Synthesis of 11*cis*, 15*cis*- and 10*cis*, 15*cis*-Octadecadienoic Acid, the Probable Precursors of 4*cis*-Heptenal in Autoxidized Butterfat

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Abstract

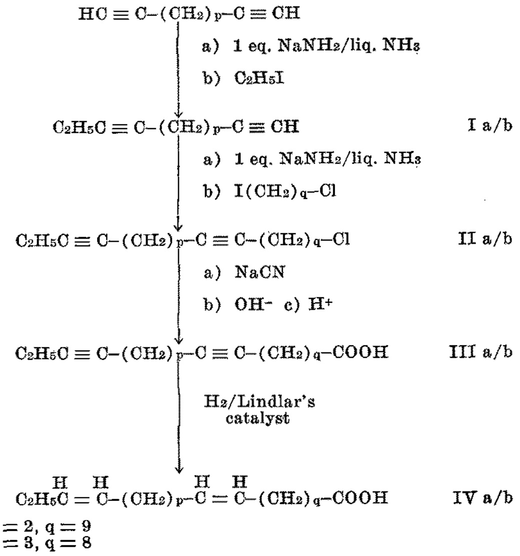
11*cis*,15*cis*- and 10*cis*,15*cis*-Octadecadienoic acid are considered to be precursors of 4*cis*-heptenal occurring in autoxidized butterfat. The synthesis of these acids was carried out as follows. In liquid ammonia, 1-sodio-1,5-octadiyne was coupled with 1-chloro-9-iodononane and 1-sodio-1,6-nonadiyne with 1-chloro-8-iodooctane. The 1-chloro-10,14- and -9,14-heptadecadiynes thus obtained were converted into 11,15- and 10,15-octadecadiynoic acid. Stereospecific partial hydrogenation of the 11,15-diynoic acid, or of the methyl 10,15-diynoate, and subsequent saponification, yielded the acids desired.

Introduction

During the isolation and identification of cream flavor, it was demonstrated (1) that the substance responsible for this flavor is identical with 4*cis*-heptenal. Its concentration in autoxidized butterfat, from which it was obtained, was estimated to 1.5 × 10^{-3} mg/kg. In the non-conjugatable *cis,cis*-isolinoleic acid fraction of butterfat (ca. 20 mg/kg) the presence of 11,15- and 10,15-octadecadienoic acid was confirmed (2–4). The latter acids were considered to be precursors of 4*cis*-heptenal, according to Farmer's oxidation theory (see ref. 5 for a survey). In this paper we describe the synthesis of these acids, which on standing indeed developed a faint cream flavor.

Methods and Results

For the preparation, synthesis of the corresponding octadecadiynoic acids, followed by stereospecific partial hydrogenation was chosen. Working analogous to the method described for all-*cis*-9,15-, -8,15- and -7,15-octadecadienoic acid (6), would involve coupling of 1-bromo-3-hexyne (1-bromo-4-heptyne) with 11-chloro-1-sodio-1-undecyne (10-chloro-1-sodio-1-decyne). These reactions are considered to be either unsuccessful or not to lead to high yields (cf. refs. 7,8). Therefore, alkylation of 1,5-hexadiyne (1,6-heptadiyne) first with ethyl iodide and then with 1-chloro-9-iodononane (1-chloro-8-iodooctane), followed by conversion into carboxylic acid was used. The alkadiynes were prepared by known procedures (9,10).



Using this scheme, 11*cis*,15*cis*-octadecadienoic acid (IVa) and 10*cis*,15*cis*-octadecadienoic acid (IVb) were obtained in 15% and 8.5% overall yield respectively.

Experimental Procedures

All temperatures are uncorrected. The melting points were determined with a Büchi apparatus. The IR spectra were recorded on a Unicam SP 100 spectrometer, the mass spectra on an AE1-MS 9 mass spectrometer and the NMR spectra (60 MHz) on a Varian A 60 NMR spectrometer. Samples dissolved in CCl_4 or $CDCl_3$ were used for the latter recordings. First-order chemical shifts (δ-values) are quoted in ppm relative to internal tetramethylsilane; they are assigned to the type of protons mentioned. The ratios of integrated peaks are given in parentheses. Where necessary, commercially available chemicals were dried and purified by standard methods; purified nitrogen was used as cover gas.

Alkadiynes (I)

1,5-Octadiyne (Ia). Ia was prepared by coupling 0.53 mole ethyl iodide with 1-sodio-1,5-hexadiyne, prepared from 0.46 mole $NaNH_2$ and 0.44 mole 1,5-hexadiyne (9) in 500 ml liquid NH_3/70 ml diethyl ether. Yield 46%, bp 50–55 C/22 mm; n_D^{15} 1.4580, n_D^{25} 1.4530 (bp 45–47 C/21 mm; n_D^{15} 1.4580; ref. 11); purity (GLC) 98%.

