Isolation of 11-cyclohexylundecanoic acid from butter

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SUMMARY After fractionation using fractional distillation, recrystallization, urea treatment hydrogenation, and repeated urea treatment, a hitherto unknown acid has been isolated from butter fatty acid methyl esters. Gas–liquid chromatography followed by mass and infrared spectroscopy showed that the acid is saturated and it contains 17 carbon atoms and a terminal cyclohexyl group.

Synthetic 11-cyclohexylundecanoic acid appeared to be identical with the isolated acid.

Butter contains at least 0.01% of this acid.

KEY WORDS butter · 11-cyclohexylundecanoic acid · isolation · carbon numbers

UNTIL 1940 ONLY A LIMITED NUMBER of saturated and unsaturated, even-numbered straight-chain fatty acids were known to occur in butterfat. Since then many more unsaturated acids, as well as odd-numbered and branched-chain acids have been identified. The present knowledge in this field has been reviewed by Garton (1).

In the course of our investigation into the composition of butter fatty acids we have isolated a fatty acid whose unusual structure has now been elucidated.

METHODS

An amount of 1070 g of dry butterfat was heated to 80° and added to a boiling solution of 3.2 g of Na in 240 ml of methanol. The mixture was boiled for 2 hr and the glycerol layer was removed. The ester layer was washed three times with water at 60°, dried over $MgSO_4$, and subsequently distilled as rapidly as possible at 0.16 mm. The yield was 780 g of methyl ester.

The methyl ester was roughly fractionated at 10^{-6} mm and 70–85°, using the vacuum system as described by De Bruyn and Schogt (2). Four fractions were obtained. The last fraction (410 g), which contained only traces of fatty acid esters with chain length shorter than 16, was recrystallized from 500 ml of acetone at $-40°$. By cooling the mother liquor (containing 150 g of esters) to $-60°$, 113 g of crystals was obtained, 37 g of material remaining in the mother liquor. The mother liquor was treated with 655 ml of methanol and 148 g of urea. After being kept at room temperature overnight 15 g of non-adduct could then be isolated (fraction A).

An additional fractionation was achieved by passing part of fraction A over a column of silicic acid impregnated with silver nitrate (3). In this way acids with three or more double bonds were removed. The remaining mixture (fraction B) was subjected to GLC on the polar immobile phase PEGA (Fig. 1*a*). The peaks with C-numbers (4) 18.3 and 19.7 were assumed to be attributable to methyl oleate and linoleate respectively. The C-number 18.65 was not that of any fatty acid known by us to occur in butter; it was unchanged after hydrogenation (Fig. 1*b*).

This does not prove conclusively that the unknown acid is saturated, for the peak at $C_{18.65}$ after hydrogenation could be due to the hydrogenation product of an ester with a higher C-number. Fraction B was once more submitted to GLC and all esters with a C-number $>$ 19.0 were collected and subsequently hydrogenated. The gas chromatogram of the hydrogenated product displayed no peak in the 18.65 position.

In this way proof has been obtained that the unknown acid in butter is *saturated.*

In order to collect sufficient amounts of this acid for further identification, we converted by hydrogenation all unsaturated acids into palmitic and stearic esters, which should be more readily separated from the unknown acid. A small amount (1.7 g) of fraction A was fully hydrogenated over a PtO_2 catalyst, and the 16:0 and 18:0 esters were removed by recrystallization from 10 volumes of acetone at 0°. The mother liquor (con-

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Abbreviations: GLC, gas—liquid chromatography; C-number, carbon number; PEGA, polyethylene glycol adlipate; IR, infared.

