heat. The electron diffraction pattern of B_5H_9 was calculated for the present model, and a possible vibrational assignment offered for B_2H_6.

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[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY,[1] PHILADELPHIA, PENNSYLVANIA]

Catalytic Air Oxidation of Methyl Oleate and Characterization of the Polymers Formed[2]

BY DANIEL SWERN, H. B. KNIGHT, JOHN T. SCANLAN AND WALDO C. AULT

Reaction of oxygen with unsaturated fatty materials is a complex phenomenon and, although much has been published on this subject, the mechanisms involved are not understood. The natural triglycerides, on which much of the work has been done, are complex mixtures. This, together with the fact that some investigators[3] have based their conclusions upon analytical data obtained on unfractionated oxidation mixtures, has made it difficult to determine the real nature of the reactions. It is true that within the last fifteen years some workers in this field[4,5,6,7] have directed their investigations to relatively simple materials of known structure and, in general, of high purity, but even with such materials the occurrence of many simultaneous reactions was observed. In some of these cases, the simple monomeric oxidation products were isolated and identified, but in every instance a large proportion of high-boiling material remained uncharacterized.

The purpose of the present investigation was to determine the effect of catalytic air oxidation upon pure methyl oleate, with particular emphasis on the characterization of the high-boiling substances produced. Methyl oleate, with cobalt oleate as catalyst, was oxidized at 65° with air until the iodine number became substantially constant. The product, an orange-red oil, was saponified with aqueous sodium hydroxide. When the resulting product was acidified, a mixture of an ether-insoluble, white solid and an ether-soluble oil was precipitated. The white solid was the high melting 9,10-dihydroxystearic acid. The ether-soluble material was converted to methyl esters and steam distilled under reduced pressure from a Claisen flask. The volatile material was fractionally distilled (Table I). Pelargonic, azelaic, and both the low and high melting 9,10-dihydroxystearic acids were identified in the distillate. This corroborated substantially the findings of Skellon[4] and Ellis,[5] who also identified these substances in addition to numerous others, such as octanoic and suberic acids. These workers did not, however, fractionate and characterize the material corresponding either to fraction 4, Table I, or to our original distillation residue. The latter was a dark, reddish-brown, viscous oil and constituted about 30 to 40% of the total oxidation products. By molecular distillation, this residue was separated into fractions of increasing molecular weight, ranging in color from light yellow to dark brown (Table II).

Fraction 4, Table I, was converted to free acids, and by fractional crystallization both 9,10-dihydroxystearic acids were isolated and identified. The oil obtained from the crystallization filtrate (usually at least 80% by weight of fraction 4) was reconverted to methyl esters. On the basis of the analytical characteristics alone, it might be concluded that this material consists of 35% unreacted methyl oleate, 25% methyl 9,10-dihydroxystearate (or 60% methyl 8- and 11-monohydroxyoleate[7a]) and 40% methyl esters of polymeric acids, probably dimers. This hypothesis is untenable, since oxidative splitting of this material with potassium permanganate in acetone solution yielded only minor quantities of pelargonic and azelaic acids. If fraction 4 consisted mainly of methyl oleate and methyl 9,10-dihydroxystearate, or methyl 8- and 11-hydroxyoleate, considerable quantities of pelargonic and azelaic acids would have been obtained. The major scission products consisted of heptanoic, pimelic, suberic and sebacic acids, as well as a mixture of short-chain scission products with a much lower boiling point than that of heptanoic acid. We believe that the isolation of such a variety of split products, considered in conjunction with the analytical characteristics of fraction 4, is reasonably satisfactory evidence for the presence in this fraction of methyl esters of several isomeric monohydroxy derivatives of one or more mono-unsaturated acids in which the double bond has been shifted from the 9,10-position. No previous evidence of a double-bond shift during oxidation of methyl oleate has come to our attention, although previous investigators have demonstrated that the double bonds of poly-unsaturated compounds are shifted during oxidation and have suggested that such shifts might also occur in mono-olefinic substances.[8] The residue remaining after distillation of the products of the permangate oxidation of

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(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

(2) Original manuscript received August 31, 1944.

(3) Overholt and Elm, *Ind. Eng. Chem.*, **32**, 378, 1348 (1940); **33**, 658 (1941); Powers, Overholt and Elm, *ibid.*, **33**, 1257 (1941).

(4) Skellon, *J. Soc. Chem. Ind.*, **50**, 382 (1931).