IR spectrum: bands at 3310 and 2135 cm^{-1} ($HC \equiv C-$), 1325 cm^{-1} ($-C \equiv C-CH_2-$), 1381 and 2935 cm^{-1} (CH_3-), and 785 cm^{-1} (C_2H_5-).

NMR spectrum:

distorted triplet at δ 1.09 ($J = 7$ Hz) (3) ($-CH_3$)

$$\left.\begin{array}{l}\text{complex at } \delta\ 1.89\\ \text{complex at ca. } \delta\ 2.1\\ \text{complex at } \delta\ 2.3\end{array}\right\}\ (7)\ \left\{\begin{array}{l}(HC \equiv C-)\\ (-CH_2-C \equiv C-)\\ (-C \equiv C-CH_2-CH_2-C \equiv C-)\end{array}\right.$$

1,6-Nonadiyne (Ib). Ib was obtained analogously from 0.49 mole ethyl iodide and 1-sodio-1,6-heptadiyne, prepared from 0.49 mole $NaNH_2$ and 0.45 mole 1,6-heptadiyne (10). Yield 56%, bp 64 C/17 mm; n_D^{15} 1.4595; purity (GLC) 86%.

IR spectrum: bands at 3310 and 2130 cm^{-1} ($HC \equiv C-$), 1325 cm^{-1} ($-C \equiv C-CH_2-$), 1381 and 1438 cm^{-1} (CH_3-), and 785 cm^{-1} (C_2H_5-). Moreover, bands at 918, 998, 1645 and 3080 cm^{-1} ($H_2C = CH-$).

1-Chloro-heptadecadiynes (II)

1,Chloro-10,14-heptadecadiyne (IIa). To a suspension of $NaNH_2$, prepared from 5.1 g (0.22 mole) sodium in 700 ml liquid NH_3 with $Fe(NO_3)_3 \cdot 9H_2O$

as catalyst, 22.6 g (0.21 mole) Ia was added in 35 min and the mixture stirred for another 60 min. Subsequently, 55 g (0.19 mole) 1-chloro-9-iodononane (12), bp 95–102.5 C/0.09 mm; n_D^{25} 1.5080 (lit. n_D^{25} 1.5074; ref. 13) was added dropwise in 4 hr. After stirring for 2.5 hr, the mixture was kept overnight in a Dewar vessel at −70 C and the next day stirred for another 2.5 hr. The NH_3 was evaporated on a waterbath, 150 ml water was added and the mixture extracted with ether (4 × 150 ml). The combined ether layers were washed with 1 N H_2SO_4, and with water until acid-free, dried over Na_2SO_4 and evaporated. Distillation of the residue yielded 25.6 g (50%) IIa bp 130 C/0.11 mm; n_D^{25} 1.4813.

1-Chloro-9,14-heptadecadiyne (IIb). In the same way as above, IIb was prepared by coupling the 1-sodio derivative of 30 g (0.25 mole) Ib with 68.6 g (0.25 mole) 1-chloro-8-iodooctane (12), bp 82–85 C/0.08 mm; n_D^{25} 1.5114 (lit. n_D^{25} 1.5113; ref. 13) in 400 ml liquid NH_3. Yield 37.5 g (56%) IIb; bp ca. 120 C/0.05 mm; n_D^{25} 1.4795.

Octadecadiynoic Acids (III)

11,15-Octadecadiynoic Acid (IIIa). Five grams (0.02 mole) IIa was converted into its nitrile by adding it in 5 min to a heated (95 C) suspension of 1.3 g (0.03 mole) NaCN in 6.6 ml dimethyl sulfoxide, raising the temperature to 150 C and maintaining it for 15 min (14,15). After cooling, the mixture was poured into 100 ml water, extracted with ether (4 × 50 ml) and the combined ether layers were evaporated. The residue (5.0 g)—dissolved in 70 ml 0.47 N 80% ethanolic NaOH—was boiled under reflux for 24 hr and subsequently poured into 200 ml water. After extraction with ether (2 × 100 ml) to remove undesired by-products the water layer was acidified with 4 N H_2SO_4 and again extracted with ether (4 × 100 ml). This ether extract was washed with water until acid-free, dried over Na_2SO_4 and evaporated. The residue, dissolved in light petroleum and decolored by treating with active carbon, was finally crystallized from light petroleum at −5 C to −15 C.

Yield 3.3 g (64%) IIIa; mp 76–77.1 C. Found: C, 78.0; H, 10.1. Calculated for $C_{18}H_{28}O_2$ (M = 276.40): C, 78.2; H, 10.2.

NMR spectrum:

$$\left.\begin{array}{l}\text{distorted triplet at } \delta\ 1.09\ (J = 7\ \text{Hz})\\ \text{complex at } \delta\ 1.3\end{array}\right\}\ (17)\ \left\{\begin{array}{l}(CH_3-)\\ (-CH_2-)\end{array}\right.$$
complex at δ 1.8–2.6 (10) ($-CH_2-C\equiv C-$ and $-CH_2-COO-$)
singlet (1) ($-COOH$)

A sample was esterified with diazomethane in ether and completely hydrogenated over Adams' catalyst; methyl stearate content (GLC) >99%.

