tive, it has been indicated that a substituent, either hindering or facilitating cleavage of the linkage between oxygen and the substituted phenyl group, is more effective in para position than in ortho position.

NOTRE DAME, INDIANA RECEIVED DECEMBER 24, 1936

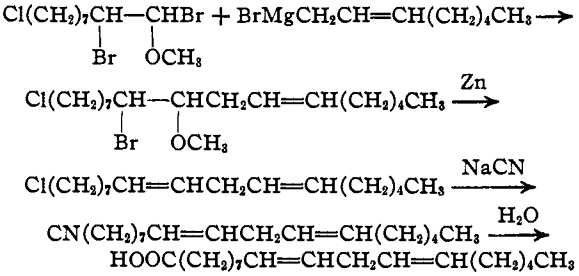
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

The Synthesis of Unsaturated Fatty Acids. II. Linoleic and 11-*n*-Amyl-9,12-tridecadienoic Acids

BY C. R. NOLLER AND M. D. GIRVIN

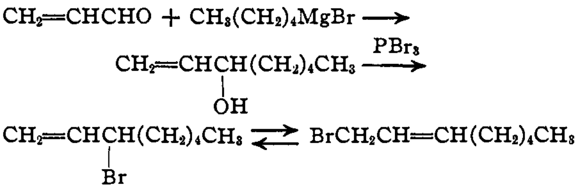
The synthesis of linoleic acid (9,12-octadecadienoic acid) is desirable not only because the commonly accepted structure is periodically questioned[1] but also because linoleic acid is apparently one of the accessory food factors, designated by Evans and his co-workers[2] as vitamin F, which is necessary for the growth and fertility of both male and female rats.

Using the following series of reactions which is similar to that previously used for the synthesis of oleic and elaidic acids[3] we have succeeded in synthesizing a product which contains α-linoleic acid.



$$\mathrm{Cl(CH_2)_7\underset{Br}{CH}-\underset{OCH_3}{CH}Br + BrMgCH_2CH{=}CH(CH_2)_4CH_3 \longrightarrow}$$
$$\mathrm{Cl(CH_2)_7\underset{Br}{CH}-\underset{OCH_3}{CH}CH_2CH{=}CH(CH_2)_4CH_3 \xrightarrow{Zn}}$$
$$\mathrm{Cl(CH_2)_7CH{=}CHCH_2CH{=}CH(CH_2)_4CH_3 \xrightarrow{NaCN}}$$
$$\mathrm{CN(CH_2)_7CH{=}CHCH_2CH{=}CH(CH_2)_4CH_3 \xrightarrow{H_2O}}$$
$$\mathrm{HOOC(CH_2)_7CH{=}CHCH_2CH{=}CH(CH_2)_4CH_3}$$

The 1-bromooctadecene-2 from which the Grignard reagent was prepared was obtained by the series of reactions



$$\mathrm{CH_2{=}CHCHO + CH_3(CH_2)_4MgBr \longrightarrow}$$
$$\mathrm{CH_2{=}CH\underset{OH}{CH}(CH_2)_4CH_3 \xrightarrow{PBr_3}}$$
$$\mathrm{CH_2{=}CH\underset{Br}{CH}(CH_2)_4CH_3 \rightleftarrows BrCH_2CH{=}CH(CH_2)_4CH_3}$$

It was realized at the outset that a mixture of 1-bromooctadecene-2 and 3-bromooctadecene-1 would result but the work of Winstein and Young[4] on analogous compounds indicated that the primary bromide would be formed in larger amount. Moreover, it was expected that the products arising from the secondary bromide would be the lower boiling and would be partially removed during the purification of the intermediate products of the synthesis.

The final product of the synthesis had the correct neutralization equivalent, iodine value, and molecular refraction for linoleic acid. Bromination of the product, however, gave none of the solid tetrabromide characteristic of α-linoleic acid. Since in the synthesis of oleic and elaidic acids[3] the equilibrium mixture of the two stereoisomers was obtained, it seemed unlikely that a mixture now had been obtained in which the geometrical isomer corresponding to α-linoleic acid was missing. Nevertheless a quantity of the synthetic material was elaidinized with Poutet's reagent[5] and the product again treated with bromine. Again no solid tetrabromide was obtained.

