C_{18}-Saturated Cyclic Acids from Linseed Oil: A Structural Study[1]

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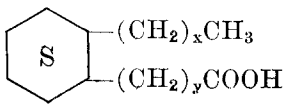
Abstract

The preparation of C_{18}-saturated cyclic acids from linseed oil by heat treatment in the presence of alkali, followed by hydrogenation and subsequent isolation of the cyclic fraction, gives rise to a series of at least 11 isomers as evidenced by GLC. Eight of these isomers have now been shown to be geometric pairs of positional isomers with the following general formula:



$x + y = 10$

An unequivocal synthesis of isomers (x = 0,1,2 and 3) indicates that the principal positional isomer (ca. 55%) of HCal is 9-(2′-*n*-propylcyclohexyl)-nonanoic acid. This isomer undoubtedly results from the cyclization of 10,12,14-octadecatrienoic acid present in the isomerized mixture. The predominance of this isomer is further substantiated by mass spectral analysis. The four positional isomers prepared constitute about 80% of the mixture as determined by gas-liquid chromatography. The four synthetic aromatic positional isomers show single peaks whereas their hydrogenated counterparts show two peaks. Thus each of the positional isomers of saturated cyclic acids is composed of two geometric isomers.

Introduction

THE FORMATION of cyclic compounds from polyunsaturated fatty acids has been recorded in the literature frequently since Cloez (4) first reported the presence of monomeric cyclic fatty acid (CFA) in heat-treated tung oil fatty acids. Cyclic structures are generally postulated for the liquid, nonurea-adducting, fatty acid fractions obtained from polyunsaturated fatty acids and oils by various types of processing. These processes include heat treatment (with and without a hydrogenation catalyst), alkaline isomerization and catalytic hydrogenation. For the most part, research on CFA has fallen into four categories: studies of conditions which favor their formation (1,5,16,24), methods of purification (10, 17), evaluation of their toxicity (6–8), and synthesis and evaluation of selected derivatives (2,9,14,15,22). Very little has been done to elucidate their structures specifically.

Rossmann (26) in 1933 was among the first to postulate a specific structure for CFA made by heat-treating eleostearic acid. He concluded that the CFA was a 5,6-disubstituted 1,3-cyclohexadiene, more specifically 8-(2-*n*-butylcyclohexa-3,5-dienyl)octanoic acid. Rivett (25) also reported evidence for 1,2-dialkyl-3,5-cyclohexadiene structures in heat-treated β-eleostearate. Five years later McInnes et al. (21) separated CFA from heated linseed oil into three fractions by preparative gas-liquid chromatography (GLC). On the basis of their infrared (IR) spectra and analysis of their oxidation products it was concluded that all three fractions had the same carbon skeleton, 1-propyl-2-alkenecarboxycyclohexene but that they differed in the position of the double bond in the side chain.

In seeming contrast to this finding Hutchison and Alexander (18) reported the isolation and identification of ethyl 11-(2-methylcyclohex-2-enyl)undec-*trans*-9-enoate in a mixture of CFA ethyl esters from heated linseed oil. This compound was separated from the mixture by preparative GLC, and its carbon skeleton was determined by comparison of its hydrogenated and aromatized derivatives with a model synthetic compound. More recently Coenen, Wieske, and co-workers (5) state that under certain conditions catalytic hydrogenation of linseed oil leads to the formation of *o*-disubstituted benzene monocarboxylic acids. The predominant aromatic isomer (85% of the mixture) was reportedly 9-(2′-propylphenyl)-nonanoic acid. This structure was again verified by comparison with an authentic model compound.

Research at the Northern Laboratory on cyclic acids has been directed toward their potential utility as industrial chemicals. This research is part of the program undertaken to find new and extended uses for linseed oil. The linseed cyclic acids (Cal) are produced by prolonged alkaline isomerization of linseed oil at high temperatures in a suitable solvent.