(5) Ellis, *Biochem. J.*, **26**, 791 (1932); *ibid.*, **30**, 753 (1936).

(6) Henderson and Young, *J. Phys. Chem.*, **46**, 670 (1942).

(7) (a) Farmer and Sutton, *J. Chem. Soc.*, 119 (1943); (b) Sutton, *ibid.*, 242 (1944).

(8) Farmer, Koch and Sutton, *ibid.*, 541 (1943).

TABLE I

FRACTIONS OBTAINED BY REDISTILLATION OF VOLATILE MATERIAL (369 G.) PRODUCED BY AIR OXIDATION OF METHYL OLEATE

Fraction	B. p. °C.	B. p. Mm.	Physical appearance	Odor	Weight, g.	Iodine number	Sapn. equivalent	Main components
1	54–66	0.2	Colorless	Fruity	76	4.0	168	Methyl pelargonate
2	70–106	0.2	liquid	Coconut	77	7.3	128	Dimethyl azelate
3	84–154	0.003–0.007	Straw-yellow liquid	Odorless	125	41.3	255	Methyl oleate, satd. esters present in starting material
4	154–185	0.007	Yellow semi-solid	Odorless	46	27.9	271	Methyl 9,10-dihydroxystearates, methyl esters of hydroxy unsatd. acids, methyl esters of dimeric acids
Residue			Dark-brown viscous liquid	Odorless	24	42.4	278	Methyl esters of polymeric substances

TABLE II

PRODUCTS OBTAINED BY DISTILLATION IN A CYCLIC MOLECULAR STILL OF THE MIXTURE OF POLYMERIC SUBSTANCES PRODUCED BY AIR OXIDATION OF METHYL OLEATE

Pass no.	Temp., °C. (press. 4–8 μ)	Weight, g.	Sapn. equiv.	Mol. wt.	I_2 no. (Wijs, one-half hour)	$n^{30}D$	d^{30}_4	Specific refraction[a]	Mol. refr.	Carbon, %	Hydrogen, %	Oxygen, % (by diff.)	Hydroxyl, %
Original charge	...	163.0	247	850	41.6	....	....	...	...	70.73	10.26	19.01	1.35
1	150	6.8	246	..	42.2	1.4690	....	...	...	69.36	10.58	20.06	2.70[b]
2	170	9.9	245	461	43.7	1.4708	0.9795	0.285	131	70.33	10.76	18.91	..
3	180	6.8	246	475	45.0	1.4718	.9811	.286	136	69.99	10.53	19.48	..
4	190	18.1	248	548	45.7	1.4745	.9847	.286	157	70.78	10.25	18.97	1.32
5	190	6.9	247	593	43.6	1.4752	.9875	.285	169	71.12	10.59	18.29	..
6	200	4.7	250	619	42.8	1.4767	.9901	.285	176	70.24	10.52	19.24	..
7	220	7.9	241	643	43.1	1.4779	.9943	.285	183	70.58	10.89	18.53	1.48
8	240	6.1	238	735	42.6	1.4798	.9977	.285	209	71.18	10.58	18.24	..
9	260	8.5	239	851	43.9	1.4809	1.0000	.285	242	70.40	10.32	19.28	1.36
Residue	...	86.0	239	1713	40.5	1.4868	1.0130	.284	487	71.62	10.79	17.59	1.09
Constants for methyl oleate (given for comparison)	...	...	296.5	296.5	85.6	1.4482	0.8669	0.3088	91.6	76.97	12.24	10.79	0

[a] The formula employed was $\frac{n^2 - 1}{n^2 + 2} \cdot \frac{1}{d}$ = specific refraction. [b] The high hydroxyl value of this fraction is probably due to residual methyl dihydroxystearate.

fraction 4 closely resembled the dimer fractions obtained by molecular distillation of the methyl esters of the original oxidation polymers (passes 2 and 3, Table II). We must assume, therefore, that fraction 4, Table I, contains methyl esters of dimeric acids in addition to the monohydroxy unsaturated acids mentioned above.

