Structural Relationships in the Natural Unsaturated Higher Fatty Acids.

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IN natural fats and fatty oils the most familiar, and indeed also the most abundant, constituent acid is oleic (*cis-n*-octadec-9-enoic), $CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$, but nearly forty analogous natural unsaturated acids have so far been recorded in various fats, and of these the constitutional formulæ are, for the most part, known with reasonable certainty. A large number of these naturally occurring unsaturated fatty acids contain the same normal carbon chain of eighteen carbon atoms which is present in oleic acid, but in others the chain may be shorter or longer. Unsaturated acids containing as few as ten, and as many as twenty-six, carbon atoms in their molecules have been reported, and all the intervening "even-numbered" members are represented in the natural acids. Those belonging to the C_{16}, C_{20}, and C_{22} series are, however, more abundant than any others except those with a chain of eighteen carbon atoms. Moreover, in different kinds of natural fats, all degrees of unsaturation from monoethenoid to hexaethenoid occur in their unsaturated acids; but polyethenoid unsaturation is much more frequent in the longer chain (C_{18} and upwards) than in the shorter chain acids. Indeed, no natural polyethenoid fatty acid containing less than sixteen carbon atoms has yet been observed.

Many of these acids share common constitutive features, and attention will be largely directed, in the present discussion, to considering these similarities in structure and their possible implications in regard to the genesis of the natural fatty acids in the living organism. Before doing so, however, it is perhaps desirable to try to obtain in rough perspective the relative quantities of the many different fatty acids which are so freely produced in different organisms. From a quantitative standpoint, the amount of many of the unsaturated acids produced in nature is extremely small (and often restricted to a single species or group of related species) in comparison with the relatively abundant production of a few—notably oleic, linoleic, hexadecenoic (palmitoleic), and the highly unsaturated acids of the C_{20} and C_{22} series which are especially typical of fats from marine organisms.

It is of course not possible to offer even a rudimentary statistical estimate of the natural production in the world of individual fatty acids, since data as to the total production in Nature of different fats are largely lacking, even in those cases (still only a fraction) in which the proportions of their component acids are known. Some years ago, however, the Dutch chemist Boekenoogen (*Oliën Vetten Oliezadan*, 1941, **26**, 143) made an interesting statistical survey of the fatty acids produced annually in Nature in a group of fats of industrial interest of which the world production and fatty acid compositions were both known with some approach to accuracy. His survey was limited to twenty fats from vegetable sources, including sunflower-seed, olive, groundnut, soya-bean, rape, coconut, palm-kernel, linseed, and a few other similar oils. Boekenoogen reached the conclusion that, over the range of oils employed, the percentage natural production of different fatty acids was as follows: oleic, 34; linoleic, 29; palmitic, 11; lauric, 7; linolenic, 6; myristic, stearic, and erucic (each), 3; and *all others together* 4%.

These ratios would be altered somewhat if the whole range of vegetable fats could be similarly assessed, and still more if the large amounts of fat synthesised by land animals and by marine organisms (from vegetable or animal plankton to the large fishes and marine mammals) were brought into the picture. It is not unreasonable to expect that more fat may be produced by aquatic organisms than the combined production of land vegetables and animals. At all events, fats from aquatic sources must represent a very substantial proportion of the total world production, and in these fats, although oleic again forms the major component of the fatty acids (usually of the order of 30 ± 10%), important proportions of hexadec-9-enoic (palmitoleic) acid and polyethenoid unsaturated acids of the C_{20} and C_{22} series may also each amount on an average to, perhaps, 20 ± 5% of the total acids, with about 10—15% of (saturated) palmitic acid also present. Again, the main components of most land animal body fats consist of about 30% of palmitic acid with larger amounts of oleic acid and with stearic acid contents varying from about 10 to 25%; whilst their milk fats are somewhat similar in composition except for the frequent presence of about 10—20% of acids (mainly saturated) with shorter carbon chains (C_{12}, C_{10}, C_8, C_6, and C_4) than in most other fats.

