Anal. Calcd. for $C_{18}H_{18}O_2Br_2$: C, 50.9; H, 3.8. Found: C, 50.7; H, 4.0.

This oil liberates iodine from potassium iodide-acetone solution, yielding the ketonic modification of the bromo diketone, melting at 72°.

Summary

In this paper are reported the preparation and many of the chemical properties of the α-diketone, 2,4,6-trimethylbenzylphenylglyoxal.

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[CONTRIBUTION FROM THE LABORATORY OF PHYSIOLOGICAL CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Studies on the Chemistry of the Fatty Acids. XII. The Preparation of Alpha- and Beta-Linoleic Acids by Debromination in Various Solvents and Observations on the Chemistry of These Acids

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In a previous report from this Laboratory, it was shown that α-linoleic acid[2] which is prepared by debromination of pure, petroleum ether-insoluble tetrabromostearic acid is a mixture of isomeric acids.[5] The principal component amounting to about 88% of the mixture, is an acid of high tetrabromide number (Tb. N. 102.9); it is believed to be the *cis–cis* modification of 9,12-octadecadienoic acid. The lesser component is believed to be either the *cis–trans* or *trans–cis* modification of this dienoic acid, or a mixture of acids none of which yields the usual insoluble bromide. It seems probable that these isomers of linoleic acid were formed by isomerization during the debromination reaction. These conclusions concerning α-linoleic acid were based mainly on one preparation of the acid, carried out in methyl alcohol to which was added only small amounts of hydrochloric acid to promote the debromination, and also on other experience in this Laboratory.

One of the objectives of the present work was to try the effect of debromination solvent on the composition of the resultant alpha-acid. In addition to methyl alcohol and pyridine, which have been used as debromination solvents by previous workers, four new solvents were tried, namely, ether, isopropyl ether, dioxane and glacial acetic acid. The first three of these gave excellent results and were found to be much more convenient than either methyl alcohol or pyridine. When methyl alcohol is used, there are always formed variable amounts of esters which must be removed. With pyridine, this difficulty is not encountered, but there is always some trouble in removing the pyridine. Ether, isopropyl ether and dioxane are neutral solvents and, after the debromination reaction, it is only necessary to wash out the last traces of zinc bromide, to remove the solvent and to distill the product. Yields with these solvents were comparable to usual experience with methyl alcohol debrominations. Yields were slightly lower when pyridine was used, but the product was satisfactory. Debromination in glacial acetic acid gave a product of low iodine value and tetrabromide number. Incidentally, attempts to debrominate in petroleum ether were without success. Although, except in the case of acetic acid, the iodine values of the several products described in detail in Table I are practically the theoretical for 9,12-octadecadienoic acid, the tetrabromide numbers varied from 81.3 to 102.4, indicating linoleic acid (*cis–cis* 9,12-octadecadienoic) contents of 81–99%, along with one to nineteen per cent. of isomeric acids. It is of special interest to note that one of the preparations in pyridine gave almost the same tetrabromide number, 102.4, as that obtained for the pure acid[5] (102.9), although the melting point was still 2° low. These results verify our previous con-

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[2] The following nomenclature is used in this paper: *linoleic acid, cis–cis*, 9,12-octadecadienoic acid, the principal naturally occurring acid of this series; *α-linoleic acid*, the mixture of octadecadienoic acids resulting from debromination of the 114–115° melting tetrabromides; *β-linoleic acid*, the product of debromination of the liquid tetrabromides, which result from bromination of α-linoleic acid or linoleic acid; *crystallization linoleic acid*, the product obtained by applying the method of Frankel and Brown to the fatty acids of semi-drying oils. This acid is ninety-five to one hundred per cent. linoleic acid[3,4] *isomeric linoleic acids or isomeric octadecadienoic acids*. These may be the *trans–cis* or the *cis–trans* 9,12-octadecadienoic acids, but not the *trans–trans* modification, since the acids in question give only liquid tetrabromides. In a general sense, other isomers with double bonds in other than the 9–12 position, but with theoretical iodine values, are not precluded.

[3] Frankel and Brown, THIS JOURNAL, **63**, 1483 (1941).

[4] Frankel, Stoneburner and Brown, *ibid.*, **65**, 259 (1943).

[5] Matthews, Brode and Brown, THIS JOURNAL, **63**, 1064 (1941).

clusions regarding the multiple nature of α-linoleic acid, the composition of which is apparently affected by debromination conditions. Melting points of the several products ranged from −6.0 to −11.6° in comparison with the −5.2° melting point of linoleic acid from which most of these isomers have been removed by repeated crystallization.[5]

Several recent investigations have attempted to clarify the conflicting views of Rollett[6] and Bedford[7] as to the nature of α- and β-linoleic acids. On the one hand, McCutcheon,[8] Riemenschneider, Wheeler and Sando,[9] and Kass and co-workers[10] have claimed that the acids regenerated from the solid and liquid tetrabromides are essentially identical. On the other hand, Green and Hilditch[11] and Hilditch and Jasperson[12] have shown that the two products differ fundamentally with respect to certain analytical constants, especially with respect to the yield of petroleum ether-insoluble bromides.

