3-Phenetyl-5-anisyl Isoxazole (XX). A. From the Isoxazoline (XVIII).—A solution of 2 g. of the isoxazoline (XVIII) in 100 cc. of glacial acetic acid was heated to 80° and 1.34 g. of chromic oxide was added. The reaction mixture was stirred for 45 minutes and then poured into 400 cc. of cold water. The resulting precipitate was filtered, washed with water and then washed with a little cold ethanol. The precipitate was boiled with a quantity of ethanol insufficient for complete solution. The residue remaining after quickly decanting off the hot alcoholic solution was recrystallized from ethyl acetate and subsequently from ethanol to yield colorless needles melting at 125.5°.

B. From the Dibromide (VIII).—To a hot solution of 5 g. of the dibromide (VIII) in 40 cc. of ethanol was added a solution of 2 g. of hydroxylamine hydrochloride in 3 cc. of water after which a solution of 4.5 g. of potassium hydroxide in 5 cc. of water was immediately added to the mixture. The solution became reddish-brown and the product precipitated rapidly on refluxing. It was filtered, washed with water and recrystallized from ethanol as colorless needles weighing 2.6 g., and melting at 126°.

C. From the α-Bromochalcone (X).—A solution of 0.57 g. of hydroxylamine hydrochloride in 5 cc. of water was added to a solution of 1.5 g. of the α-bromo unsaturated ketone (X) in 30 cc. of ethanol after which a solution of 1.4 g. of potassium hydroxide in 5 cc. of water was added to the mixture. The solution turned dark red while refluxing for one hour. After cooling, the precipitate which was formed was recrystallized from methanol as colorless needles to yield 0.18 g. melting at 126°.

Mixture of Isoxazoles (XIX) and (XX) from Diketone (XII).—To a solution of 1 g. of the enolic material (XII) in 25 cc. of ethanol was added a solution of 0.25 g. of hydroxylamine hydrochloride in 4 cc. of water and the mixture was refluxed for one hour, during which interval a colorless material precipitated. This material recrystallized from ethanol as colorless silky needles weighed 0.54 g. and melted at 131.6°.

Anal. Calcd. for $C_{18}H_{17}O_3N$: C, 73.2; H, 5.8. Found: C, 73.3; H, 5.7.

The melting points of the mixtures of varying proportions of the isoxazoles (XIX) and (XX) were found to vary irregularly between 125.6° to 138.6°. The melting point of a mixture of the isoxazoles, prepared by dissolving approximately equal quantities—about 30 mg. each—in ethanol, allowing the solvent to evaporate and then intimately mixing was 132°.

Summary

1. We have reported the preparation of two β-diketones which are 100% enolic in methanol.

2. We have shown that each β-diketone yields a mixture of two isoxazoles—each a derivative of one or the other of the resonating enol pair.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY, GENERAL MILLS, INC.]

Hydroxylated Stearic Acids. I. Action of Prévost's Reagent on Oleic and Elaidic Esters: Evidence for Configuration of the Hydroxy Acids[1]

BY HAROLD WITTCOFF AND SIDNEY E. MILLER

The Prévost reagent,[2] silver iodobenzoate, was applied to methyl oleate and to elaidic acid by Green and Hilditch,[3] who reported that the former, after saponification, yielded a mixture of the high and low melting forms of 9,10-dihydroxystearic acids, whereas the latter yielded only the low melting form.[3a,4] Repetition of the work in this Laboratory has shown, in contrast to the results of the English workers, that subsequent to saponification the interaction of silver iodobenzoate and methyl oleate (*cis* double bond) yields exclusively the low melting form of 9,10-dihydroxystearic acid. Likewise there results from methyl elaidate (*trans* double bond) after similar treatment the high melting form of the dihydroxy acid. Furthermore, by changing the order of the addition of the reagents, and by extending the time of reaction, it has been possible to increase the yields considerably over those reported by the previous workers.