Hence, although it is clearly impossible to attempt any reasonably precise estimate, one may offer the opinion that, of all the fatty acids synthesised in Nature, oleic acid probably forms not much less than about 40%, and that no other acid approaches it in amount, with the single exception of the most characteristic member of the saturated series, palmitic, which may well form about 15% of the total natural fatty acid production. The characteristic C_{16} and C_{20-22} acids of fats of aquatic orgin, and linoleic acid which is so frequent a constituent of vegetable fats, with possibly stearic acid (mainly from certain classes of land animals), are probably the only other fatty acids which would contribute a significant individual contribution in a survey of world production; this might be (speculatively) estimated at, say, 5—7% in each case. If these figures bear any near relation to the actual facts, they imply that the rest of the natural higher fatty acids (saturated and unsaturated) together account for only about 15—25% of the total world production—and much of this proportion would be accounted for by acids such as lauric, myristic, erucic, linolenic, and a few others which predominate in seed fats of certain plant families. Thus many of the unsaturated acids to which reference will now be made are only produced in Nature in relatively minute quantities in comparison with the natural production of oleic acid and a few other unsaturated fatty acids.

Having thus endeavoured to give a picture—albeit necessarily very crude—of the relative occurrence of the many different unsaturated acids, let us now proceed to a more detailed consideration of their constitutive resemblances and dissimilarities.

Natural Unsaturated Acids which contain a Structure Identical with One or Other Half of the Oleic Acid Molecule ($CH_3\cdot[CH_2]_7CH\colon$ *or* $\colon CH\cdot[CH_2]_7\cdot CO_2H$).

Many natural straight-chain ethenoid acids of fats share a somewhat singular partial resemblance to oleic acid in that one or other part of their molecules is identical with that of one half of the oleic acid molecule.

Natural Unsaturated Acids with a Common Grouping, $\colon CH\cdot[CH_2]_7\cdot CO_2H$.—Table I shows the constitution of six monoethenoid acids (C_{10} to C_{20}) of the " even-numbered " homologous series in which unsaturation occurs uniformly at the 9th carbon atom from the acidic end of the molecules.

TABLE I.

Monoethenoid acids, $R\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$.

$C_{10}H_{18}O_2$	Dec-9-enoic	$CH_2\colon CH\cdot[CH_2]_7\cdot CO_2H$
$C_{12}H_{22}O_2$	Dodec-9-enoic	$CH_3\cdot CH_2\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$
$C_{14}H_{26}O_2$	Tetradec-9-enoic (myristoleic)	$CH_3\cdot[CH_2]_3\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$
$C_{16}H_{30}O_2$	Hexadec-9-enoic (palmitoleic)	$CH_3\cdot[CH_2]_5\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$
$C_{18}H_{34}O_2$	Octadec-9-enoic (oleic)	$CH_3\cdot[CH_2]_7\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$
$C_{20}H_{38}O_2$	Eicos-9-enoic (gadoleic)	$CH_3\cdot[CH_2]_9\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$

On the whole, acids of exclusively animal origin preponderate in Table I, but it must be recalled that hexadecenoic acid (though only present in traces in most land vegetable fats) is as ubiquitous in Nature as is oleic acid itself, and that hexadecenoic and gadoleic acid occur in some quantity in fats of aquatic origin, vegetable as well as animal. On the other hand, the polyethenoid acids of the C_{18} series—linoleic, linolenic, elæostearic, licanic, parinaric—which are characteristic and major components of many of the more unsaturated kinds of vegetable fatty oils (illustrated in Table II) share the same constitutive feature with those of the monoethenoid acids in Table I : unsaturation begins in each at the 9th carbon atom from the carboxyl group, irrespective of whether the polyethenoid structure is conjugated or not.

TABLE II.

Polyethenoid acids, $R\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$ (*of vegetable fats*).