These acids contain a cyclohexadiene ring (17) and can be either hydrogenated to the cyclohexane derivative (HCal) or aromatized (ACal) as shown in the flow diagram (Fig. 1). Both HCal and ACal are mixtures of isomers as demonstrated by GLC. Since relatively little is known about the specific structures of this class of compounds, generally referred to as cyclic acids, and since there appears to be some disagreement among those who have reported specific structures, we initiated a detailed structural study to identify the isomers of ACal and HCal. Our approach was to synthesize the pure individual positional isomers believed to be present in ACal, hydrogenate a portion of each, and then compare these model compounds with ACal and HCal by IR, GLC, NMR, and mass spectrometry. This paper describes the synthesis of the model compounds and reports the comparative studies.

Experimental

The synthesis of model compounds is shown schematically in Fig. 2.

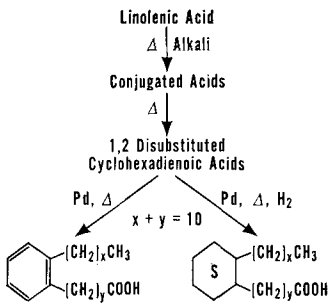


FIG. 1. Preparation of hydrogenated and aromatic cyclic acids from linseed oil.

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[2] No. Utiliz. Res. Dev. Div., ARS, USDA.

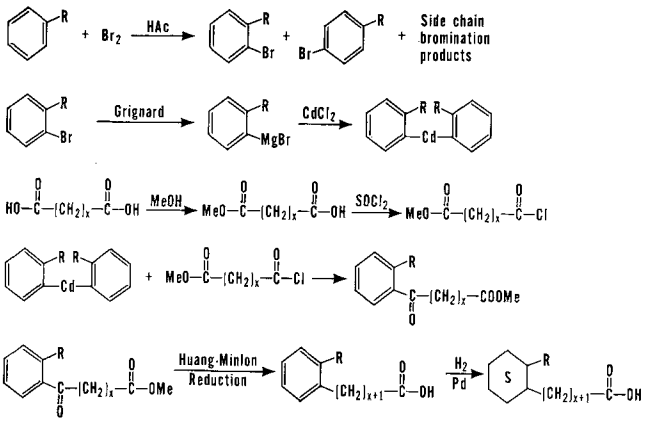


FIG. 2. Synthesis of individual pure aromatic isomers.

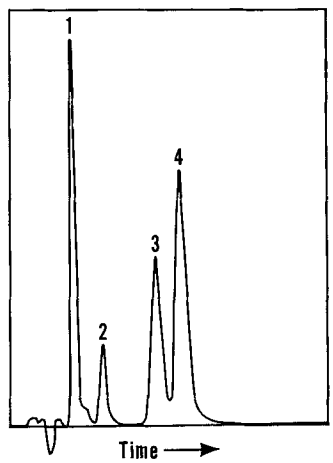


FIG. 3. Gas chromatogram of brominated *n*-butylbenzene, Pye Argon chromatograph, 4-ft × ¼-in. column, EGSSX on 100–120 Gas Chrom, 136C, 21 cc/min, (1) *n*-butylbenzene (2) 1-phenylbutene (3) *o*-bromo-*n*-butylbenzene (4) *p*-bromo-*n*-butylbenzene.

Bromination of n-alkylbenzenes

o-Bromotoluene and *o*-bromoethylbenzene were purchased from the Aldrich Chemical Company (28) and used without further purification. The bromination of commercially obtained *n*-propyl- and *n*-butylbenzene was carried out according to the method of Lamneck (20). The reaction vessel was a 500-cc, jacketed, three-necked, round-bottom flask. The flask was equipped with an addition funnel, condenser with drying tube, and thermistor probe for temperature control. The thermistor controller operated a centrifugal pump which circulated cool water through the jacket of the flask. Adequate agitation was achieved with a magnetic stirrer. All glass equipment was painted black to eliminate light. The reactions were carried out for four days at 17–18C.