We have attempted to throw further light on this question by preparing a series of beta-acids by debromination of liquid tetrabromides in various solvents. The results are recorded in Table II. Excluding the product from acetic acid, the important differences between the alpha- and beta-acids are summarized below.

	LINOLEIC ACID	
	Alpha-	Beta-
Yield, %	80–93	30–94
Iodine value	179.7–181.0	161.2–174.9
Tb. N.	81.3–102.4	15.2–54.5
Octadecadienoic from I. V. %	100	78–94
Linoleic from Tb. N.	81–99	15–53
Isomeric acids	1–19	32–70
Melting points	−6.0 to −11.6	−17.2 to −22.2[a]

[a] The product from pyridine melted at −2°.

One of the important differences in the preparation of the alpha- and beta-acids in methyl alcohol is the yield. In the former instance, this is nearly the theoretical but in the case of the beta-acid a great deal is lost in the final distillation, showing the probable presence of much easily polymerizable material in the undistilled beta-acids. It is interesting to note that when ether is employed as the debromination solvent, the yields are comparable with those obtained for the alpha-acid. Nevertheless, the content of isomeric acid in the product ranged from 40–63%.

In addition to the data cited above, oxidation experiments on the alpha- and beta-acids show decided differences, the former giving about 50% yield of the usual sativic acids, while the latter gives only small amounts of these sativic acids, and, in some instances, only indefinite oily products. Further, in another report[13] employing spectroscopic methods, it has been shown that the alpha-acid contains 1.0 to 1.2% of conjugation, while the beta-acid contains 1.9 to 6.4% of this type of material.

We believe that our data justify the following conclusions. The alpha-acid is composed mainly of linoleic acid, but in addition contains variable amounts of isomeric acids, depending on the debromination conditions. These isomeric acids add iodine monochloride quantitatively and do not yield the 114–115° melting tetrabromides. They would seem to be either the *trans–cis* or the *cis–trans*, 9,12-octadecadienoic acid, or both. β-Linoleic acid differs mainly from the alpha-acid in its low linoleic acid content (15–53%) and its comparatively high content of isomeric octadecadienoic acids (32–70), and also in the presence of two to six per cent. of conjugated material. Again, these isomeric acids, which are estimated from differences in iodine value and Tb. N., we believe to be mainly *cis–trans* or *trans–cis* modifications, and definitely not the *trans–trans* acid, which yields a solid tetrabromide melting at 78°. They may also include other octadecadienoic acids of theoretical iodine value. In addition to the linoleic acid and isomeric acids mentioned above, the several preparations of beta-acid contained 6–22% of acids which have been more profoundly altered. These have been calculated as of the iodine value of octadecenoic acid, 89.9 which, of course, is an assumption. Part of this material is reported as conjugated acids which would not give the theoretical iodine value. We have shown later with two different preparations of beta-acid that the iodine value does rise decidedly with time, as would be expected with conjugated acids, but the spectroscopic results show that this low iodine number is only in part explained by conjugation.

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(6) Rollett, *Z. physiol. Chem.*, **62**, 410, 422 (1909).

(7) Erdmann and Bedford, *Ber.*, **42**, 1324 (1909); *Z. physiol. Chem.*, **66**, 76 (1910).

(8) McCutcheon, *Can. J. Research*, **16**, 158 (1938).

(9) Riemenschneider, Wheeler and Sando, *J. Biol. Chem.*, **127**, 391 (1939).

(10) Kass and Burr, THIS JOURNAL, **61**, 1062 (1939); Kass, Lundberg and Burr, *Oil & Soap*, **17**, 50 (1940).

(11) Green and Hilditch, *Biochem. J.*, **29**, 1552 (1935).

(12) Hilditch and Jasperson, *J. Soc. Chem. Ind.*, **58**, 233 (1939).

(13) Brode, Patterson, Brown and Frankel, to be published in *Ind. Eng. Chem.*

Another possibility is the presence of additional dienoic acids with one double bond too close to the carboxyl to give the theoretical iodine value. Still another possibility is that the molecule has been altered by oxidation or by cyclization.

Our debromination experiments gave two unexpected results which we believe to be important, but which we are not prepared to discuss without further study. One of these is the high melting point of the beta-acids prepared in pyridine, which was 3° higher than that of linoleic acid, and about 20° higher than those of the beta-acids prepared in other solvents. The other anomalous result is the low iodine number of both alpha- and beta-acids prepared in acetic acid, suggesting that hydrogenation was taking place along with debromination.