$C_{18}H_{32}O_2$	Octadeca-9 : 12-dienoic (linoleic)	$CH_3\cdot[CH_2]_4\cdot CH\colon CH\cdot CH_2\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$
$C_{18}H_{30}O_2$	Octadeca-9 : 12 : 15-trienoic (linolenic)	$CH_3\cdot CH_2\cdot CH\colon CH\cdot CH_2\cdot CH\colon CH\cdot CH_2\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$
$C_{18}H_{30}O_2$	Octadeca-9 : 11 : 13-trienoic (elæostearic)	$CH_3\cdot[CH_2]_3\cdot CH\colon CH\cdot CH\colon CH\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$
$C_{18}H_{28}O_3$	4-Keto-octadeca-9 : 11 : 13-trienoic (licanic)	$CH_3\cdot[CH_2]_3\cdot CH\colon CH\cdot CH\colon CH\cdot CH\colon CH\cdot[CH_2]_4\cdot CO\cdot[CH_2]_2\cdot CO_2H$
$C_{18}H_{28}O_2$	Octadeca-9 : 11 : 13 : 15-tetraenoic (parinaric)	$CH_3\cdot CH_2\cdot CH\colon CH\cdot CH\colon CH\cdot CH\colon CH\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H$

Natural Unsaturated Acids with a Common Grouping $CH_3\cdot[CH_2]_7\cdot CH\colon$.—There are apparently just as many instances in which the converse state of affairs obtains to that considered in Tables I and II. The acids shown in Table III originate exclusively in vegetable fats, with the exception of selacholeic or nervonic (tetracos-15-enoic) acid which has been observed in the fats of Elasmobranch fish (Tsujimoto, *J. Soc. Chem. Ind., Japan*, **1927**, **30**, 1868) and of cerebrosides (Klenk, *Z. physiol. Chem.*, **1927**, **66**, 287), and, of course, of oleic acid itself which is common to all fats.

TABLE III.

Monoethenoid acids, $CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_n\cdot CO_2H$.

$C_{14}H_{26}O_2$	Tetradec-5-enoic	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_3\cdot CO_2H$
$C_{18}H_{34}O_2$	Octadec-9-enoic (oleic)	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$
$C_{20}H_{38}O_2$	Eicos-11-enoic	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_9\cdot CO_2H$
$C_{22}H_{42}O_2$	Docos-13-enoic (erucic)	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_{11}\cdot CO_2H$
$C_{24}H_{46}O_2$	Tetracos-15-enoic (selacholeic)	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_{13}\cdot CO_2H$
$C_{26}H_{50}O_2$	Hexacos-17-enoic (ximenic)	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_{15}\cdot CO_2H$
$C_{30}H_{58}O_2$	Tricos-21-enoic (lumequic)	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_{19}\cdot CO_2H$

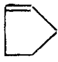
It is natural, owing to the universal presence of oleic acid in natural fats (usually in major proportion), to wonder whether the homologous unsaturated acids in Tables I and III may not result from some chemical transformation of pre-formed oleic acid or glycerides. At first sight this idea gains some support from the circumstance that the acid with almost the longest carbon chain in Table I, and with almost the shortest carbon chain in Table III, is oleic acid, thus suggesting (*a*) that the lower homologues in Table I might arise by shortening of the alkyl chain $CH_3\cdot[CH_2]_7\cdot CH{:}$ of oleic acid, and (*b*) that the higher homologues in Table III might similarly be the result of prolongation of the oleic skeleton of carbon atoms by interaction at the carboxyl group with other, shorter-chain, acidic groups. Such possibilities must be regarded for the present, however, as purely speculative.

It is, indeed, probable that the production of homologous monoethenoid acids down to dec-9-enoic acid, which is specific so far only in milk fats, is the result of shortening of the alkyl chain (two carbon atoms at a time) in the oleic groups of blood glycerides during their transformation in the mammary gland into milk-fat glycerides; further similar action may well account for the short-chain saturated acyl groups (butyric, hexoic, etc.) which characterise the milk fats (Hilditch, " Chemical Constitution of Natural Fats ", 2nd Edition, 1947, pp. 117—120, 306—310). On the other hand, the exclusive production of hexadec-9-enoic acid by degradation of oleic acid seems much less likely, since in the fats of aquatic organisms and of some bacteria and of some other lower forms of flora hexadec-9-enoic acid is a major component comparable in amount with that of oleic acid. Apart from the special case of the milk fats, it cannot yet be said that there is any real evidence to support the possible conversion *in vivo* of oleic acid or its glycerides into lower unsaturated homologues.