Purification of Bromoalkylbenzenes

The crude reaction products were poured into a separatory funnel, and the lower layer containing unreacted bromine, iodine and iron salts in acetic acid was drawn off. The upper layer was diluted with chloroform and washed three times with water, once with dilute sodium bisulfite, and finally with bicarbonate. The chloroform solution was then dried over anhydrous sodium sulfate and the chloroform subsequently stripped off. Flash distillation of the stripped products at 45 mm removed the unreacted alkylbenzenes. Based on their recovery, conversion of both *n*-propyl- and *n*-butylbenzene was about 45%. The remaining brominated derivatives were refluxed at atmospheric pressure for 4 hr to decompose side-chain bromination products. HBr was given off, and the resultant dark products were washed and dried before fractionation. GLC of these products showed four principal peaks. The chromatogram of brominated *n*-butylbenzene (Fig. 3) is typical.

Distillation of these products was carried out in a 2-ft × 13-mm Podbielniak column containing stainless steel Helipac. The pressure was 46 mm, and the reflux ratio was 40:1. The composition of the distilled fractions was monitored by GLC. Material corresponding to peaks 1 and 2 were easily separated from 3 and 4 and were shown, respectively, to be unreacted *n*-alkylbenzenes and alkenyl benzenes produced by the decomposition of side-chain bromination products. Compounds corresponding to peaks 3 and 4 were not cleanly separated from each other. Those fractions rich in 3 were redistilled through the same column at about 400 mm, yielding pure compounds as shown by GLC. IR absorbance at 750 cm^{-1} for 3 and at 820 cm^{-1} for 4 indicated that they were the *ortho*- and *para*-isomers, respectively.

Preparation of Grignard Reagents

The reaction of *o*-bromotoluene and *o*-bromoethylbenzene with Mg in dry ether proceeds without difficulty by standard techniques; however, as the size of the alkyl group on the aromatic ring increases, the reaction becomes more difficult to initiate and proceeds slowly. To form the Grignard reagent of *o*-bromo-*n*-butylbenzene, the following techniques were combined. The equipment was flame-dried and dry air was subsequently metered through the system for several hours. Magnesium (10% excess) that had been activated with HCl and dried in vacuum was then added to the flask. About 3 parts ether and 1 part benzene, previously dried over sodium, were distilled from sodium directly into the reaction vessel. The *o*-bromo-*n*-butylbenzene was then introduced; the mixture was stirred and warmed to reflux, and a crystal of iodine and several "active" chips of magnesium taken from a tube of ethyl bromide in ether were added. Ether was then slowly distilled until the temperature of the reaction mixture became high enough to initiate the reaction. About 6 hr were required for complete reaction.

Preparation of Organo-Cadmium Reagents

This reaction proceeded quite smoothly with the addition of anhydrous $CdCl_2$ powder directly to the Grignard reagent. A 10% excess of $CdCl_2$ was added slowly with stirring to prevent the solvent from refluxing too vigorously. (Care must be taken to ensure that the $CdCl_2$ is anhydrous.) Dry benzene was then added, and the ether stripped off.

Preparation of Methyl (ω-chloroformyl) n-alkanoates

These compounds were prepared by adding 100% molar excess of $SOCl_2$ to appropriate methyl hydrogen alkanoate at 0–5C and then slowly warming to room temperature (3). When the reaction subsided, the mixture was refluxed for 4 hr. Excess $SOCl_2$ was then removed under house vacuum, and the residue was fractionated in a short Vigreux column at 0.075 mm. These compounds, obtained in high yield (>90%), were quite pure (>98%) as determined by potentiometric titration and GLC of their methanol-derived diesters.

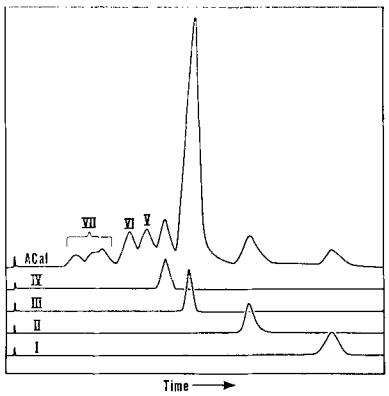


FIG. 4. Gas chromatogram of aromatic cyclic acids derived from linseed oil and pure individual aromatic isomers: Barber Colman chromatograph, 200-ft × 0.01-in. column, column coated with an experimental nitrile silicone resin No. 238–149–99 produced by General Electric, 200C. I = methyl 11-(*o*-methylphenyl)undecanoate, II = methyl 10-(*o*-ethylphenyl) decanoate, III = methyl 9-(*o*-*n*-propylphenyl)nonanoate, IV = methyl 8-(*o*-*n*-butylphenyl)octanoate, V, VI, and VII have not been identified.

