Synthesis of *cis* 9, 15-, 8, 15-, and 7, 15-Octadecadienoic Acid[1]

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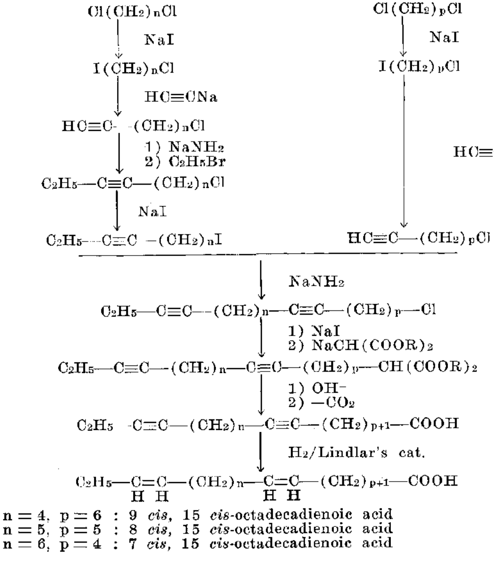
Abstract

In connection with the study of autoxidation of some *iso*-linoleic acids, the 9,15-, 8,15-, and 7,15-octadecadienoic acids have been synthesized by partial hydrogenation of the corresponding diynoic acids. These acids were prepared by coupling ω-iodo-3-alkynes with ω-chloro-1-alkynes by means of sodium amide in liquid ammonia to form ω-chlorohexadiynes, followed by condensation of the corresponding iodine compounds with sodium malonic ester.

Introduction

During the hydrogenation of linolenic acid-containing oils, such as linseed and soybean oil, *iso*-linoleic acids are formed. Autoxidation of some of these acids results in the formation of 6-nonenal, which is the substance responsible for the typical hardening flavor (1). Especially 9,15-octadecadienoic but also 8,15-octadecadienoic acid are regarded as precursors of 6-nonenal. Theoretically it is not to be expected that 6-nonenal is produced from 7,15-octadecadienoic acid by autoxidation (2). To confirm these assumptions, sufficient amounts of pure 9,15-, 8,15-, and 7,15-octadecadienoic acid were required. Their natural occurrence is not very frequent. De Jong and Van der Wel (3) could detect them in milk fat but only in extremely low concentrations. Little has been reported in the literature about the preparation of these dienoic acids however. Some investigators (4–7) have isolated the 9,15-octadecadienoic acid from a fatty acid mixture which was obtained by reduction of linolenic acid with hydrazine. The amounts were small, and only one of the dienoic acids could be obtained by this method.

A convenient route can now be described for the synthesis of all the three acids via the corresponding diynoic acids, according to the following scheme:



$n = 4,\ p = 6$: 9 *cis*, 15 *cis*-octadecadienoic acid
$n = 5,\ p = 5$: 8 *cis*, 15 *cis*-octadecadienoic acid
$n = 6,\ p = 4$: 7 *cis*, 15 *cis*-octadecadienoic acid

Experimental Section

Synthesis of ω-Chloro-1-Alkynes

Dichloroalkanes were converted into the chloro-iodo compounds by refluxing with NaI in acetone according to the method of Ahmad et al. (8). These compounds gave ω-chloro-1-alkynes by reacting with sodium acetylide in liquid ammonia, as described by Newman and Wotiz (9). The following compounds were obtained:

1-chloro-5-hexyne, found: bp 68–69C/53 mm; n_D^{25} 1.4485; lit. (10): bp 47–48C/17 mm; n_D^{25} 1.4480.

1-chloro-6-heptyne, found: bp 60–61C/13.5 mm; n_D^{25} 1.4514 (corr.); lit. (9): bp 166C/1 atm.; n_D^{25} 1.4507.

1-chloro-7-octyne, found: bp 65–67C/7 mm; n_D^{20} 1.4547 (corr.); lit. (11): bp 69–70C/10 mm; n_D^{20} 1.4534–1.4542.