As regards the acids in Table III, Boekenoogen (*Fette u. Seifen*, **1939**, **46**, 717), who first observed the C_{26} and C_{30} acids of this group in the seed fat of *Ximenia americana*, drew attention to the sequence of increase of four methylene groups between ethenoid and carboxylic groups in the series tetradecenoic–oleic–erucic–ximenic–lumequic acids of vegetable fats; but the implication of this is at present obscure. Moreover, the C_{24} acid conforming with the structural feature of this group is animal in origin, whilst an eicos-11-enoic acid (intermediate between oleic and erucic) has now been shown to be a minor component of seed fats (Cruciferæ) in which erucic acid occurs in quantity. At present, therefore, it seems wise merely to draw attention to the structural resemblances disclosed in Tables I and III, and to regard speculation as to the implications, if any, of the various common constitutional features as largely premature until further evidence can be provided. (Some recent investigations of seed fats of the family Cruciferæ, in which erucic acid is shown to be accompanied not only by small proportions of the eicos-11-enoic acid mentioned, but also by small amounts of a docosadienoic acid, will be referred to later in this discussion.)

Natural Unsaturated Acids which do not contain either of the C_9 *Groupings Present in Oleic Acid.*

Many natural unsaturated fatty acids are known which, unlike those listed in Tables I, II, and III, do not coincide with oleic acid in the constitution of either of the saturated carbon chains of their molecules. These acids, however, again fall into groups in which coincidences of structure are equally as well defined as in the preceding cases.

Natural Cyclic Unsaturated Acids.—A few species of the family Flacourtiaceæ, notably some of the genus *Hydnocarpus*, have long been known to produce seed fats of therapeutic value in leprosy and other skin affections, owing to their content of cyclic unsaturated acids in which the molecule terminates in a *cyclo*pentene group. Of these acids, chaulmoogric, $C_{18}H_{32}O_2$,  $C\cdot[CH_2]_{12}\cdot CO_2H$, and hydnocarpic, $C_{16}H_{28}O_2$, are the most abundant, but Cole and Cardoso

(*J. Amer. Chem. Soc.*, 1939, **61**, 2349) have shown that very small proportions of lower analogues down to $C_6H_8O_2$ accompany them; a cyclic diethenoid acid, $C_{18}H_{30}O_2$ (gorlic acid), is also often present in small quantities in these fatty oils. In chaulmoogra and the related oils, small quantities of oleic glycerides are also present, whilst some other species of this family contain no cyclic unsaturated acids, but only the more usual linoleic and oleic acids.

A summary of the natural cyclic unsaturated fatty acids is given in Table IV.

TABLE IV.

Cyclic unsaturated acids.

$C_{18}H_{32}O_2$	Chaulmoogric	13-*cyclo*Pent-2-enyl-*n*-tridecoic
$C_{18}H_{30}O_2$	Gorlic	13-*cyclo*Pent-2-enyl-*n*-tridec-6-enoic
$C_{16}H_{28}O_2$	Hydnocarpic	11-*cyclo*Pent-2-enyl-*n*-undecoic
$C_{14}H_{24}O_2$	Alepric	9-*cyclo*Pent-2-enyl-*n*-nonoic
$C_{12}H_{20}O_2$	Aleprylic	7-*cyclo*Pent-2-enyl-*n*-heptoic
$C_{10}H_{16}O_2$	Aleprestic	5-*cyclo*Pent-2-enyl-*n*-pentoic
$C_6H_8O_2$	Aleprolic	*cyclo*Pent-2-enylcarboxylic

Natural Unsaturated Acids with a Common Grouping, ${:}CH\cdot[CH_2]_4\cdot CO_2H$.—An isomer of oleic acid, *cis*-octadec-6-enoic (petroselinic) acid, was discovered by Vongerichten and Köhler (*Ber.*, 1909, **42**, 1638) in parsley-seed oil, and has since been found to be present in all other seed fats of the Umbelliferæ which have been examined, and also in the seed fat of ivy and of a few rare species of tropical plants belonging to the Simarubaceæ. No diethenoid acid similarly corresponding to linoleic acid has yet been reported, but Heiduschka and Luft (*Arch. Pharm.*, 1919, **257**, 33) observed that the fatty oil from evening-primrose seeds contains an octa-6 : 9 : 12-trienoic acid isomeric with linolenic acid; whilst as already mentioned the cyclic gorlic acid contains an ethenoid bond in the aliphatic chain in the Δ^6-position.