Coupling Reaction

A 50% solution of the methyl (ω-chloroformyl)*n*-alkanoate in dry benzene was added slowly with stirring to the appropriate organo-cadmium reagent previously described. After reflux due to the reaction subsided, the mixture was heated and reflux maintained for ½-hr. The crude product in benzene was acidified with HCl, and the benzene layer containing the coupled product washed several times with water. The dried organic layer was then stripped of benzene under house vacuum, and the crude product fractionated under high vacuum (0.05 mm) through a short Vigreux column. The fraction boiling 125–145C showed strong IR absorption at 1683 cm^{-1} (ketone) 760, 1495, and 1600 cm^{-1} (*ortho*-disubstituted benzene) and 1175, 1200, 1250 cm^{-1} (methyl ester).

Reduction of Coupled Product

The methyl ω-(2′-*n*-alkylbenzoyl)-*n*-alkanoates were reduced without further purification by the Huang-Minlon modification of the Wolff-Kishner reduction. The recovered crude reduction products were fractionally distilled at 0.035 mm through a short-path microdistillation apparatus. A water-white fraction bp 128–134C was collected, which showed the same IR spectrum as the coupled product except for the absence of the band at 1683 cm^{-1} (ketone). Each methyl ester of these products [methyl 11-(*o*-methylphenyl)undecanoate (I), methyl 10-(*o*-ethylphenyl) decanoate (II), methyl 9-(*o*-*n*-propylphenyl)nonanoate (III), and methyl 8-(*o*-*n*-butylphenyl)octanoate IV] showed essentially one peak by GLC (Fig. 4). The yield of I based on the *o*-bromo-toluene (limiting reagent) was 76.5%. The yields of II, III, and IV were only 15 to 20%; the low yields can be traced directly, at least in part, to moisture in the supposedly anhydrous $CdCl_2$.

Hydrogenation of Aromatic Isomers I-IV

These isomers were hydrogenated at high pressure in acetic acid with a Pd-C catalyst (13). The UV, IR, and GLC analyses of the recovered products [methyl 11-(2′-methylcyclohexyl)undecanoate (IH), methyl 10-(2′-ethylcyclohexyl)-decanoate (IIH), methyl 9-(2′-*n*-propylcyclohexyl)nonanoate (IIIH), and methyl 8-(2′-*n*-butylcyclohexyl)octanoate (IVH)] showed no trace of residual aromatic contaminants.

Preparation of Linseed Cyclic Acids and Their Aromatic and Hydrogenated Derivatives

Cal was prepared by alkaline isomerization of linseed oil in ethylene glycol according to the method

