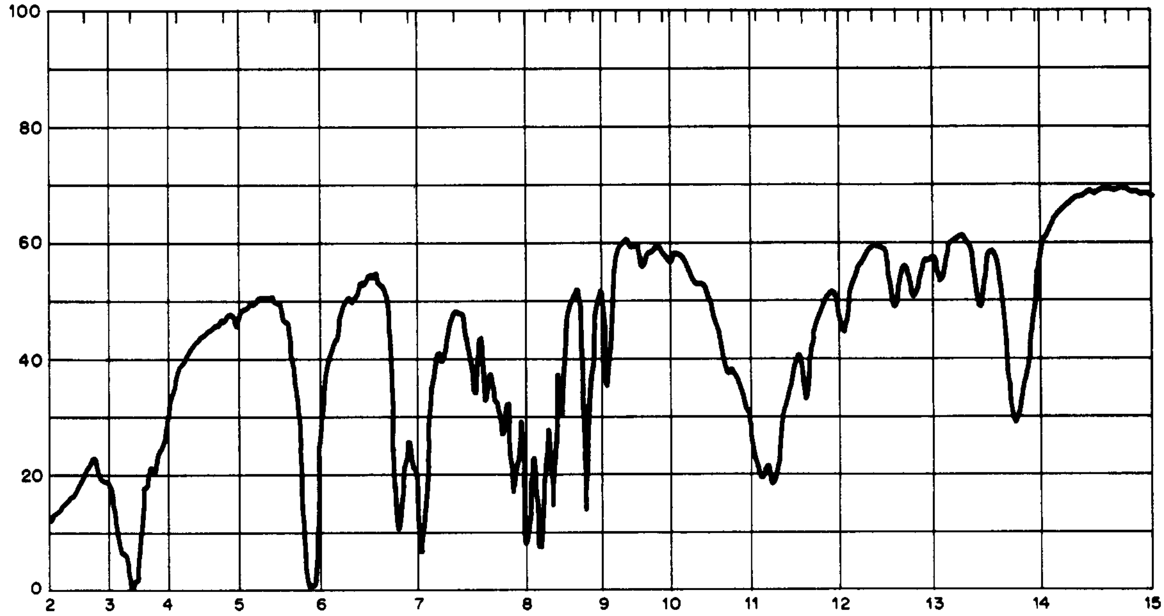

FIG. 2. INFRARED ABSORPTION SPECTRA OF α-IODOPALMITIC ACID.

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[8] The authors wish to thank Henry J. Noebels of Beckman Instruments, Inc. for the absorption spectra and analysis.