Examination of Table II reveals that the saponification equivalents and specific refractions of the fractions are fairly constant, whereas the molecular weights and molecular refractions increase with increasing distillation temperature. These properties indicate that these products are polymeric, but comparison of the saponification equivalents with that of methyl oleate indicates that these polymers are not multiples of C_{18} monomers. The major portion of the polymeric material isolated as a distillation residue, has an average molecular weight of about 1700. The iodine numbers of the fractions are essentially constant at a value equal to about half that of methyl oleate. The hydroxyl values are also constant but at a relatively low level. The oxygen content of the product is not entirely accounted for as hydroxyl, peroxide or carbonyl oxygen. These high oxygen values may be accounted for by assuming that the polymers are linked by oxygen. This concept is supported by the fact that the densities of the polymers are considerably higher than those of carbon-to-carbon linked polymers prepared by Bradley and Johnston[9] by heating fatty acid esters at high temperatures with exclusion of oxygen. The oxygen linkage is probably an ether type since the polymers are not saponifiable to monomer units.

The existence of polymers linked by ether oxygen has been suggested by previous investigators, who have studied the oxygen oxidation of cyclohexene and related hydrocarbons and have proposed mechanisms for the formation of such polymers.[10] No individual polymer was isolated by

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(9) Bradley and Johnston, *Ind. Eng. Chem.*, **33**, 86 (1941).

(10) Farmer, Bloomfield, Sundralingam and Sutton, *Trans. Faraday Soc.*, **38**, 348 (1942); Farmer and Sundralingam, *J. Chem. Soc.*, 121 (1942).

these workers, who drew their conclusions from the fact that their analytical data corresponded to oxygen-linked polymers.

The formation of polyfunctional substances during the air oxidation of methyl oleate offers a rational explanation for the formation of infusible, insoluble gels during the drying of oil paints and varnishes, in accordance with accepted theories of functionality. It is not necessary to assume that increase in molecular weight during the drying of a paint or varnish film is due to some form of association dependent upon "extra valence" forces.

Experimental

Materials.—The methyl oleate employed was a colorless, odorless liquid, the preparation of which has been reported previously.[11] Representative samples had iodine numbers of about eighty-four and thiocyanogen numbers of about eighty-three. The composition of this material ranged from 95 to 96% methyl oleate, 3 to 4% saturated esters, and 1% methyl linoleate.

Cobaltous oleate was prepared from oleic acid of comparable purity. Oleic acid (20 g.) was dissolved in 20 cc. of 95% ethanol, and an equivalent quantity of aqueous *N* sodium hydroxide was added with stirring. The temperature of the soap solution was reduced to about 5° by the addition of crushed ice. In an atmosphere of carbon dioxide or nitrogen, a cold aqueous solution containing 10.2 g. of cobalt nitrate hexahydrate was added with vigorous stirring. The resulting mixture was filtered, washed once with alcohol and dried, the product being kept in an inert atmosphere during all these operations. The tacky, purple mass, obtained in quantitative yield, was used as soon as it was alcohol-free.

Oxidation Procedure.—To 806 g. (2.7 moles) of methyl oleate in a three-liter, three-necked flask, 26.6 g. of freshly prepared cobalt oleate was added, and solution was effected by gentle heating. The flask was then equipped with a thermometer, a reflux condenser, and two fritted-glass disks immersed in the solution. A vigorous stream of air was passed through the solution while the temperature was maintained at 65°. At eight-hour intervals, samples were withdrawn for analysis. The acid number rose steadily throughout the oxidation to a maximum of about 130. The peroxide value was fairly constant at 20 to 40 millimoles per kilogram. The oxidation was stopped when the iodine number became substantially constant, which required about 170 hours. The final iodine number was usually below 15. The product obtained was an orange-red oil with a fruity odor. Including the samples withdrawn for analysis, its weight was 900 g. This represented a gain in weight of 8%.

Isolation and Identification of Products.—The oxidation products (875 g.) were refluxed for eight hours with two liters of 3 *N* aqueous sodium hydroxide, acidified with dilute sulfuric acid while hot, and stirred vigorously. A viscous, dark-brown, upper layer was formed. The product at this point usually had an iodine number from 10 to 15 units higher than would be expected from the iodine number of the crude oxidation product. We cannot explain this, but it corroborates the generally accepted belief that analytical data on crude oxidation products are not reliable. After the mixture had cooled to room temperature, it was treated with ether. The ether layer, in which a white solid was suspended, was washed with water until free of sulfuric acid, cooled to 0 to 5°, and filtered. The solid was washed once with cold ether. This material was high-melting 9,10-dihydroxystearic acid, somewhat impure; m. p., 124.5-126.5°; yield, 39 g.

Anal. Calcd. for $C_{18}H_{36}O_4$: neut. equiv., 316.5. Found: neut. equiv., 314-320.