Perhaps the most arresting feature in this group, however, is the occurrence of a natural ethynoid acid, tariric acid, in the seed fats of a few species of *Picramnia*, a South American genus of the Simarubaceæ family. This almost unique appearance of an acetylenic fatty acid has been rivalled recently by the discovery of a still more unusual acid in the glycerides of the seed fat of *Onguekoa Gore*, a West African shrub, a fatty oil which is also abnormal in its content of hydroxy-unsaturated glycerides. Steger and van Loon (*Fette u. Seifen*, 1937, **44**, 243) first reported the presence in the fat of a diethynoid acid which they termed isanic acid, but Boekenoogen (*ibid.*, p. 344) and Castille (*Annalen*, 1939, **543**, 104) showed that the acid (termed by them erythrogenic acid) was even more remarkable in that it contained a terminal vinyl group and two acetylenic groups; it differs from tariric acid in that the first acetylenic group is in the Δ^9 and not the Δ^6 position; and its possible structures are shown in Table V, which also incorporates the other natural unsaturated acids which belong structurally to this group. It will be noticed that all the acids in Table V belong to the C_{18} series.

TABLE V.

Ethenoid and ethynoid acids, $R\cdot C(H){:}C(H)\cdot[CH_2]_4\cdot CO_2H$.

$C_{18}H_{34}O_2$	Octadec-6-enoic (petroselinic)	$CH_3\cdot[CH_2]_{10}\cdot CH{:}CH\cdot[CH_2]_4\cdot CO_2H$
$C_{18}H_{30}O_2$	Octadeca-6 : 9 : 13-trienoic	$CH_3\cdot[CH_2]_4\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot[CH_2]_4\cdot CO_2H$
$C_{18}H_{32}O_2$	Octadec-6-ynoic (tariric)	$CH_3\cdot[CH_2]_{10}\cdot C\vdots C\cdot[CH_2]_4\cdot CO_2H$
$C_{18}H_{20}O_2$	Octadec-17-endi-9 : (11 or 15)-ynoic	$CH_2{:}CH\cdot[CH_2]_4\cdot C\vdots C\cdot C\vdots C\cdot[CH_2]_7\cdot CO_2H$ or $CH_2{:}CH\cdot C\vdots C\cdot[CH_2]_4\cdot C\vdots C\cdot[CH_2]_7\cdot CO_2H$

Natural Unsaturated Acids with a Common Grouping, $:CH\cdot[CH_2]_9\cdot CO_2H$.—There remain a few monoethenoid acids in which 9 methylene groups separate the carboxyl group from the double bond. These are illustrated in Table VI.

TABLE VI.

Monoethenoid acids, $CH_3\cdot[CH_2]_n\cdot CH{:}CH\cdot[CH_2]_9\cdot CO_2H$.

$C_{18}H_{34}O_2$	Octadec-11-enoic (vaccenic)	$CH_3\cdot[CH_2]_5\cdot CH{:}CH\cdot[CH_2]_9\cdot CO_2H$
$C_{20}H_{38}O_2$	Eicos-11-enoic	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_9\cdot CO_2H$
$C_{22}H_{42}O_2$	Docos-11-enoic (cetoleic)	$CH_3\cdot[CH_2]_9\cdot CH{:}CH\cdot[CH_2]_9\cdot CO_2H$

Vaccenic acid was first observed by Bertram (*Biochem. Z.*, 1928, **197**, 433) in beef fat and butter fat, in both of which it is present only in minute proportions; Bertram considered it to be *trans*-octadec-11-enoic acid in view of the scission products obtained from it on oxidation.

Since his work appeared, the structure of the acid does not appear to have received independent confirmation. Boeseken, van Krimpen, and Blanken (*Rec. Trav. chim.*, 1930, **49**, 247), however, showed that *trans*-octadec-11-enoic acid, identical with the natural vaccenic acid, was present amongst the products of partial hydrogenation of elæostearic esters.