Synthesis of ω-Iodo-3-Alkynes

1-Iodo-5-Octyne. The sodium compound of 1-chloro-5-hexyne, obtained with the aid of sodium amide in liquid ammonia, was coupled according to Newman and Wotiz (9) with ethyl bromide to form 1-chloro-5-octyne (bp 74C/12 mm; n_D^{20} 1.4580; yield 66%; lit. (12): bp 188C/740 mm; n_D^{25} 1.4590). This compound was converted into 1-iodo-5-octyne (bp 104.5C/105 mm; n_D^{25} 1.5196 (corr.); yield 88.4%) by refluxing with an excess of NaI in acetone for 20 hr (9).

1-Iodo-6-Nonyne. In a similar way 1-chloro-6-heptyne was converted into 1-chloro-6-nonyne (bp 80–83C/8 mm; n_D^{25} 1.4596 (corr.); yield 64.5%), which gave 1-iodo-6-nonyne (bp 110–112C/8 mm; n_D^{20} 1.5166 (corr.); yield 90.4%) with NaI in acetone.

1-Iodo-7-Decyne. Similarly 1-chloro-7-octyne was converted into 1-chloro-7-decyne (bp 108–110C/13 mm; n_D^{25} 1.4609; yield 65%), which gave 1-iodo-7-decyne (bp 71–74C/0.5 mm; n_D^{20} 1.5134 (corr.); yield 69.3%) with NaI in acetone.

Coupling of ω-Chloro-1-Alkyne with ω-Iodo-3-Alkyne

1-Iodo-7,13-Hexadecadiyne. To a suspension of sodium amide, prepared from 15.0 g (0.65 mole) of sodium in one liter of liquid ammonia with $Fe(NO_3)_3 \cdot 9\ H_2O$ (1.5 g) as catalyst, a solution of 93.9 g (0.65 mole) of 1-chloro-7-octyne in 150 ml of dry ether was added in 30 min with stirring. After stirring was continued for another hour at −35C, a solution of 152.4 g (0.65 mole) of 1-iodo-5-octyne in 150 ml of dry ether was added.[3] Stirring was continued for 5 hr at −35C under reflux, then the ammonia was allowed to evaporate overnight. To the residue, one liter of water was added; the water layer was separated and extracted three times with ether. The combined ether layers were washed with water and subsequently dried over $MgSO_4$. After

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[3] More than the usual amount of liquid ammonia and addition of dry ether was necessary to keep the organic components in suspension and/or in solution.

evaporation of the ether, 88 g (53.6%) of 1-chloro-7,13-hexadecadiyne (bp 134–136C/0.5 mm; n_D^{25} 1.4816; IR spectrum: bands at 660 cm^{-1} [$-CH_2Cl$] and 1320 cm^{-1} [$-CH_2-C\equiv C-$], no terminal triple bond could be detected) were isolated from the mixture by fractionated distillation. The compound was converted into 1-iodo-7,13-hexadecadiyne (bp 143–146C/0.6 mm; n_D^{20} 1.5120 (corr.); yield 75.4%) by refluxing with 100% excess of NaI in acetone for 20 hr (9).

1-Iodo-6,13-Hexadecadiyne. To a suspension of sodium amide, prepared from 14.6 g (0.635 mole) of sodium and 1.5 g of $Fe(NO_3)_3 \cdot 9H_2O$ in one liter of liquid ammonia, a solution of 1-chloro-6-heptyne (82.9 g; 0.635 mole) in dry ether (150 ml) was added in 30 min with stirring. After another 60 min of stirring, a solution of 1-iodo-6-nonyne (158.8 g; 0.635 mole) in dry ether (150 ml) was added.