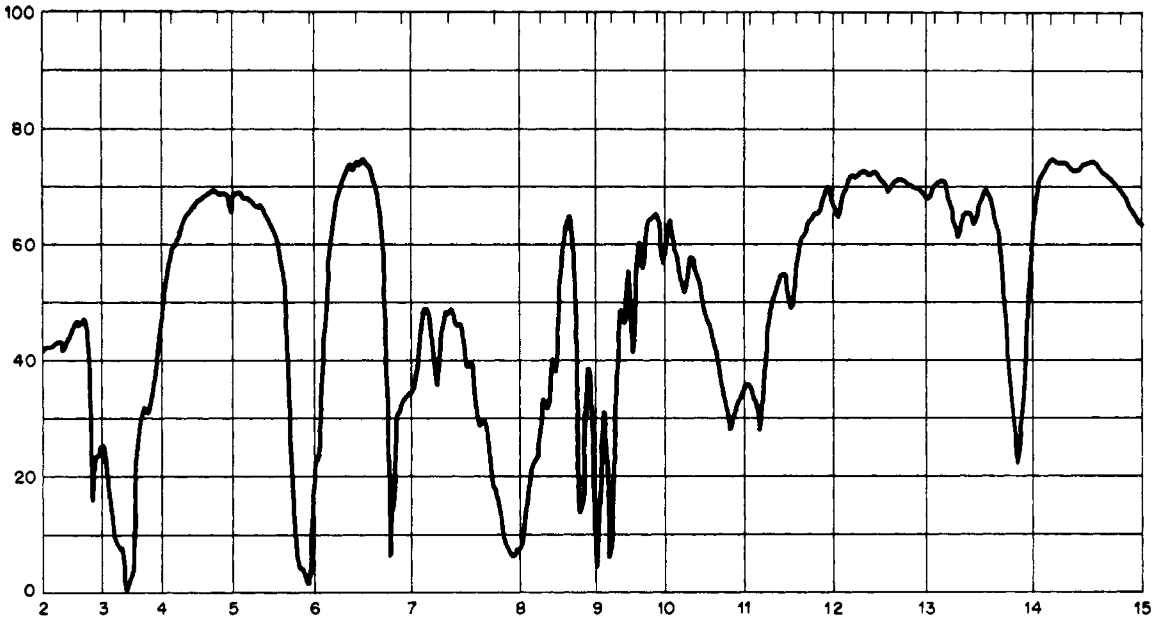

FIG. 3. INFRARED ABSORPTION SPECTRA OF α-HYDROXYPALMITIC ACID.

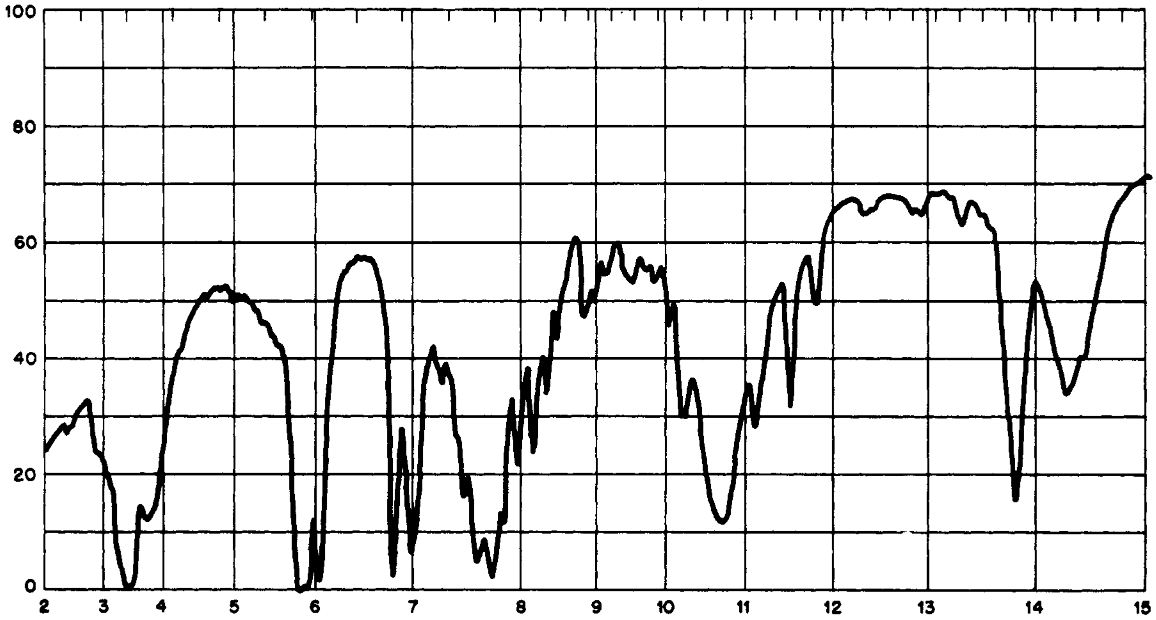

FIG. 4. INFRARED ABSORPTION SPECTRA OF 2-HEXADECENOIC ACID.

Figures 1 to 4. The determinations were made on a Beckman I R-2 A infrared spectrophotometer utilizing the pressed KBr technique since carboxylic acids usually exist in solution in the dimeric form.

In all the curves the sharp band at 2.85 is presumably due to the OH stretching, the band at 3.4 to the CH stretching, the strong band at 5.9 to the C=O, carbonyl, and the sharp band at 6.8 to the scissor-like bending of the methylene groups. As might be expected the 2.85 band is most pronounced in the hydroxy palmitic acid. No explanation can be given to the 14.4 band in the α-bromo acid and the 14.3 band for the unsaturated acid.