A portion of elaidinized product was next oxidized with permanganate according to the modified Hazura procedure used by Green and Hilditch[6] when a quantity of tetrahydroxystearic acids was obtained from which both α- and β-sativic acids were isolated. This proves definitely that α-linoleic acid was present. The amount of crude tetrahydroxy acids was about seven-tenths of that obtained from a sample of elaidinized natural α-linoleic acid and this would indicate that the amount of α-linoleic acid present in the synthetic mixture was of the order of 70%. The crude hydroxy acids from the synthetic product, however, were quite gummy and the total amount of once recrystallized product was only about 28% of that obtained from the natural product.

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[1] Takahashi, *J. Chem. Soc. Japan*, **42**, 130 (1921); *C. A.*, **15**, 2273 (1921); Haworth, *J. Chem. Soc.*, 1456 (1929); Nunn and Smedley-McLean, *Biochem. J.*, **29**, 2742 (1935).

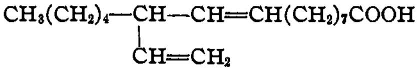
[2] Burr and Burr, *J. Biol. Chem.*, **82**, 345 (1929); **86**, 587 (1930); Burr, Burr and Miller, *ibid.*, **97**, 1 (1932); Evans and Lepkovsky, *ibid.*, **96**, 143 (1932); Evans, Lepkovsky and Murphy, **106**, 431, 441, 445 (1934).

[3] Noller and Bannerot, THIS JOURNAL, **56**, 1563 (1934).

[4] Winstein and Young, *ibid.*, **58**, 104 (1936).

[5] Griffiths and Hilditch, *J. Chem. Soc.*, 2315 (1932).

[6] Green and Hilditch, *Biochem. J.*, **29**, 1554 (1935).

The other constituent of the synthetic mixture is undoubtedly 11-*n*-amyl-9,12-tridecadienoic acid  $CH_3(CH_2)_4—CH(CH=CH_2)—CH=CH(CH_2)_7COOH$ arising from the 3-bromooctadecene-1. Ozonation gave an amount of formaldehyde corresponding to 16% of the calculated amount for this compound. Pure undecylenic acid, however, under the same conditions gave only 44% of the calculated amount of formaldehyde so that as high as 30% of the second isomer is indicated. It was noted that the synthetic product did not become viscous when exposed to air as readily as did α-linoleic acid and it is likely that a large amount of α-linoleic acid in the synthetic product was lost during the course of the numerous fractional distillations by which it was hoped to remove the lower boiling isomer.

The amount of synthetic material obtained during the course of this work was not sufficient for feeding experiments. Because of the numerous steps, poor yields and uncertainty concerning the exact composition of the product, it would seem desirable to develop a more satisfactory method of synthesis rather than attempt to produce synthetic linoleic acid in quantity by this method.

Experimental

_n_-Amylvinylcarbinol was prepared from *n*-amylmagnesium bromide and acrolein in 47–49% yields observing the precautions recommended by Bouis.[7] After two fractionations the main product boiled at 78–81° at 20 mm. This alcohol has been prepared previously by Levene and Walti[8] who give the boiling point as 81–82° at 20 mm. but give no details concerning the preparation.

1-Bromooctadecene-2 and 3-Bromooctadecene-1.—A mixture of these bromides was prepared from the above alcohol and phosphorus tribromide according to the procedure of Bouis.[7] The yield of product, b. p. 87–89° at 20 mm., was 79%; n^{23}D 1.4768; $d^{23}{}_4$ 1.1314.

Anal. Calcd. for $C_8H_{15}Br$: Br, 41.88. Found: Br, 41.70, 41.85.

Because of the high boiling point and the ease with which rearrangement takes place,[4] no attempt was made to separate the mixture into pure isomers. On rapid redistillation at 20 mm. the first 5 cc. of distillate showed n^{23}D 1.451 and the last 5 cc. n^{23}D 1.477. After long standing the equilibrium value was n^{23}D 1.472. Assuming the first and last fractions to be pure secondary and primary bromides, respectively, the equilibrium mixture would contain about 80% of the primary bromide.

1-Chloroheptadecadiene-8,11 and 1-Chloro-10-_n_-amyldodecadiene-8,11.—The mixed bromides were converted into the Grignard reagent in 75% yields, condensed with 8,9-dibromo-9-methoxynonyl chloride, and the bromine and methoxyl groups removed according to the procedure previously used for the synthesis of 1-chloroheptadecene-8.[3] None of the intermediate product was isolated in a pure state and the over-all yield based on the ω-chlorononylaldehyde was 12–15% boiling at 165–171° at 6 mm. after three fractional distillations; n^{24}D 1.4604; $d^{24}{}_4$ 0.8912; mol. ref. calcd., 84.6; found, 83.4.