10,15-Octadecadiynoic Acid (IIIb). In the same way as described above 10.7 g (0.04 mole) IIb was converted into 7.1 g (65%) IIIb mp 48–49 C.

Found: C, 78.1; H, 10.3. Calculated for $C_{18}H_{28}O_2$ (M = 276.40): C, 78.2; H, 10.2.

NMR spectrum:

$$\left.\begin{array}{l}\text{distorted triplet at } \delta\ 1.09\ (J = 7\ \text{Hz})\\ \text{complex at } \delta\ 1.12\text{–}1.86\end{array}\right\}\ (17)\ \left\{\begin{array}{l}(CH_3-)\\ (-CH_2-)\end{array}\right.$$
complex at δ 1.86–2.8 (10) ($-CH_2-C\equiv C-$ and $-CH_2-COO-$)
singlet (1) ($-COOH$)

Cis,cis-Octadecadienoic Acids (IV)

11cis,15cis-Octadecadienoic Acid (IVa). A solution of 1.274 g (0.005 mole) IIIa and 0.3 g quinoline in 40 ml light petroleum was hydrogenated in the presence of 0.5 g Lindlar's catalyst (16,17). H_2-Uptake: 211 ml (0 C, 760 mm Hg; calc.: 207 ml). After removal of the catalyst by filtration and quinoline by extraction with 1 N HCl (2 × 10 ml), the light petroleum was washed acid-free with water, dried over Na_2SO_4 and evaporated. Yield: 1.29 g oil (~ 100%), mp ca. 11 C; n_D^{25} 1.4672; purity (GLC of methyl ester) >98%.

IR spectrum: bands at 720 and 3010 cm^{-1} ($-\overset{H}{C}=\overset{H}{C}-$), 1717 cm^{-1} (–COOH); content of trans isomer <2%.

Mass spectrum: parent peak (molecule ion) at m/e 280 (calc. 280).

NMR spectrum:

distorted triplet at δ 0.95 (J = 7 Hz) (3) (CH_3-)
singlet at δ 1.30 (14) ($-CH_2-$)
complex at δ 1.83–2.5 (10) ($-CH_2-\overset{|}{C}=\overset{|}{C}-$ and $-CH_2-COO-$)
complex at δ 5.25 (4) ($-\overset{H}{C}=$)
singlet (1) ($-COOH$)

The double bonds were located as follows (3): The methyl ester was treated with OsO_4 (less than 0.4 mole per mole of ester). Subsequently, hydrogenation with PtO_2 as catalyst, followed by hydrolysis of the osmate ester and cleavage with HIO_4 of the resulting diol mixture, yielded a mixture of heptanal, propanal (trace), and almost equal amounts of methyl 11-oxoundecanoate and 15-oxopentadecanoate. This means that the double bonds are at the 11- and 15-position.

10cis,15cis-Octadecadienoic Acid (IVb). An amount of 6.4 g (0.02 mole) IIIb was esterified with a solution of diazomethane in ether and distilled to give 5.0 g (74%) methyl-10,15-octadecadiynoate. An amount of 2.78 g (0.01 mole) of this ester and 0.25 g quinoline were dissolved in 25 ml of light petroleum and subsequently hydrogenated in the presence of 0.22 g of Lindlar's catalyst. H_2-Uptake: 425 ml (0 C, 760 mm Hg; calc. 430 ml). After working up, 2.57 g (91%) methyl-10*cis*,15*cis*-octadecadienoate was obtained. An amount of 1.57 g was saponified by boiling for 30 min with 25 ml 0.25 N ethanolic KOH. After cooling, the mixture was acidified and worked up as usual to give 0.925 g IVb (62%; 42% calc. on IIIb) n_D^{25} 1.4685; purity (GLC of methyl ester) >97%.

IR spectrum, methyl ester: bands at 720 and 3010 cm^{-1} ($-\overset{H}{C}=\overset{H}{C}-$) and 1745 cm^{-1} ($-COOCH_3$); content of trans isomers <2%.

Mass spectrum, methyl ester: parent peak (molecule ion) at m/e 294 (calc. 294).

NMR spectrum, methyl ester:

distorted triplet at δ 0.96 (J = 7 Hz) (3) (CH_3-)
complex at δ 1.12–1.73 (14) ($-CH_2-$)
complex at δ 1.73–2.4 (10) ($-CH_2-\overset{|}{C}=\overset{|}{C}-$) and $-CH_2-COO-$)
singlet at δ 3.55 (3) ($-COOCH_3$)
complex at δ 5.23 (J = 4.5 Hz) (4) ($-\overset{H}{C}=$)

In order to locate the double bonds, *IVb*, methyl ester, was treated as described for *IVa*, methyl ester. The result was a mixture of octanal, propanal (trace), and almost equal amounts of methyl 10-oxodecanoate and 15-oxopentadecanoate, which means that the double bonds are at the 10- and 15-position.

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