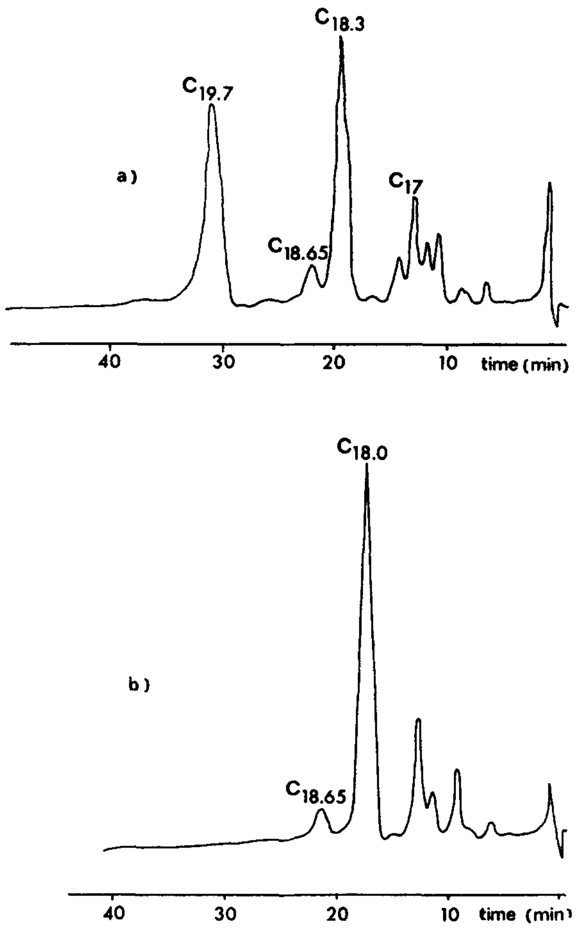


FIG. 1. Gas chromatograms of partially purified unknown ester (fraction B) (*a*) before hydrogenation, (*b*) after hydrogenation. Column 120 × 0.4 cm, 10% PEGA on Celite 545 (100–120 mesh), temperature 188°.

taining 416 mg) was treated with 1.6 g of urea and 6 ml of methanol. The nonadduct weighed 60 mg (fraction C) and was further analyzed by GLC (Fig. 2*a*). The fraction with C-number 18.65 on PEGA was collected separately and rechromatographed on Apiezon C (Fig. 2*b*), on which its C-number was 18.05.

IDENTIFICATION

IR Spectrum

The IR spectrum of the ester isolated by GLC (with C-number 18.65 on PEGA) shows the following unusual features (Fig. 3):

1. Two bands at 842 and 890 cm^{-1}, giving strong evidence for the presence of a cyclo-alkane ring (also one of the few possibilities left by the gas-chromatographic evidence), probably cyclohexyl.

2. A broad band with a maximum at 1455 cm^{-1}, instead of the doublet at 1440 and 1465 cm^{-1} characteristic of normal fatty acid esters.

The absorption at 1455 cm^{-1} could originate from a $—CH_3$ asymmetrical bending or a $>CH_2$ scissoring vibration (which occur in cyclopentane and cyclohexane derivatives). In the first case a corresponding band at about 1375 cm^{-1} ($—CH_3$ symmetrical bend) should occur. A rather weak band could indeed be detected in the free acid at 1373 cm^{-1}. Nevertheless this interpretation is not necessarily correct, because the spectrum of the acid between 1180 and 1380 cm^{-1} shows a regular spacing of the frozen rotational isomers, suggesting that the absorption at 1373 cm^{-1} could also be a crystallization band.

From the IR spectrum it was concluded, therefore, that the isolated compound was derived from a fatty acid of unknown chain length with a cyclohexyl group. The presence of a cyclopentyl ring in combination with a methyl group was considered to be less probable.

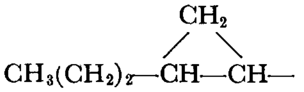
Mass Spectrum

The salient points of the mass spectrum of the methyl ester, part of which is recorded in Fig. 4, are:

(*a*) The parent peak (P) has a mass number of 282 ($C_{18}H_{34}O_2$).

(*b*) The spectrum is clearly not that of an unsaturated compound, therefore the molecular formula gives evidence for the presence of an alicyclic ring.

(*c*) The pattern of fragments containing the two oxygen atoms of the ester group is identical with that of the saturated esters up to the C_{11}-fragments. Of the higher ones, apart from the parent peak, only the C_{14}-fragments are prominent.

Part of the molecule is therefore $—(CH_2)_{10}—COOH$, leaving C_6H_{11} as an unknown part of the structure. The fact that the (P minus C_3H_7) fragment (mass 239) gives a prominent peak in the spectrum might indicate a  $CH_3(CH_2)_2\text{—}\overset{CH_2}{\overset{\diagup\ \ \diagdown}{CH\text{—}CH}}\text{—}$ structure for the remainder of the molecule, although the C_3H_7 fragment is always formed with long-chain aliphatic esters by loss of the α-, β-, and γ-carbon atoms through cleavage and recombination of the fragments (5). The cyclopropyl structure was shown to be out of the question by the IR spectrum, as the cyclopropyl absorption at 1023 cm^{-1} was absent from all spectra. GLC results also made a cyclopropane ring very unlikely, esters of acids which contain a cyclopropane ring having on Apiezon C a lower C-number than the corresponding straight-chain compounds.

It was decided therefore to disregard the mass spectral evidence for a propylcyclopropyl fragment, and to proceed on the hypothesis that the substance isolated was the methyl ester of 11-cyclohexylundecanoic acid (I).