In general, our results are in agreement with and amplify the conclusions of Hilditch and coworkers, and do not agree with the observations of other workers, previously mentioned, that the alpha- and beta-acids are essentially identical.

We have already made some attempts to separate the several constituents of the beta-acids by low temperature crystallization. So far, the results have been disappointing, but we are continuing work in this direction.

Experimental

The Preparation and Properties of α- and β-Linoleic Acids.—The general procedure for preparing the alpha- and beta-acids in methyl alcohol was the following. The purified petroleum ether-insoluble tetrabromides from corn oil fatty acids, or from α linoleic acid, and, in the case of the beta-acid, the liquid bromides obtained by bromination of the alpha-acid, were dissolved in hot methyl alcohol and zinc powder was added cautiously in small amounts. The heat of reaction was sufficient to keep the alcohol boiling. From time to time, a few drops of hydrochloric acid were added to prevent lag in the reaction. After more than the calculated quantity of zinc had been added, the mixture was refluxed about an hour. The alcohol was then removed from the residual zinc and zinc bromide, either by suction filtration or centrifugation, the residue was washed several times with hot acidulated methyl alcohol and the combined solutions concentrated to about one-fourth volume by distillation. The remaining alcohol was removed by addition of water. To assure complete recovery of the product, this was extracted by several washings with ether. The ether was distilled off, and the resulting linoleic acid, containing about 5% of methyl ester, was distilled, saponified and after addition of hydrochloric acid the resulting acid was again distilled.

Debrominations in pyridine were carried out by the method of Kaufmann and Mestern.[14] Debrominations in other solvents, such as ether, isopropyl ether and dioxane, were carried out similarly. Since no ester formation is involved, as in the case of methyl alcohol, no final saponification was necessary to remove esters. The following is a typical experiment with ether: 30 g. of corn oil tetrabromides was dissolved in 350 cc. of ethyl ether and 15 g. of zinc powder was added in small portions. The addition of zinc at first produced no reaction, but a vigorous reaction began upon the addition of a few drops of concd. hydrochloric acid. Repeated additions of the zinc and hydrochloric acid kept the reaction going, a total of 7 cc. of the acid being finally added. The mixture was refluxed for one and one-half hours, transferred to a separatory funnel, and washed successively with 2 cc. of concd. hydrochloric acid, 500 cc. of dilute hydrochloric acid and finally with distilled water. It was then dried over anhydrous sodium sulfate, the ether was distilled off, and the product distilled under reduced pressure; yield, 13 g., practically water-white (see Table I).

The results of two series of debrominations of solid and liquid tetrabromides in various solvents are described in Tables I and II.

Partial Oxidation Experiments.—Specimens of alpha- and beta-acids were oxidized either by the method of Hazura[15] or the Lapworth and Mottram[16] modification of this method. For example, 4.8 g. of alpha-acid was dissolved in 200 cc. of water containing 3 g. of potassium hydroxide. To this was added 150 g. of powdered ice and slowly 5 g. of potassium permanganate in 200 cc. of ice-water. After standing at 0° for twenty-four hours, the solution was decolorized with sulfur dioxide gas, and 150 cc. of concd. hydrochloric acid added. The precipitated sativic acids were filtered off, washed free of hydrochloric acid and dried. They were extracted with ether to remove impurities and crystallized from hot water and 95% alcohol; yield, 3.2 g. crude acids which were resolved into 1.1 g. of an acid melting at 164° and 1.1 g. melting at 173°. The yields of sativic acids accounted for in the latter two products amounted to about 40%. Several other attempts gave similar results, the highest yield being about 60%. The two acids just mentioned correspond very closely to the products isolated by Riemenschneider, *et al.*,[6] during the repeated crystallization of 15 g. of crude sativic acids from the alpha-acid.

Our results with the beta-acid were not as clear-cut. In several attempts, we isolated very small amounts of the high melting sativic acids. In several others, we got 0.7–16% yields of an acid melting at 144°. In still other attempts only an oily product could be isolated. Generally speaking, results by other workers have been inconsistent as to the melting points of the sativic acids which were isolated from the beta-acid, but consistent in the observation that the beta-acid gives only small yields of the usual sativic acids. It should be noted that Riemenschneider and co-workers did obtain a 39% yield in one instance. We do not report our results in more detail at present because we feel that the principal difficulty so far is due to the complexity of the mixture which constitutes the beta-acid. Not only is it next to impossible to isolate pure sativic acids from such a mixture, but also apparently a large proportion of the material in the mixture is disruptively oxi-

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[14] Kaufmann and Mestern, *Ber.*, **69B**, 2684 (1936).

[15] Hazura, *Monatsh.*, **8**, 151 (1887).

[16] Lapworth and Mottram, *J. Chem. Soc.*, **127**, 1628 (1925).