The ether solutions were combined and dried over anhydrous calcium sulfate. The brown residue obtained after recovery of the solvent was converted to methyl esters by refluxing for eight hours with a large excess of anhydrous methanol (catalyst, sulfuric acid). The dark-brown methyl esters weighed 675 g. and had the following characteristics: iodine number, 26; acid number, 10; saponification equivalent, 215; hydroxyl, 2.55%. It is believed that the material lost consisted of volatile and water-soluble substances. This would account only in part for the increase in iodine number.

Six hundred and fifty-seven grams of these methyl esters was then steam distilled under reduced pressure (1.5-2.5 mm.) to a maximum pot temperature of 220° until no further distillate was obtained.[12] During the steam distillation, an additional 20 g. was withdrawn from the non-volatile portion for analysis.

Steam-volatile (Monomeric) Fraction.—This fraction weighed 390 g. and had the following characteristics: iodine number, 22; acid number, 7; saponification equivalent, 191. It was fractionally distilled, and the data obtained are shown in Table I.

Since the material comprising the fractions up to and including methyl oleate (fraction 3, Table I) has previously been carefully examined by Skellon[4] and Ellis,[5] no work was done on them beyond that recorded in Table I.

A 25-gram portion of fraction 4, Table I, was saponified with aqueous sodium hydroxide and acidified with sulfuric acid. The water-insoluble semi-solid upper layer was dissolved in ether, and washed acid free. The ether solution was cooled to 5°, and the precipitate which formed was filtered and washed once with cold ether. This precipitate (1.7 g.) was high-melting 9,10-dihydroxystearic acid, somewhat impure; m. p., 127.5-128.5°. When it was mixed with 9,10-dihydroxystearic acid prepared from oleic acid by oxidation with potassium permanganate its melting point was unchanged. From the ether filtrate, a light-brown semi-solid was obtained (21 g.). This was dissolved in 105 cc. of acetone and cooled to −20°. The precipitate (1 g.) was low-melting 9,10-dihydroxystearic acid, somewhat impure; m. p., 87.5-89.5°. When it was mixed with 9,10-dihydroxystearic acid prepared from oleic acid by peracetic acid oxidation its melting point was unchanged. The acetone filtrate yielded a light-brown oil (20 g.). This was combined with similar fractions from two other oxidations of methyl oleate and the mixture was converted to methyl esters. These had the following characteristics: iodine number, 31; saponification number, 214; saponification equivalent, 262; ester number, 207; % hydroxyl, 2.6; molecular weight, 362.

Fifty grams was oxidized with potassium permanganate in acetone solution by the method of Armstrong and Hilditch.[13] After solution of the manganese dioxide, the acidified mixture was extracted with two successive portions of ether. The ether solution was dried and the ether recovered. The residue was reconverted to methyl esters. The yield was 37 g. (iodine number, 3). These were fractionally distilled (15 plates) under vacuum. From the distillate (23 g.), heptanoic, pelargonic, pimelic, suberic, azelaic and sebacic acids were identified. Pelargonic and azelaic acids were present in only minor proportions. The residue (4 g.) was a dark-brown, viscous oil (iodine number, 22; saponification equivalent, 240; n^{30}_{D} 1.4714) which closely resembled the dimer fractions obtained by molecular distillation of the methyl esters of the original oxidation polymers (passes 2 and 3, Table II). The trap material (7 g.), which had a distinct fruity odor and was fairly volatile, had a saponification number of 98. No aldehyde, ketone or alcohol derivative could be prepared from the trap material.

Non-volatile (Polymeric) Fraction.—The steam distillation residue (analytical data shown in the first line of Table II) was a dark-brown, viscous, odorless oil (223 g.). It was vacuum-distilled in a cyclic molecular still. The

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(11) Swern, Knight and Findley, *Oil and Soap*, **21**, 133 (1944).

(12) In subsequent work, it was found that distillation from a Claisen flask in a stream of inert gas gave the same results and was easier to carry out.

(13) Armstrong and Hilditch, *J. Soc. Chem. Ind.*, **44**, 43T (1925).

results of the distillation and subsequent analysis are shown in Table II.

Analytical Methods Employed.—Iodine numbers were determined by the standard Wijs (one-half hour) method. Molecular weights were determined cryoscopically in benzene on methyl esters only. Per cent. hydroxyl was determined by a method recently developed by C. L. Ogg, W. L. Porter and C. O. Willits,[14] of this Laboratory.