After stirring was continued for 5 hr, the product was worked up in the way as described above. Fractionated distillation yielded 88.3 g (55.1%) of 1-chloro-6,13-hexadecadiyne (bp 131–133C/0.4 mm; n_D^{25} 1.4806 (corr.), which was converted into 1-iodo-6,13-hexadecadiyne (bp 146–150C/0.5 mm; n_D^{25} 1.5102 (corr.); yield 78.2%) with an excess of NaI in acetone.

1-Iodo-5,13-Hexadecadiyne. To a suspension of sodium amide, prepared from 12.5 g (0.54 mole) of sodium and 1.5 g of $Fe(NO_3)_3 \cdot 9\ H_2O$ in one liter of liquid ammonia, a solution of 1-chloro-5-hexyne (62.9 g; 0.54 mole) in dry ether (150 ml) was added. After stirring was continued for another 60 min, a solution of 1-iodo-7-decyne (142.6 g; 0.54 mole) in dry ether (150 ml) was added. The purified 1-chloro-5,13-hexadecadiyne (bp 142–144C/0.7 mm; n_D^{25} 1.4820 (corr.); yield 68.3 g, 50.1%) was converted into 1-iodo-5,13-hexadecadiyne (bp 143–146C/0.6 mm; n_D^{25} 1.5087 (corr.); yield 75.6%).

Condensation of ω-Iodohexadecadiynes with Sodium Malonic Ester

9,15-Octadecadiynoic Acid. The diynoic acid was prepared by the method of Raphael and Sondheimer (13). The 1-iodo-7,13-hexadecadiyne (86 g; 0.25 mole) was heated under reflux with a previously prepared solution of sodium (15.2 g; 0.66 mole) and ethyl malonate (110 g; 0.69 mole) in one liter of absolute EtOH for 16 hr. After saponification with an excess of KOH at room temperature for 48 hr, the solution was acidified and the hexadecadiynyl malonic acid which was formed was subsequently decarboxylated at 150–170C. The product (62 g) which was obtained after distillation was recrystallized from 20 parts of light petroleum (bp 40–60C) at −20C, then from 40 parts at −40C. Yield 43.2 g (62.2%); mp 52.7C (corr.); n_D^{65} 1.4626; NV (neutralization value), calc. 203.3; found: 203.6; purity (GLC) ca. 100%.

Analysis: calc.: C, 78.25; H, 10.15; found: C, 78.1; H, 10.2. IR spectrum: bands at 1320 cm^{-1} ($-CH_2-C\equiv C-$) and 1700 cm^{-1} ($-COOH$). NMR spectrum: triplet at δ 1.1 (3 methyl protons); methylene envelope δ 1.2–1.8 (14 protons); and multiplet δ 1.8–2.5 (10 protons next to isolated carbon-carbon triple bond and to carboxyl group).

The typical sharp triplet at the characteristic δ value (1.10) indicates the presence of the fragment $CH_3-CH_2-C\equiv C-$. Although it is impossible to locate exactly the second triple bond in the chain, this bond is not conjugated with the first triple bond or the carboxyl group, nor is it separated from this bond or group by only one methylene group (14).

8,15-Octadecadiynoic Acid. In an analogous way 8,15-octadecadiynoic acid (41 g; 68.7%) was prepared from 1-iodo-6,13-hexadecadiyne (75.6 g; 0.22 mole) and a solution of sodium (13.3 g; 0.58 mole) and ethyl malonate (97.5 g; 0.61 mole) in absolute EtOH (900 ml). The IR and NMR spectra were in agreement with the proposed structure. Mp 42.2C (corr.); n_D^{65} 1.4625; NV, calc.: 203:3; found: 203.7; purity (GLC) > 99%. Analysis: calc.: C, 78.25; H, 10.15; found: C, 78.0; H, 10.1.