Anal. Calcd. for $C_{17}H_{31}Cl$: Cl, 13.1; iodine no., 187.6. Found: Cl, 13.0; iodine no., 185.8.

A large amount of low boiling material was obtained which was not investigated.

1-Cyanoheptadecadiene-8,11 and 1-Cyano-10-_n_-amyldodecadiene-8,11.—To 12 g. of the mixed chlorodienes in 90 cc. of 95% alcohol was added 3 g. of sodium cyanide and the mixture refluxed for ninety-six hours. The sodium chloride was filtered from the solution and washed with alcohol, the alcohol distilled from the filtrates, and the residue fractionated under reduced pressure. There was obtained 7 g. (60.5%) b. p. 160–170° at 6 mm. Refractionation gave 5 g. (43%) of b. p. 165–170° at 6 mm.

Anal. Calcd. for $C_{18}H_{31}N$: N, 5.36; iodine no., 194.3. Found: N, 5.21; iodine no., 194.8.

9,12-Octadecadienoic and 11-_n_-Amyl-9,12-tridecadienoic Acids.—A solution of 7 g. of nitrile, 2 g. of sodium hydroxide in 10 cc. of water, and 90 cc. of 95% alcohol was refluxed for one hundred and twenty hours. The alcohol was distilled, the residue taken up in 200 cc. of water and extracted three times with petroleum ether. The aqueous solution was acidified and the acids extracted. The solvent was removed and the residue fractionated under reduced pressure. There was obtained 3 g. (40%); b. p. 200–205° at 6 mm. or 185–187° at 3 mm.; n^{27}D 1.4640; $d^{27}{}_4$ 0.8948; mol. ref. calcd. 85.9; found: 86.4.

Anal. Calcd. for $C_{17}H_{31}COOH$: neut. equiv., 280.2; iodine no., 180.8. Found: neut. equiv., 281.4; iodine no., 179.2.

The synthetic product after standing for several days at 10° deposited a small amount of solid which after filtration and recrystallization from petroleum ether melted at 59–61° and was saturated to bromine. It was thought that the prolonged heating with alkali may have converted some of the linoleic acid into palmitic or myristic acids, but mixed melting point determinations showed that the solid compound was not either. It was not investigated further.

Chemical Investigation of the Synthetic Product.—Bromination in petroleum ether under conditions that readily yielded the characteristic tetrabromide from natural α-linoleic acid[9] gave no solid bromide. The same results were obtained on samples of the synthetic and natural acids after isomerization with Poutet's reagent.[5]

Oxidation of 1.0 g. of isomerized natural α-linoleic acid by potassium permanganate according to the modified

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(7) Bouis, *Ann. chim.*, [10] **9**, 407 (1928).

(8) Levene and Walti, *J. Biol. Chem.*, **94**, 593 (1931).

(9) Natural α-linoleic acid used for comparison purposes was prepared from cottonseed oil through the tetrabromide (m. p. 114.5–115°) and the methyl ester by Rollett's procedure [*Z. physiol. Chem.*, **62**, 414 (1909)]. It was noted in another run where debromination of the tetrabromide was carried out in the absence of acid and without going through the methyl ester that the product solidified in the cold room at 10°. The highest melting point previously recorded for pure α-linoleic acid is −7° [Holde and Gentner, *Ber.*, **58**, 1067 (1925)] and we hope to investigate this product further.

Hazura procedure recommended by Hilditch[6] gave 0.57 g. of solid tetrahydroxystearic acids. Hilditch states that the tetrahydroxy acids were "separated by fractional crystallization from ethyl acetate." We used absolute ethyl acetate and found that the lower melting acid could be extracted and recrystallized from this solvent but that the higher melting acid was too insoluble to be recrystallized from it. After extraction of the lower melting acid with absolute ethyl acetate, the higher melting acid was recrystallized from 95% alcohol. There was obtained in this way 0.28 g. of tetrahydroxystearic acid, m. p. 156–157° and 0.07 g., m. p. 172–175°. When 1.0 g. of the synthetic acid was treated in exactly the same way there was obtained 0.40 g. of a sticky product from which was isolated only 0.08 g. of m. p. 151–154° and 0.02 g., m. p. 174–175°. Mixed melting points with the corresponding acids from natural α-linoleic acid were 152–155° and 173–175°.