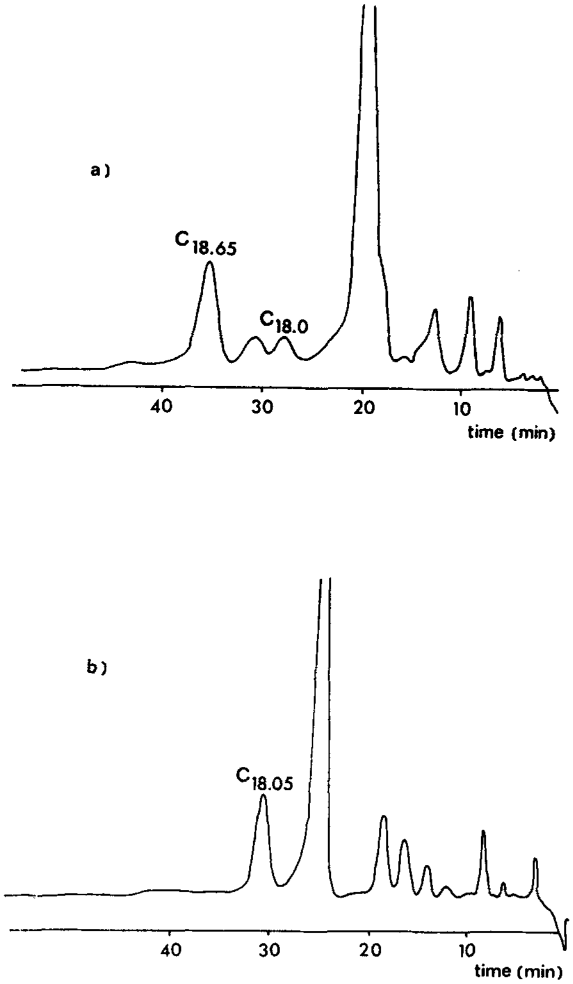
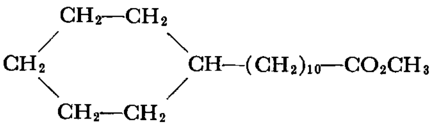


FIG. 2. Gas chromatograms of fraction C (fraction A after hydrogenation and fractionation). Columns 120 × 0.4 cm (*a*) 10% PEGA on Celite 545 (100–120 mesh), temperature 178°, (*b*) 10% Apiezon C on Celite 545 (80–100 mesh), temperature 207°.



I

Synthesis

The starting material was 10-phenyldecanoic acid (6), which was converted into 10-cyclohexyldecanoic acid by hydrogenation at 150° and 100 atm in glacial acetic acid. The melting point (52.3–53.1°) was in accordance with that given by Hiers and Adams (52.5–53.5°) (7). The methyl ester had bp 132–135° (15 mm) and $[n]_D^{20} = 1.4595$.

10-Cyclohexyldecanoic acid was converted into 11-cyclohexylundecanoic acid methyl ester by the Arndt-Eistert synthesis (8). This ester showed bp 120–124.5° (0.3 mm) and $[n]_D^{20} = 1.4617$. The free acid had mp 55.4–56.6° (reference 7: 58–59°).

Comparison of Synthetic and Natural Product

The C-numbers of the synthesized 11-cyclohexylundecanoic acid methyl ester on Apiezon L and PEGA were 18.05 and 18.65 respectively. These values are equal to those found for the methyl ester of the acid isolated from butter. (It should be noted that the C-number

TABLE 1 C-NUMBERS OF THREE ACIDS WITH A TERMINAL RING

Methyl Ester of	C-Number on Apiezon L at 205°	PEGA at 191°
11-Cyclohexylundecanoic acid (C_{17})	18.05	18.65
11-Cyclopentylundecanoic acid (dehydrohydnocarpic acid) (C_{16})	16.85	17.50
13-Cyclopentyltridecanoic acid (dehydrochaulmoogric acid) (C_{18})	18.85	19.50