EXPERIMENTAL

Preparation of α-bromopalmitic acid. 1. Hell-Volhard-Zelinsky Reaction.[9] Palmitic acid (E. K. pure grade) 100 g. (0.39 mole) and 5 g. of red phosphorus were placed in a 1 liter 3-necked flask equipped with a stirrer, dropping-funnel, and condenser protected by a calcium chloride tube. The acid was melted on a water bath at 70°, and 50 ml. (0.975 mole) of dry bromine was dropped in over 8 hours with continuous stirring, then heated and stirred for an additional 4 hours at which time the evolution of HBr ceased. The clear, dark red reaction mixture was heated on a boiling water-bath at 30 mm. until all the excess bromine had been removed, giving a clear straw-colored oil.

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[9] Gilman and Blatt, *Org. Syntheses*, Coll. Vol. 1, 2nd ed., 115 (1941). See also, W. J. Hickinbottom, *Reactions of Organic Compounds*, 2nd ed. Longman's, Green and Co., New York, 1948, page 239.

The hot product was poured into 2 l. of water and allowed to stand overnight. The hydrolyzed acid was washed several times with water, and finally was heated in water with stirring. The cooled gel was taken up in 500 ml. of ether. The ether solution was washed until the washings were neutral to litmus and was dried over sodium sulfate. On removal of the ether 121 g. of the bromo acid, 92%, was obtained.

After recrystallization from petroleum ether with Norit and finally from ethyl alcohol the product gave a melting point 52.3–52.5° (corr.); N.E.: Found, 335.2, 335.9; Theoretical, 335.38; Bromine[10]: Found, 23.8, 23.4; Calculated, 23.8.

2. Method of Schwenk and Papa. Using an all-glass system consisting of a 500-ml. 2-necked flask fitted with a dropping-funnel and condenser protected by a calcium chloride drying tube, 50 g. (0.195 mole) of palmitic acid was dissolved in purified thionyl chloride, and converted to the acid chloride by warming on a hot plate for 1.5 hours. Then 42 g. (0.262 mole) of bromine was dropped in over a three-hour period at the reflux temperature, and refluxing was continued for an additional 3 hours. (In other runs additional refluxing with ultraviolet light did little to improve the reaction.)

The thionyl chloride was distilled off on a boiling water-bath, the last traces being removed at the pressure of a water pump. The clear light red oil remaining was poured into 1.5 l. of water and was stirred while heating. The acid chloride hydrolyzed slowly, hydrolysis being complete at 80°. The mixture was allowed to cool and the crystalline product which separated was again heated in water with stirring. The final steps of the isolation were the same as in the first method described. The yield of the crude product obtained was 64.2 g. (0.192 mole), 98%.

Preparation of ethyl α-bromopalmitate. The α-bromopalmityl halide secured in either of the foregoing procedures may be used without purification at this point. In one experiment starting with 100 g. (0.39 mole) of palmitic acid, after removal of excess bromine, the hot crude acid bromide was added slowly with stirring to 200 ml. (3.6 moles) of absolute ethanol with cooling. The solution was boiled on a water bath for 4 hours and the excess alcohol was distilled off. The ester was poured into water, taken up in 250 ml. of ether and the ether solution was washed with sodium bicarbonate solution, and finally with water. The ether solution was dried, the ether removed, and the oil distilled at reduced pressure to give 129.3 g. (0.357 mole) of a clear light yellow oil; 91.7%.

The ethyl α-bromopalmitate had the following constants: boiling point 177–178° at 2 mm.; *sp. gr.* 28/28 1.0484; n^{20}_{D} 1.4560; M_D: Calculated, 94.52; Theoretical, 94.77.[11]

Preparation of α-iodopalmitic acid. To a 1-l. flask fitted with a condenser protected by a soda-lime tube was added 62.7 g. (0.187 mole) of α-bromopalmitic acid, 56 g. (0.374 mole) of sodium iodide, and 600 ml. of dry methyl ethyl ketone. The mixture was refluxed for 8 hours, and then the solvent was distilled off on a water-bath, traces being removed at the pressure of a water pump. The product was added to 1.5 l. of water, acidified to litmus with dilute sulfuric acid and sufficient 10% sodium bisulfite solution was added to discharge the color of the solution. The solid clumps were filtered, resuspended in water, stirred, and heated with the addition of sufficient sodium bisulfite solution to discharge all the color. The mixture was cooled, filtered, the solid acid dissolved in dilute sodium carbonate, reprecipitated by the addition of sulfuric acid, and the solid washed with water. There was obtained 66.5 g. (0.174 mole, 93%) of the crude iodo acid.