A solution of 1.536 g. (0.00548 mole) of synthetic acids in 20 cc. of absolute ethyl acetate was ozonized and the solution decomposed with zinc dust and water according to the procedure of Whitmore and Church[10] without removal of the solvent. After distillation and extraction of the aqueous layer with ethyl acetate the formaldehyde was estimated iodimetrically.[11] A blank run was made in which 20 cc. of ethyl acetate was ozonized for the same length of time and decomposed in the same manner as the sample. The amount of formaldehyde from the sample, corrected by the blank, was 0.000883 mole, indicating the presence of 16% of 11-*n*-amyl-9,12-tridecadienoic acid. Pure undecylenic acid, however, gave only 44% of the calculated amount of formaldehyde under the same conditions. The water–zinc dust decomposition of the ozonides does not seem to be very satisfactory for compounds giving water insoluble products since the latter tend to coat the zinc dust and cause it to agglomerate.

The formaldehyde was identified positively by conversion into the 2,4-dinitrophenylhydrazone which after four crystallizations from methyl alcohol melted at 158–162°. The mixed melting point with pure formaldehyde-2,4-dinitrophenylhydrazone (m. p. 166–167°) was 159–163°.

An attempt to isolate the *n*-hexoic and *n*-heptoic acids which also should be formed on ozonation of the synthetic product gave a small amount of mixed acids distilling at 200–260° but conversion to the anilides gave an oil which could not be made to crystallize.

Summary

A series of reactions has been carried out which led to the synthesis of a mixture of linoleic acid and 11-*n*-amyl-9,12-tridecadienoic acid.

STANFORD UNIVERSITY, CALIF.

RECEIVED FEBRUARY 1, 1937

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[10] Whitmore and Church, THIS JOURNAL, **54**, 3712 (1932).

[11] Feinberg, *Am. Chem. J.*, **49**, 89 (1913).

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Studies of Absorption Spectra. I. Crotonaldehyde and Acrolein

BY FRANCIS E. BLACET, WILLIAM G. YOUNG AND JACK G. ROOF

In connection with problems in photochemistry and in the synthesis of pure stereoisomeric compounds, a quantitative study of the absorption spectra of crotonaldehyde and acrolein in the vapor phase has been made. The object of this investigation was (1) to determine the types of absorption in different regions of the spectrum, (2) to compare the absorption of these two closely related compounds, and (3) in the case of crotonaldehyde, to test by spectroscopic means for the presence of *cis*-crotonaldehyde in the purified commercial product.

Although a number of investigators have studied these compounds,[1] the work for the most part was done with solutions in which the band structure of absorption, as shown by the vapors, was not observed. However, two exceptions to this generalization should be mentioned. Lüthy[1c] reported the fine structure but did not attempt to calculate extinction coefficients from studies of the vapor phase. Eastwood and Snow[1h] also have done nothing with extinction coefficients, but by means of a 21-foot (6.3 meter) grating have shown that some of the prominent maxima of acrolein may be resolved into very narrow bands which they attribute to rotational levels in the molecule.

Experimental Part

Purification and Treatment of Samples.—In an attempt to detect the presence of *cis*-crotonaldehyde in the purified commercial product, samples were prepared in two different ways and their absorption spectra studied. The first of these, which is hereafter called the "original" sample, was made in such a way that any mixture of the *cis* and *trans* forms would be preserved. The second or "irradiated" sample was treated with hydrochloric acid and sunlight by a procedure which is known to cause similar compounds to be converted into the *trans* form.[2]

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[1] (a) Bielecki and Henri, *Ber.*, **46**, 3627 (1913); (b) Purvis and McClelland, *J. Chem. Soc.*, **103**, 433 (1913); (c) Lüthy, *Z. physik. Chem.*, **107**, 284 (1923); (d) Henri, *Compt. rend.*, **178**, 844 (1924); (e) Purvis, *J. Chem. Soc.*, **127**, 9 (1925); (f) Henri, *Compt. rend.*, **199**, 849–851 (1934); (g) Thompson and Linnett, *Nature*, **134**, 937 (1934); (h) Eastwood and Snow, *Proc. Roy. Soc.* (London), **A149**, 446 (1935).

[2] (a) Wislicenus, *Ann.*, **248**, 341 (1889); (b) Blaise, *Ann. chim. phys.*, [8] **11**, 116 (1907).