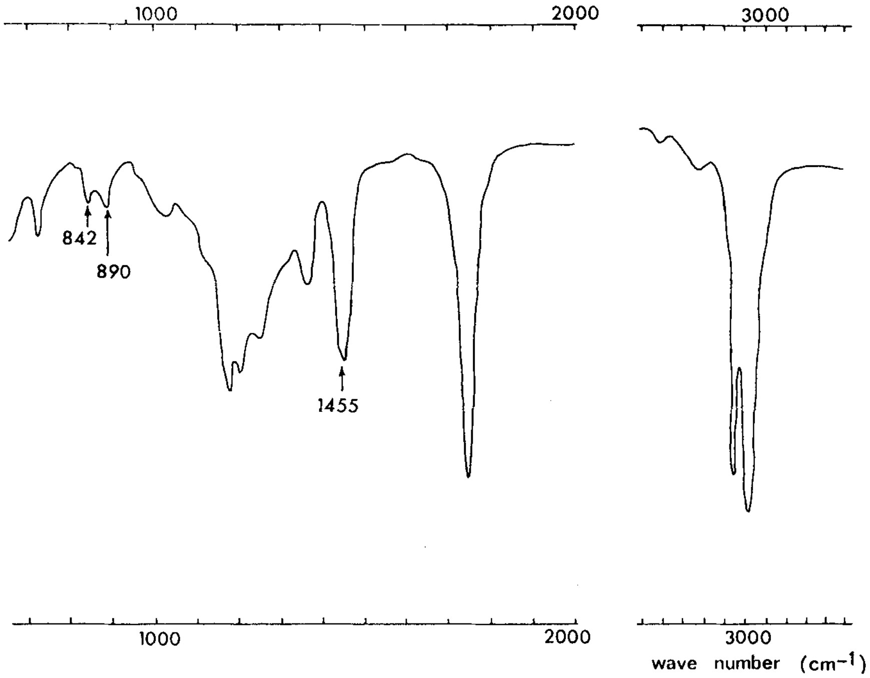


FIG. 3. IR spectrum of the isolated fatty acid methyl ester, recorded on a Unicam SP 100.

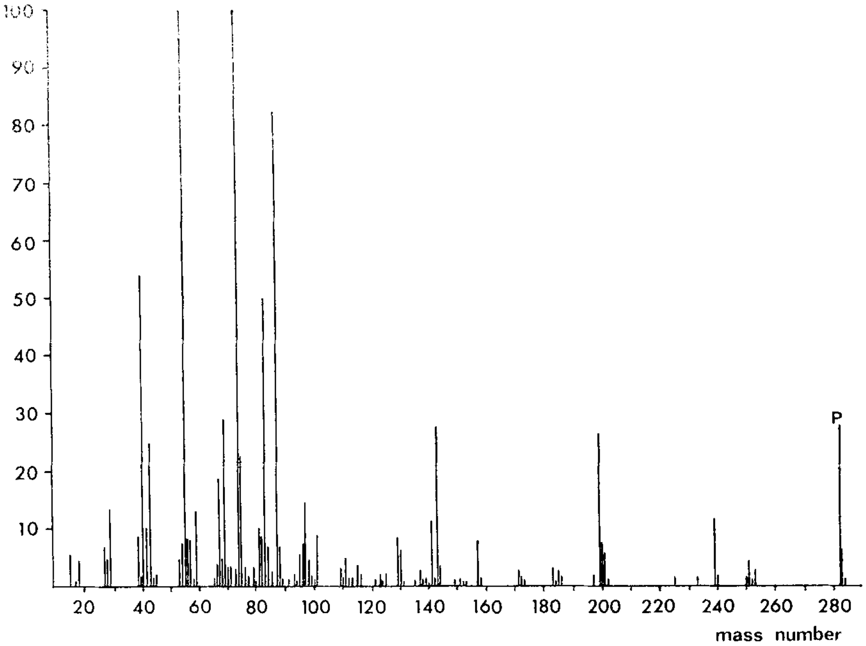


FIG. 4. Mass spectrum of the isolated fatty acid methyl ester, recorded with an AEI-type MS 2 H mass spectrometer with an inlet temperature of 200°.

on Apiezon L steadily decreased as a column was repeatedly used; after some months it was 17.45.)

For comparison we have also determined the C-numbers for two acids having a terminal five-membered ring (see Table 1). Table 2 shows the melting points (unc) of the isolated and the synthesized acids, as well as those of their respective anilides, prepared by the method of De Jonge, van der Ven, and den Hertog (9). IR and mass spectra of the synthetic product were identical with those of the ester obtained from butter.

TABLE 2 MELTING POINTS (UNC) OF THE SYNTHETIC AND NATURAL 11-CYCLOHEXYLUNDECANOIC ACIDS AND OF THEIR ANILIDES

	Acid	Anilide
Synthetic 11-cyclohexylundecanoic acid (A)	55.4–56.6	84.9–86.6
Acid from butter (B)	53.4–54.0	83.5–84.5
Equal parts of A and B	54.6–56.1	85.7

The evidence presented above is considered as proof for the structure of the naturally occurring acid. Its content in butter is estimated to be at least 0.01%.

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