7,15-Octadecadiynoic Acid. Similarly 7,15-octadecadiynoic acid (34 g; 63.2%) was prepared from 1-iodo-5,13-hexadecadiyne (67.1 g; 0.195 mole) and a solution of sodium (11.8 g; 0.51 mole) and ethyl malonate (85.5 g; 0.535 mole) in absolute EtOH (800 ml). The IR and NMR spectra were in agreement with the proposed structure. Mp 51.3C (corr.); n_D^{65} 1.4625; NV, calc.: 203:3; found: 204.3; purity (GLC) about 100%. Analysis: calc.: C, 78.25; H, 10.15; found: C, 78.1; H, 9.9.

Partial Hydrogenation of Octadecadiynoic Acids

9,15-Octadecadienoic Acid. A mixture of EtOH (10 ml), quinoline (0.35 g), and Lindlar's catalyst (3.5 g), was stirred in a hydrogen atmosphere till no further hydrogen was taken up (15). Subsequently 9,15-octadecadiynoic acid (7 g), dissolved in 25 ml of EtOH, was added, and stirring under hydrogen was then continued. The absorption of hydrogen ceased after an uptake of 1344 ml (calc.: 1368 ml) of hydrogen. The catalyst was filtered off; ether and water were added to the filtrate, and the ether layer was washed with dilute sulfuric acid to remove the quinoline. Yield 6.7 g (94.4%); purity (GLC) ca. 99% (impurity mainly monoenoic acid); n_D^{20} 1.4691; n_D^{65} 1.4530; NV, calc.: 200.3; found: 200.0; IV, calc.: 181.3; found: 181.5. Analysis: calc.: C, 77.14; H, 11.43; found: C, 77.1; H, 11.5. The presence of the double bond at the 9th and 15th position could be confirmed by oxidative degradation by means of osmium tetroxide (3,16).

IR spectrum: bands at ca. 700 and 1650 cm^{-1} ($-CH=CH-$), 1700 cm^{-1} ($-COOH$), and 3020 cm^{-1} ($-CH=$); *trans* content $< 0.5\%$. NMR spectrum: triplet at δ 0.95 (3 methyl protons); methylene envelope δ 1.2–1.7 (14 protons); multiplets δ 1.7–2.5 (10 protons next to isolated carbon-carbon double bond and to carboxyl group) and δ 5.3 (4 olefinic protons).

The typical sharp triplet at the characteristic δ value (0.95) indicates the presence of the fragment $CH_3-CH_2-CH=CH-$. Although it is impossible to locate exactly the second double bond in the chain, this bond is not conjugated with the first double bond or the carboxyl group nor is it separated from this bond or group by only one methylene group (14).

8,15-Octadecadienoic Acid. In the same way 8,15-octadecadiynoic acid (7 g) was converted into 8,15-octadecadienoic acid by partial hydrogenation. Hydrogen uptake: 1360 ml (calc.: 1366 ml). Yield 6.8 g (95.8%); purity (GLC) > 98%; the IR and NMR spectra were in agreement with the proposed structure, *trans* content $< 0.5\%$; n_D^{20} 1.4691; n_D^{65} 1.4531; NV, cal.: 200.3; found: 200.6; IV, calc.: 181.3; found: 180.1. Analysis: calc.; C, 77.14; H, 11.43; found: C, 77.1; H, 11.5. The position of the double bonds was confirmed by oxidative degradation by means of osmium tetroxide.

7,15-Octadecadienoic Acid. By the same method 7,15-octadecadiynoic acid (7 g) was converted into 7,15-octadecadienoic acid by partial hydrogenation. Hydrogen uptake: 1346 ml (calc.: 1356 ml); yield 6.7 g (94.4%); purity (GLC) ca. 98%; the IR and NMR spectra were in agreement with the proposed structure; only traces of *trans* isomers were present. n_D^{20} 1.4690; n_D^{65} 1.4529; NV, calc.: 200.3; found: 200.9; IV, calc.: 181.3; found: 180.3. Analysis: calc.: C, 77.14; H, 11.43; found: C, 77.1; H, 11.7. The position of the double bonds was confirmed by oxidative degradation with osmium tetroxide.

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