The product was recrystallized twice from petroleum ether using Norit. The α-iodopalmitic acid thus obtained had m.p. 59.5–59.9° (corr.), N.E.: Found, 382.3, 383.0; Theoretical, 382.3. Analysis for iodine:[10] Found, 32.8, 32.7; Calculated, 33.1.

Preparation of 2-hexadecenoic acid. To a 1-l. flask fitted with a condenser equipped with soda-lime and drying tubes was added 51 g. (0.134 mole) of purified α-iodopalmitic acid, 27 g. (0.482 mole) of potassium hydroxide, and 600 ml. of 95% ethyl alcohol. The mixture was refluxed for 10 hours on a steam-bath, and then the bulk of the alcohol was distilled off, the last traces being removed at the pressure of a water pump. The product was dissolved in 1.5 l. of water at 80°, then acidified with sulfuric acid, and cooled to room temperature. The solid acid was taken up in 700 ml. of ether, and the ether solution was dried over sodium sulfate. The ether was removed and the product was taken up in warm petroleum ether. On cooling to room temperature about 10 g. of the α-hydroxypalmitic acid was filtered off. The volume of the solution was reduced to about half by evaporation and an additional 1 g. of the hydroxy acid was removed. On chilling in an ice-bath 10.5 g. of 2-hexadecenoic acid was obtained. Two more evaporations and chillings produced an additional 9 g. of the crude unsaturated acid. Total yield of crude unsaturated acid: 19.5 g. or 57%.

The crude product was purified by repeated recrystallizations from petroleum ether, and finally from 95% ethyl alcohol. This treatment produced pure white sparkling crystals. The 2-hexadecenoic acid thus obtained gave m.p. 48.7–49.0° (corr.), N.E.: Found, 254.3, 254.9; Theoretical, 254.3.

Preparation of α-hydroxypalmitic acid. Pure α-bromopalmitic acid (80.0 g., 0.248 mole) was refluxed with 28 g. (0.5 mole) of potassium hydroxide in 500 ml. of 95% ethyl alcohol for 10 hours on a steam-bath. The product was isolated in the same manner as described for 2-hexadecenoic acid through the recovery from the ether solution. The pure white product thus obtained was twice suspended in 500 ml. of petroleum ether and filtered. This product was recrystallized from 95% ethyl alcohol and dried. Yield of α-hydroxypalmitic acid: 63 g. or 93%. This product melted at 81–82°, N.E.: Found, 273.0; Theoretical, 272.4.

The α-hydroxypalmitic acid thus obtained was identical in all respects with that obtained as a by-product in the preparation of the unsaturated acid.

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(10) The halogen content of the acids was determined by the Volhard method on samples previously ignited in an electric Parr Peroxide Bomb. For ignition 0.2-g. samples were used with sucrose as accelerator. The melt was removed from the fusion cup and head with water in the usual way. In case of the iodide especially, care was required in dissolving the melt slowly enough so that the frothing from the Na_2O_2 did not boil out of the beaker. Hence it was found advisable to use 100 ml. of hot water in a liter beaker.

After the melt had dissolved the solution and combined washings were heated almost to boiling and 0.5 g. of hydrazine sulfate was added to reduce any bromate or iodate that might have been formed. The cooled solution was allowed to stand for at least two hours and then was acidified with 50 ml. of nitric acid (1:1). Low results were obtained when the nitric acid solution was prepared from concentrated acid stored in a colorless glass bottle. It was assumed that oxides of nitrogen were present to attack the thiocyanate used in the back titration. See, Rieman, Neuss and Naimen, *Quantitative Analysis*, McGraw Hill Book Co. New York, 1951, page 271.

An excess of 0.1 *N* $AgNO_3$ (5 ml.) was added to the solution and the unreacted silver nitrate was back titrated with 0 1 *N* potassium thiocyanate using one ml. of a saturated solution of ferric ammonium sulfate as indicator.

(11) Shriner and Fuson, *Identification of Organic Compounds*, 3rd ed. John Wiley and Sons Inc., New York, 1949, page 45.