TABLE I

ANALYTICAL DATA ON α-LINOLEIC ACIDS PREPARED BY DEBROMINATION IN VARIOUS SOLVENTS

Origin of tetrabromide	Debromination solvent	Yield, %	I. V.	Tb. N.	% Linoleic from Tb. N.	M. p., °C.
Corn oil acids	Methyl alcohol	90.0	180.9	90.6	88	− 7.0
Corn oil acids	Ethyl ether	92.8	180.3	88.7	86	− 6.2
Pure linoleic acid	Ethyl ether	93.2	180.7	96.9	94	− 6.0
Corn oil acids	Isopropyl ether	90.5	181.0	81.3	79	− 8.2
Pure linoleic acid	Isopropyl ether	90.4	181.0	83.8	81	−11.6
Corn oil acids	Dioxane	91.8	180.0	86.6	84	− 8.2
Pure linoleic acid	Dioxane	86.7	180.6	85.0	82	− 8.6
Pure linoleic acid	Pyridine	88.2	179.7	102.4	99	− 7.0
Pure linoleic acid	Pyridine	80.0	181.0	93.8	91	− 7.0 to −6.8
Corn oil acids	Glacial acetic	76.0	138.6	34.5	34	−11.0 to −9.4
Corn oil acids	Glacial acetic	78.0	127.2	18.9	18	−11.0 to −9.4

TABLE II

ANALYTICAL DATA ON β-LINOLEIC ACIDS PREPARED BY DEBROMINATION IN VARIOUS SOLVENTS

Debromination solvent	Yield, %	I. V.	Tb. N.	% Purity by I. V.[a]	% Purity by Tb. N.[b]	Isomeric acid, %[c]	M. p., °C.
Methyl alcohol	50	167.8	52.5	85	51	34	....
Methyl alcohol	31	161.2	47.7	78	46	32	....
Methyl alcohol	40	161.5	40.7	78	39	39	....
Methyl alcohol	54	168.7	54.5	85	53	32	−17.2
Methyl alcohol	30	165.7	26.3	82	25	57	−20.2
Methyl alcohol	51	167.8	52.4	85	51	34	−20
Pyridine	49	173.5	21.3	91	21	70	− 2.0
Pyridine	38	172.2	31.1	90	30	60	− 2.0
Ethyl ether	70	169.0	44.6	87	43	44	−21.8
Ethyl ether	90	174.9	53.8	94	52	42	−19.8
Ethyl ether	85	174.6	54.1	94	53	41	−21.8
Ethyl ether	85	171.6	47.1	90	46	44	−21.8
Ethyl ether	91	168.2	15.2	78	15	63	−19.0
Isopropyl ether	77	166.3	43.6	83	42	41	−22.2
Dioxane	94	174.1	47.7	94	46	48	−22.2
Acetic acid	68	89.8	0.0	..	..	..	+ 1.0

[a] Total octadecadienoic acid of I. V., 181.0. [b] Total linoleic acid (*cis*, *cis*-9,12-octadecadienoic) from Tb. N. [c] Octadecadienoic acids of I. V., 181.0 but of 0.0 Tb. N.

dized even at the low temperature employed in the oxidation.

Action of Wijs Solution on β-Linoleic Acid.—In some preliminary studies, we had available a number of concentrates of β-linoleic acid which had been prepared from the crude liquid tetrabromides of the unsaturated fatty acids of corn oil. The regenerated beta-acid in this instance was originally contaminated with variable amounts of oleic acid, but the latter had been largely removed by repeated crystallization. Also, there had been some separation of the constituents of the beta-acid by this crystallization. Two of these concentrates were treated with Wijs reagent for one, five and twenty-four hours. These and other analytical results follow:

Specimen	I. V. 1 hr.	I. V. 5 hrs.	I. V. 24 hrs.	Tb. N.	Diene no.	M. p., °C.
A	167.7	168.5	173.9	26.1	5.0	solid at −20
B	157.8	162.8	173.3	34.9	2.0	liquid at −20

A specimen of the alpha-acid under similar conditions increased in iodine number only 0.9. This increase in iodine number may be due to (a) conjugation, or (b) position of one double bond in relation to the carboxyl. The former would appear to be more important in Specimen A, and the latter in Specimen B.

Summary

α- and β-linoleic acids were prepared by debromination of solid and liquid tetrabromostearic acids, respectively, in methyl alcohol, pyridine, ether, isopropyl ether, dioxane and glacial acetic acid. Ether was shown to be the best solvent for the debromination reaction, although the other solvents tried, with the exception of acetic acid, were satisfactory. Yields of the beta-acid in ether were comparable to those obtained in methyl alcohol for the alpha-acid. The properties of the alpha- and beta-acids were compared and conclusions were drawn as to their chemical nature.

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