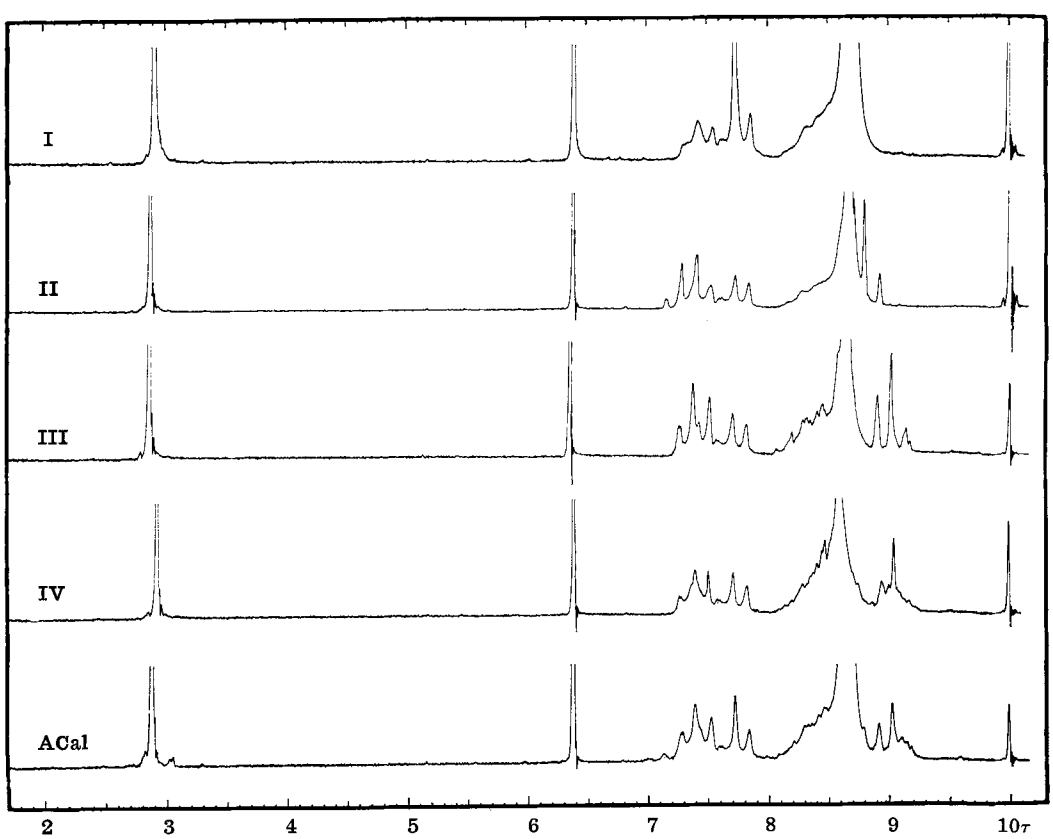


FIG. 5. NMR spectra of ACal and pure individual aromatic isomers: I-IV as in Figure 4.

of Eisenhauer et al. (12). The dehydrogenation of Cal to ACal in the presence of Pd has been previously described (13). Hydrogenation of Cal to HCal has also been reported earlier by Eisenhauer et al. (11).

Discussion

The GLC curves of ACal and the pure aromatic isomers (I–IV (Fig. 4) show that the principal isomer in ACal is III and, by an approximation of the areas under the curve, III constitutes about 56% of the sample, II and IV about 9%, and I about 6%. The two peaks V (6%) and VI (8%), which immediately precede IV, have not been identified but are believed to be methyl 7-(2′-*n*-pentylcyclohexyl)heptanoate and methyl 6-(2′-*n*-hexylcyclohexyl)hexanoate. Peak VII (6%), also not yet identified, represents at least three minor components. These three peaks may be residual cyclohexadiene structures resulting from incomplete dehydrogenation.

The NMR spectra of ACal and the pure aromatic isomers I–IV (Fig. 5) show common signals at 2.9τ (aromatic protons), 6.4τ (methoxy protons), and 8.5–8.7τ (isolated methylene). The large signal exhibited by I at 7.7τ is caused by the methyl group attached directly to the ring. The absence of a triplet between 8.7 and 9.2τ in I also indicates no methylene between the methyl group and the ring. In II, the downfield band of this triplet is nearly lost in the isolated methylene signal. This triplet in III and IV is more typical of long-chain terminal methyls. The relatively stronger signal at 7.7τ in ACal as compared to those of II, III, and IV indicates the presence of small amounts of I in the mixture. The signal in II at 7.15τ, which is part of a quadruplicate 7.15 to 7.5τ, is also evident in ACal. The most striking overall similarity, however, is between III and ACal, which is in agreement with the GLC findings.

Mass spectrographic analysis of ACal did not give the fragmentation pattern expected. Apparently both side chains are cleaved, producing only relatively light-weight fragments that do not give adequate information for establishing the position of the aromatic ring. Thus the appearance of a strong peak at mass 105 (*o*-xylyl ion) does not necessarily mean that the principal isomer is I. This contention is in agreement with the data of Meyerson (23) on the fragmentation of 1,4-di-(1-decyl)benzene.