If the benzoxylation proceeds by *trans* addition to the double bond as Prévost contends[2b] then it follows that low melting 9,10-dihydroxystearic acid is the *threo* form and is configurationally related to elaidic acid whereas the high melting form is the *erythro* form and represents the so-called normal or *cis* addition of the two hydroxyl groups to oleic acid.

The above conclusions reached from benzoxylation studies are in accord with those postulated by King[5] from epoxidation experiments. Both our conclusions and those of King, however, are opposed to the conclusions of Atherton and Hilditch[6] who, like King, employed epoxidation as a means of postulating configurational relationships. In reading Atherton and Hilditch's work, one is impressed with the fact that they have not taken full advantage of evidence which has accumulated relating to certain mechanisms upon which their postulations are dependent. Thus it has been shown that closure and fission of epoxide rings proceed with inversion.[7] Likewise, modern theory proposes the *trans* addition of hypochlorous acid to olefins.[8] Finally, hy-

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[1] Paper No. 75, Journal Series, Research Laboratories, General Mills, Inc. Presented at the 112th meeting of the American Chemical Society, New York City, Sept. 15–19, 1947.

[2] (a) C. Prévost, *Compt. rend.*, **196**, 1129 (1933); (b) *ibid.*, **197**, 1661 (1933); (c) C. Prévost and R. Lutz, *ibid.*, **198**, 2264 (1934); (d) C. Prévost and J. Wiemann, *ibid.*, **204**, 989 (1937); (e) E. B. Hershberg, *Helv. Chim. Acta*, **17**, 351 (1934).

[3] T. G. Green and T. P. Hilditch, *Biochem. J.*, **29**, 1552 (1935).

[3a] D. Swern, G. N. Billen, T. W. Findley and J. T. Scanlan, THIS JOURNAL, **67**, 1786 (1945).

[4] A. Lapworth and E. N. Mottram, *J. Chem. Soc.*, 1628 (1925).

[5] G. King, *ibid.*, 37 (1943).

[6] D. Atherton and T. P. Hilditch, *ibid.*, 204 (1943).

[7] See, for example, S. Winstein and H. J. Lucas, THIS JOURNAL, **61**, 1576 (1939).

[8] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 148.

droxylation by permanganate in basic or neutral medium is generally considered to be a *cis* addition, and the contention of Atherton and Hilditch that this mode of addition is somehow modified by excess alkali is open to serious question.

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Experimental[9]

Low Melting 9,10-Dihydroxystearic Acid.—A mixture of oven-dried silver benzoate (0.2 mole, 45.8 g., Ag content = 46.0%), iodine (0.1 mole, 25.4 g.) and anhydrous benzene (300 cc.) was heated on a steam-bath for one-half hour under reflux with adequate precaution against moisture. Thereafter methyl oleate[10] (0.1 mole, 29.7 g.), which was 96% pure as indicated by thiocyanogen and iodide number determinations, was added and the reactants were refluxed for twenty-four hours. The mixture was filtered to remove silver iodide after which the filtrate was washed successively with water, dilute sodium bicarbonate solution and again with water. The benzene solution was dried over sodium sulfate and the solvent was removed under reduced pressure to yield a reddish oil (43.5 g., 81%) which resisted attempts to induce crystallization. A portion of this material (10.0 g.) was stirred intermittently and heated on a steam-bath for three hours with 10% aqueous sodium hydroxide (50 cc.). The hot solution was stirred mechanically while being acidified with concentrated hydrochloric acid. An oily layer of the dihydroxy acid collected at the surface whereas the benzoic acid started to crystallize in the aqueous layer. After the upper layer had solidified it was separated and was triturated with dilute acid and finally with water. The washings were combined with the aqueous layer which on heating yielded a small additional amount of oily material. This was separated and combined with the original product which was dried on a clay plate. The material was dissolved in absolute ethanol and allowed to stand. There resulted five successive crops of crystals (5.0 g.) which after two crystallizations from ethyl acetate melted at 93–94° and which did not depress the melting point of an authentic sample of 9,10-dihydroxystearic acid[3a] (m. p. 95°) on admixture. Evaporation of the original mother liquor yielded a mixture of benzoic and dihydroxystearic acids which were separated by treatment with Skellysolve B in which the latter material is practically insoluble. The insoluble portion, after crystallization from 95% ethanol, yielded 0.5 g. more of low melting 9,10-dihydroxystearic acid. Thus a total of 5.5 g. of product was obtained which is a 93% yield on the basis of the benzoxylated product subjected to saponification.