Eicos-11-enoic acid was first observed by McKinney and Jamieson (*Oil and Soap*, 1936, **13**, 289) and by Green, Hilditch, and Stainsby (*J.*, 1936, 1750) in the seed-wax of *Simmondsia californica*, a plant which is peculiar in elaborating waxes (esters of eicosenoic and erucic acids with eicosenyl and docosenyl alcohols) and not glycerides in its seeds. In 1946, Hopkins (*Canadian J. Res.*, 1946, **24**, B, 211) observed that small proportions of the same acid accompanied erucic, linoleic, and oleic acids in the seed oil of hare's ear mustard (*Conringia orientalis*, Cruciferæ), and subsequently we have found that, although previously overlooked, it is similarly present in rape-seed oil and mustard-seed oil (see also p. 248).

Cetoleic acid is a docosenoic acid present in small proportions in most fish fats.

Unsaturated Acids in Fatty Oils from Aquatic Sources.

It was mentioned earlier that polyethenoid acids with four, five, and six double bonds are very prominent in fatty oils from aquatic flora and fauna; these acids appear to be constituted quite differently from any which we have considered up to the present point in this discussion, and also from the monoethenoid fatty acids which occur along with them in fats of aquatic origin.

Monoethenoid Acids of Marine-animal Fats.—To emphasise this point, it is desirable to tabulate (Table VII) the monoethenoid acids so far encountered in marine fats, although these have already appeared in one or other of Tables I, III, and VI. It is apparent from Table VII that no simple relationship, such as those to which attention has been drawn in the preceding tables, seems to be characteristic of the "marine" monoethenoid acids. The grouping $\cdot C\cdot[CH_2]_7\cdot C\cdot$ occurs, however, in all but one of these acids, whilst in the C_{20} and C_{22} members of the series the system $\cdot C\cdot[CH_2]_9\cdot C\cdot$ also appears.

TABLE VII.

Monoethenoid acids of marine-animal fats.

$C_{14}H_{26}O_2$	Tetradec-5-enoic (sperm-head)	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_3\cdot CO_2H$
$C_{14}H_{26}O_2$	Tetradec-9-enoic (myristoleic)	$CH_3\cdot[CH_2]_3\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$
$C_{16}H_{30}O_2$	Hexadec-9-enoic (palmitoleic)	$CH_3\cdot[CH_2]_5\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$
$C_{18}H_{34}O_2$	Octadec-9-enoic (oleic)	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$
$C_{20}H_{38}O_2$	Eicos-9-enoic (gadoleic)	$CH_3\cdot[CH_2]_9\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$
$C_{22}H_{42}O_2$	Docos-11-enoic (cetoleic)	$CH_3\cdot[CH_2]_9\cdot CH{:}CH\cdot[CH_2]_9\cdot CO_2H$
$C_{24}H_{46}O_2$	Tetracos-15-enoic (selacholeic)	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_{13}\cdot CO_2H$

Polyethenoid Acids of Marine-animal Fats.—When we turn to the corresponding polyethenoid acids (Table VIII) a completely different type of structure is encountered, in which the only resemblance to other natural polyethenoid acids is the frequent occurrence of the pentadiene system $\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot$. The most striking difference from other natural unsaturated fatty acids is the point (usually Δ^4) at which unsaturation begins, the unsaturated molecules terminating almost invariably in the system $\cdot CH{:}CH\cdot[CH_2]_2\cdot CO_2H$.

TABLE VIII.

Polyethenoid acids of marine-animal fats.

$C_{16}H_{26}O_2$	Hexadecatrienoic (hiragonic)	$\Delta^{6:10:14}$
$C_{16}H_{24}O_2$	Hexadecatetraenoic	$\Delta^{4:8:11:14}$ or $\Delta^{4:9:12:15}$
$C_{18}H_{28}O_2$	Octadecatetraenoic (moroctic)	$\Delta^{4:8:12:15}$
$C_{20}H_{32}O_2$	Eicosatetraenoic (arachidonic)	$\Delta^{4:8:12:16}$
$C_{20}H_{30}O_2$	Eicosapentaenoic	$\Delta^{4:8:12:15:18}$
$C_{22}H_{34}O_2$	Docosapentaenoic (clupanodonic)	$\Delta^{4:7:11:15:19}$ or $\Delta^{4:8:11:15:19}$ or $\Delta^{4:8:12:15:19}$
$C_{22}H_{32}O_2$	Docosahexaenoic (clupanodonic)	$\Delta^{4:8:12:15:18:21}$ or $\Delta^{4:8:11:14:17:20}$
$C_{24}H_{36}O_2$	Tetracosahexaenoic (nisinic)	$\Delta^{4:8:12:15:18:21}$