Hydrogenation of the pure aromatic isomers I–IV gives the corresponding cyclohexane derivatives IH–IVH. The gas chromatogram of III and IIIH (Fig. 6) shows that the hydrogenation of a pure (one) aromatic species gives rise to two cyclohexyl species. The two cyclohexyl species have a shorter retention time and appear to be present in differing amounts. These (two) species are configurational isomers of the disubstituted cyclohexanes (chair form). Because substituent groups prefer to assume the equatorial position for steric reasons, one would predict that the predominant isomer should be the *trans* (e,e + a,a) form. The lesser isomer would then be the *cis* (a,e + e,a) form. It should be pointed out that each of these forms is a racemic mixture of a *dl* pair. One would expect little if any of the (a,a) *trans* form to be present in the mixture, and the predominant *cis* form would be the one in which the alkyl group is axial and the long chain containing the ester function equatorial. This predominance may become insignificant as the alkyl group becomes larger (27).

From the chromatogram of HCal (Fig. 7) it is evident that the first peak in each pair is the larger

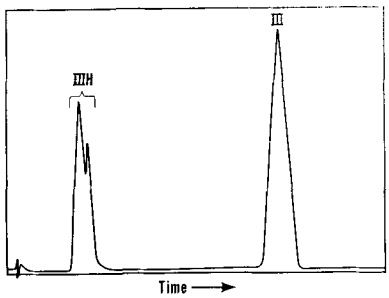


FIG. 6. Gas chromatogram of methyl 9-(*o*-*n*-propylphenyl) nonanoate III and methyl 9-(2′-*n*-propylcyclohexyl)nonanoate, Pye Argon chromatograph, 4-ft × ¼-in. column, EGSSX on 100–120 Gas-Chrom, 175C, 35 cc/min.

and should, according to previous reasoning, be the *trans* form. Because of its configuration one would expect the *trans* form to have a shorter retention time than the *cis* form. It can also be seen that as the alkyl group becomes larger, I → IV, the ratio of the two peaks also becomes larger. This observation is also in agreement with the previous reasoning, i.e., as the alkyl group becomes larger the equatorial position is favored.

The isomer pairs in HCal were identified first by comparing their retention times with the pure hydrogenated isomers IH–IVH and then by GLC analysis of mixtures of each pure isomer with HCal. A mixture of HCal with a combination of IIH–IVH is shown in Fig. 7B. It is significant that no new peaks appear and that there is obvious enrichment of the peaks corresponding to IIH–IVH. The peaks corresponding to IH and the unidentified peaks are conversely greatly suppressed.

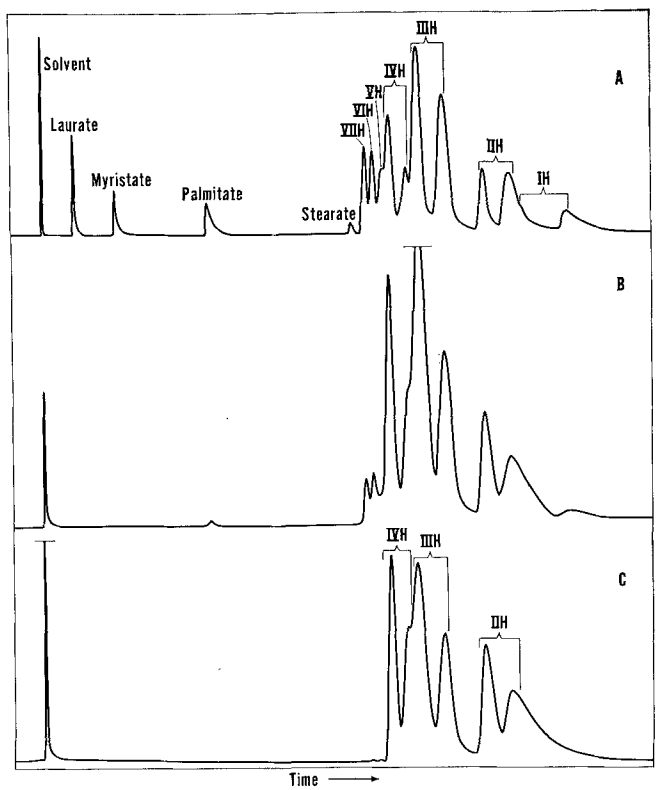
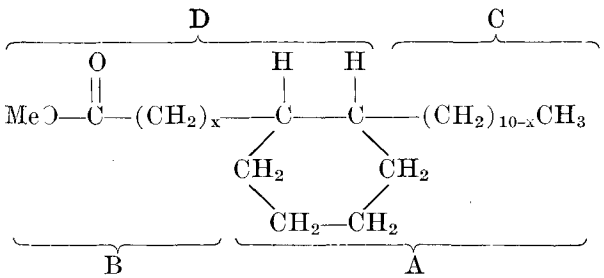