Acknowledgment.—The authors are indebted to J. C. Cowan and W. Bond of the Northern Regional Research Laboratory for conducting the molecular distillation, and to E. F. Jordan, Jr., of the Eastern Regional Research Laboratory for assistance in conducting some of the laboratory work.

Summary

The catalytic air oxidation of methyl oleate has been studied.

The high-boiling, previously uncharacterized portion of the oxidation products, obtained in 30 to 40% yield, has been fractionated by molecular distillation, yielding oxygenated polymers of dimeric and higher complexity. It is believed that these polymers are oxygen linked.

A methyl ester fraction with a boiling point intermediate between that of methyl oleate and the polymers has been isolated and extensively studied for the first time. By oxidative splitting of this fraction with potassium permanganate in acetone solution, it has been shown to consist mainly of methyl esters of several isomeric monohydroxy derivatives of one or more mono-unsaturated acids in which the double bond has been shifted from the 9,10-position, and methyl esters of dimeric acids.

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[14] Ogg, Porter and Willits, *Ind. Eng. Chem.*, *Anal. Ed.*, in press.

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY,[1] PHILADELPHIA, PENNSYLVANIA]

Nicotinic Acid. Water-insoluble Esters and Amides

BY C. O. BADGETT, RAYMOND C. PROVOST, JR., CLYDE L. OGG AND C. F. WOODWARD

Attention has been directed[2] to the need for water-insoluble forms of nicotinic acid, thiamin, and riboflavin for use in the practical fortification of cereals, such as corn grits and white rice, which are often rinsed prior to cooking. Although nicotinic acid and nicotinamide have been successfully employed in the fortification of wheat flour, their water solubility makes them disadvantageous for enrichment of the food products mentioned above.

The present paper describes the preparation of *n*-alkyl esters and N-(*n*-alkyl) amides of nicotinic acid in an attempt to obtain derivatives having the desired water-insolubility and biological activity. The N-phenyl-, N-cyclohexyl- and N-(2-pyridyl)-nicotinamides were also prepared for biological comparison.

n-Alkyl esters of nicotinic acid, in which the length of the alkyl group ranged from C_2 to C_{18}, were prepared by the reaction of the corresponding alcohols with nicotinyl chloride.[3] N-(*n*-Alkyl) nicotinamides, in which the alkyl group ranges from C_6 to C_{18}, were prepared by the following methods: reaction of *n*-alkyl amines with nicotinyl chloride,[3] aminolysis of nicotinic esters,[4,5] and the reaction of amines with nicotinic acid.[5] The latter two methods were recently employed[5] in the synthesis of the following N-substituted nicotinamides for antispasmodic and anticonvulsant tests: benzyl-, *n*-amyl-, allyl- and dibutylaminopropyl-.

Published data indicate that methyl nicotinate is active in bacterial metabolism, whereas the ethyl-, *n*-propyl- and *n*-butyl esters of nicotinic acid are active in animal metabolism and exhibit some specificity as essential factors for bacteria. N-Methyl and N,N-diethyl nicotinamide were active in tests on dogs and on dysentery bacilli.[6]

Preliminary biological data, obtained by C. A. Elvehjem, L. J. Teply and W. A. Krehl, on several of the higher amides and esters prepared in this study are summarized in Tables I and II. Although most of these derivatives are relatively inactive in *Lactobacillus arabinosus*, there is some indication that the esters are active in animal metabolism. Since N-phenyl nicotinamide was about two-thirds as active as nicotinic acid in dog assays, it is believed that the N-alkyl nicotinamides will also be active under similar test conditions.

As was to be expected, the higher *n*-alkyl esters and amides of nicotinic acid were insoluble in water. Since the rinsing of fortified cereals would not result in saturation of the wash water with the vitamin, the solubility data herein reported are indicative of the maximum vitamin loss that could be incurred. The actual loss in practice would probably be far less than the saturation value.

Experimental

The preparation of *n*-octyl nicotinate is representative of the method employed in the preparation of the fourteen

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[1] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

[2] Gunderson, *Science*, **98**, 277 (1943).

[3] Hukusima, *J. Chem. Soc.*, Japan, **61**, 121 (1940).

[4] Pictet and Sussdorff, *Arch. sci. phys. nat.*, Geneve, [4] **5**, 118; *Chem. Zentr.*, **69**, I, 677 (1898).

[5] Billman and Rendall, THIS JOURNAL, **66**, 540 (1944).

[6] For an excellent review of compounds functionally related to nicotinic acid, see Elvehjem and Teply, *Chem. Rev.*, [4] **33**, 185 (1943).