Anal. Calcd. for $C_{18}H_{36}O_4$: C, 68.31; H, 11.47. Found: C, 68.22; H, 11.30.

The exact procedure outlined by Green and Hilditch[3] was repeated in which the iodine was added to a heated mixture of methyl oleate and silver benzoate in benzene and in which the reaction time was only three hours. The product was saponified as indicated in the previous experiment. Since the English workers indicated that their acid precipitated from ether, the oily layer was dissolved in ether and was washed with dilute acid and with water. The ether solution was then dried over sodium sulfate and was allowed to stand. From 35.0 g. of benzoxylated material there resulted 6.3 g. of material which, after three crystallizations from ethyl acetate, melted at 92–93° and did not depress the melting point of an authentic sample of 9,10-dihydroxystearic acid (m. p. 95°). The original mother liquor, on standing, yielded 1.0 g. more of a mixture of benzoic and low melting 9,10-dihydroxystearic acids. Evaporation of the ether yielded a mushy solid which was entirely soluble in Skellysolve B and appeared to be chiefly benzoic acid.

High Melting 9,10-Dihydroxystearic Acid.—Methyl oleate[10] was elaidinized[11] and saponified and the resulting mixture of oleic and elaidic acids was separated by the lead salt procedure.[12] The elaidic acid (m. p. 40–42°) was then converted to its methyl ester and distilled.

Silver benzoate (0.0672 mole, 15.4 g.), iodine (0.0336 mole, 8.53 g.) and anhydrous benzene (100 cc.) were allowed to react as described in the above procedure after which methyl elaidate (0.0336 mole, 10 g.) was added and the mixture was refluxed for twenty-one hours. The reaction mixture, when processed as in the preceding experiment, yielded 16.5 g. (91.2%) of a thick reddish oil. A portion of this material (7.0 g.) was saponified as described in the first experiment (10% aqueous sodium hydroxide, 50 cc.). After three crystallizations from alcohol–benzene (1:1) there resulted 3.1 g. (76% based on benzoxylated product) of pure 9,10-dihydroxystearic acid melting at 130–131°.[4] No depression was observed on admixture with an authentic sample (m. p. 131°).

Anal. Calcd. for $C_{18}H_{36}O_4$: C, 68.31; H, 11.47. Found: C, 68.34; H, 11.05.

Summary

The reaction of silver iodobenzoate with methyl oleate has been shown, contrary to the results of Green and Hilditch,[3] to yield exclusively the low melting form of 9,10-dihydroxystearic acid after saponification. Conversely, with methyl elaidate the high melting form of the acid resulted. From these observations certain conclusions are advanced regarding the configuration of the 9,10-dihydroxystearic acids.

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[9] Melting points are uncorrected. The authors are indebted to Mr. Harold Boyd and to Miss Katherine Tellor for the performance of micro carbon and hydrogen analyses and to Mr. D. E. Terry for samples of pure methyl oleate.

[10] D. Swern, H. B. Knight and T. W. Findley, *Oil & Soap*, **21**, 133 (1944).

[11] S. H. Bertram, *Chem. Weekblad*, **33**, 3 (1936).

[12] L. V. Cocks, B. C. Christian and G. Harding, *Analyst*, **56**, 368 (1931).

[13] Original manuscript received September 23, 1946.