The structures given in Table VIII are as allocated by Tsujimoto, Toyoma, and other Japanese workers. Farmer and van den Heuvel (*J.*, 1938, 427; *J. Soc. Chem. Ind.*, 1938, **57**, 24) isolated methyl docosahexenoate from the acids of cod-liver oil by use of the molecular still, thereby avoiding risk of isomerisation and polymerisation by exposure to a temperature above 120°; from the scission products obtained by oxidation of the ester they deduced that the acid contained four $:CH\cdot CH_2\cdot CH:$ groups and one $:CH\cdot[CH_2]_2\cdot CH:$ group between the terminal groups $CH_3\cdot CH:$ and $:CH\cdot[CH_2]_2\cdot CO_2H$. Their docosahexaenoic acid therefore possessed one of the following structures :

$\Delta^{4:8:11:14:17:20}$	$CH_3\cdot CH[:CH\cdot CH_2\cdot CH]_4:CH\cdot[CH_2]_2\cdot CH:CH\cdot[CH_2]_2\cdot CO_2H$
$\Delta^{4:7:11:14:17:20}$	$CH_3\cdot CH[:CH\cdot CH_2\cdot CH]_3:CH\cdot[CH_2]_2\cdot CH:CH\cdot CH_2\cdot CH:CH\cdot[CH_2]_2\cdot CO_2H$
$\Delta^{4:7:10:14:17:20}$	$CH_3\cdot CH[:CH\cdot CH_2\cdot CH]_2:CH\cdot[CH_2]_2\cdot CH[:CH\cdot CH_2\cdot CH]_2:CH\cdot[CH_2]_2\cdot CO_2H$
$\Delta^{4:7:10:13:17:20}$	$CH_3\cdot CH:CH\cdot CH_2\cdot CH:CH\cdot[CH_2]_2\cdot CH[:CH\cdot CH_2\cdot CH]_3:CH\cdot[CH_2]_2\cdot CO_2H$
$\Delta^{4:7:10:13:16:20}$	$CH_3\cdot CH:CH\cdot[CH_2]_2\cdot CH[:CH\cdot CH_2\cdot CH]_4:CH\cdot[CH_2]_2\cdot CO_2H$

Whilst there is general agreement in the above data that unsaturation begins at the Δ^4 position in the fatty acid chain in these polyethenoid acids from marine sources of fat, Dolby, Nunn, and Smedley-MacLean (*Biochem. J.*, 1940, **34**, 1422) and Mowry, Brode, and Brown (*J. Biol. Chem.*, 1942, **142**, 671, 679) concur in finding that the arachidonic acid in animal adrenal phosphatides is eicosa-5 : 8 : 11 : 14-tetraenoic acid. This may indicate that the arachidonic acid of land animals differs from that in marine fats. However this may be, these highly unsaturated acids of natural fats stand quite apart in their constitution from any of the other natural unsaturated fatty acids, and therefore appear to be the result of quite independent synthetic processes from those which determine the production of oleic, hexadecenoic, linoleic, and most other unsaturated acids of natural fats.

Characteristic Unsaturated Acids in the Seed Fats of the Cruciferæ.

In the foregoing discussion nearly all the known natural unsaturated fatty acids have been displayed in groups which reflect well-marked similarities in their structure. It is equally interesting to consider the different types of unsaturation which are found together in fats of related biological origin (as, for instance, the fats from marine fauna which give rise to the complex mixture of unsaturated fatty acids dealt with in the preceding section). Another example which seems worthy of brief reference is the mixture of acids present in seed fats of the family Cruciferæ, both because it exhibits well-marked features peculiar to this family, and because very recent work has added to our knowledge of this group.