FIG. 7. Gas chromatograms of: (A) HCal methyl esters with saturated C_{12-18} fatty methyl ester markers; (B) mixture of A and C; and (C) pure methyl 10-(2′-ethyl cyclohexyl)decanoate (IIH), methyl 9-(2′-*n*-propylcyclohexyl)nonanoate (IIIH), and methyl 8-(2′-*n*-butylcyclohexyl)octanoate (IVH). Barber Colman chromatograph, 200-ft × 0.01-in. column, Apiezon M, 200C.

Mass spectral analyses of HCal methyl esters and the pure hydrogenated isomers IH–IVH showed a much more useful fragmentation pattern than their corresponding aromatic derivatives. Significant mass numbers corresponding to cleavage of each side chain were evident in the spectra. This cleavage is illustrated by the following general formula. The intensities of fragments A–C resulting from this cleavage were measured.



Three other significant peaks (A + 1 via rearrangement of A, D-32, and D-23-18 by further fragmentation of D) are also evident in the spectra of the hydrogenated derivatives. The only exception is the absence of D,D-32, and D-32-18 in the spectra of I. This lack is to be expected since the cleavage would involve the methyl attached to the ring. Such cleavage is not favored because of the high energy of the methyl fragment. To make a quantitative estimation of the percentage of each of the isomers IH–IVH in the mixture HCal, one prominent mass number was chosen for each pure isomer. The mass number showing the least interference from the same number in the other three isomers was used for the calculation. These mass numbers and their relative intensities in scale divisions per microliter are given in Table I. These fragments correspond to D-32-18 for IIH–IVH. Since the peak corresponding to D-32-18 does not exist for IH, the mass number corresponding to fragment A was used for this isomer. The approximate percentages of the isomers in HCal are as follows: IH—5.5%, IIH—10.5%, IIIH—53.5%, and IVH—9.5%. IIIH is undoubtedly derived from cyclization of 10,12,14-octadecatrienoic acid present in the isomerized mixture (19). The percentages are in reasonably good agreement with the percentages of I–IV as calculated from the GLC curve of ACal. Methyl 7-(2′-*n*-pentylcyclohexyl)heptanoate and methyl 6-(2′-*n*-hexycyclohexyl)hexanoate were not synthesized; therefore their contribution to the isomer mixture (HCal) cannot be definitely established. The presence of these two isomers in the mixture is evident however from the appearance of mass numbers corresponding to the fragmentation pattern shown by the other isomers. The intensity of these peaks are of the same order as IH and IVH. There is some evidence for the presence of methyl 5-(2′-*n*-heptylcyclohexyl)pentanoate in the mass spectrum of the mixture but no evidence for the remaining members of the series.

TABLE I

Selected Mass Spectral Intensities of Pure Hydrogenated Cyclic Isomers and (HCal)

Mass number	199	189	203	217
	Intensities (Scale divisions/Microliter)			
Methyl 9-(2′ methylcyclohexyl) undecanoate	*108*	1.8	1.2	1.0
Methyl 8(2′ ethylcyclohexyl) decanoate	4.3	2.0	1.6	*38.3*
Methyl 7-(2′-*n*-propylcyclohexyl) nonanoate	1.0	3.7	*58.6*	0.8
Methyl 6-(2′-*n*-butylcyclohexyl) octanoate	2.1	*94.2*	1.1	0.6
Methyl ester of hydrogenated cyclic acids (HCal)	8.5	13.5	35.9	5.0

ACKNOWLEDGMENT

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REFERENCES

1. Baldwin, W. S., D. E. Floyd and R. F. Paschke (General Mills), U.S. *2,868,815 (1959)*.
2. Bell, E. W., J. P. Friedrich, L. E. Gast and J. C. Cowan, JAOCS *42*, 876–878 (1965).
3. Blatt, A. H., Org. Syn. Collective Vol. 2, 276, (1948).
4. Cloëz, M. S., Compt. Rend. *83*, 943–945 (1876).
5. Coenen, J. W. E., Th. Wieske, R. S. Cross and H. Rinke, Unilever Research Laboratories, Hamburg-Bahrinfeld, Germany, and Vlaardingen, The Netherlands, private communication.
6. Common, R. H., E. W. Crampton, F. A. Farmer and A. S. W. DeFreitas, J. Nutr. *62*, 341–347 (1957).
7. Crampton, E. W., R. H. Common, F. A. Farmer, A. F. Wells and D. Crawford, Ibid. *49*, 333–347 (1953).
8. Crampton, E. W., R. H. Common, E. T. Pritchard and F. A. Farmer, Ibid. *60*, 13–24 (1956).
9. DeJarlais, W. J., and H. M. Teeter, JAOCS *39*, 421–424 (1962).
10. Eisenhauer, R. A., and R. E. Beal, AOCS 57th Annual Meeting, Los Angeles, Calif., 1966, Abstr. No. 73.
11. Eisenhauer, R. A., R. E. Beal, L. T. Black and J. P. Friedrich, submitted to JAOCS.
12. Eisenhauer, R. A., R. E. Beal and E. L. Griffin, JAOCS *40*, 129–131 (1963).
13. Friedrich, J. P., E. W. Bell and L. E. Gast, AOCS 54th Annual Meeting, Atlanta, Ga., 1963, Abstr. No. C-2.
14. Friedrich, J. P., E. W. Bell and L. E. Gast, JAOCS *42*, 643–645 (1965).
15. Friedrich, J. P., and L. E. Gast, AOCS 57th Annual Meeting, Los Angeles, Calif., 1966, Abstr. No. 72.
16. Friedrich, J. P., J. C. Palmer, E. W. Bell and J. C. Cowan, JAOCS *40*, 584–587 (1963).
17. Friedrich, J. P., H. M. Teeter, J. C. Cowan and G. E. McManis, Ibid. *38*, 329–332 (1961).
18. Hutchison, R. B., and J. C. Alexander, J. Org. Chem. *28*, 2522–2526 (1963).
19. Kass, J. P., and G. O. Burr, J. Am. Chem. Soc. *61*, 3292–3294 (1939).
20. Lamneck, J. H., Ibid. *76*, 1106–1107 (1954).
21. McInnes, A. G., F. P. Cooper and J. A. MacDonald, Can. J. Chem. *39*, 1906–1914 (1961).
22. Marvel, C. S., J. C. Hill, J. C. Cowan, J. P. Friedrich and J. L. O'Donnell, J. Polymer Sci. *2*, 2523–2532 (1955).
23. Meyerson, S., Appl. Spectry. *9*, 120–130 (1955).
24. Paschke, R. F., and D. H. Wheeler, JAOCS *32*, 473–478 (1955).
25. Rivett, D. E., Ibid. *33*, 635–637 (1956).
26. Rossmann, E., Fettchem. Umschau *40*, 96–102 (1933); C. A. *27*, 5057 (1933).
27. Winstein, S., and N. J. Holness, J. Am. Chem. Soc. *77*, 5562–5578 (1955).

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