The mixture of acids present in these seed fats is peculiarly difficult to determine quantitatively, but a recent analysis of the component acids in a typical rape-seed oil has given the following data, which probably give a good approximate picture of the general nature of these fats :

Saturated acids, %	Palmitic, 2·5; stearic, 1·5; arachidic–behenic–lignoceric, 3.
Unsaturated C_{16} acids, %...........	Hexadecenoic, 1.
,, C_{18} acids, %...........	Oleic, 13; linoleic, 16; linolenic, 9.
,, C_{20} acids, %...........	Eicosenoic, 5.
,, C_{22} acids, %...........	Erucic, 48; docosadienoic, 1.

The " newcomers " to this group are hexadecenoic (now recognised as a trace constituent of most vegetable seed fats, *cf.* Hilditch and Jasperson, *J. Soc. Chem. Ind.*, 1938, **57**, 84), the eicosenoic acid first observed in hare's ear mustard-seed oil by Hopkins (*loc. cit.*), and the small amount of docosadienoic acid which accompanies the large proportion of erucic acid in these fats and which was first detected by Hilditch, Laurent, and Meara (*J. Soc. Chem. Ind.*, 1947, **66**, 19). Hopkins, in his communication on hare's ear mustard-seed oil, suggested that the eicosenoic acid which he had proved to be present therein might be either absent from other Cruciferæ (*e.g.*, *Brassica*) seed fats, or that its presence in small quantities might have been overlooked. Further work by Baliga in my laboratory shows that the latter explanation is the correct one, and we have now isolated the acid from, and determined its approximate proportion in, several specimens of rape-seed oil.

Again, the facts that ester-fractions of the unsaturated C_{22} acids from an ordinary mustard-seed oil (Hilditch, Laurent, and Meara, *loc. cit.*) showed somewhat higher unsaturation than that due to methyl erucate alone, and that on treatment with alkali at 180° they gave rise to an absorption band at 234 mμ indicative of conjugated diene unsaturation, indicated the presence of small amounts of a docosadienoic acid. We have since confirmed this in a number of rape-seed oils, and have isolated the dienoic acid and determined its constitution, namely, docosa-13 : 16-dienoic acid. These results will be communicated in detail in a future paper, but may be briefly summarised here.

These minor component unsaturated acids are concentrated, during the determination of the total component acids, in the fraction of the total acids which is most soluble in acetone at a low temperature, and which contains nearly all the oleic, linoleic, and linolenic acids, with some erucic acid, in addition to most of the small amount of hexadecenoic, eicosenoic, and docosadienoic acids present. An example of the ester-fractions obtained on distillation of the methyl esters of typical concentrates of this kind from rape-seed oils is given in Table IX, together with the theoretical equivalents and iodine values of the individual methyl esters which may be present.

TABLE IX.

Typical fractionation data for methyl esters of unsaturated acids from a rape-seed oil.

Fract. No.	Wt., g.	Equiv.	Iodine value.
1	3·5	269·8	66·9
2	4·2	289·1	132·4
3	6·1	292·4	149·3
4—9	32·9	293·4—294·5	153·6—154·9
10	4·7	294·9	152·5
11	4·1	308·2	124·2
12	5·1	323·4	92·5
13	4·9	327·6	85·6
14	8·6	349·9	79·8
15—17	12·6	350·8—355·6	77·0—78·4

Ester.	Equiv.	Iodine value.
Methyl hexadecenoate	268·0	94·8
,, oleate	296·0	85·8
,, linoleate	294·0	172·8
,, linolenate	292·0	261·2
,, eicosenoate	324·0	78·4
,, erucate	352·0	72·2
,, docosadienoate	350·0	145·1

In many earlier fractional distillations of rape-seed oil esters we had often noticed the regular occurrence of small fractions with equivalents in the region of 324 ± 2, but had regarded them as intermediate mixtures between the large bulks of unsaturated C_{18} and C_{22} esters in process of separation. In view of Hopkins's work, however, we accumulated sufficient fractions of this nature for further examination; as expected, they indeed still contained both unsaturated C_{18} and C_{22} esters, but, by refractionation, we eventually obtained specimens, approximating in equivalent and iodine value to those of methyl eicosenoate, which were undoubtedly esters of an eicosenoic acid. Derivatives prepared from this acid, and the scission products obtained by oxidation of its ester, in all respects confirmed Hopkins's conclusion that the acid was eicos-11-enoic acid.

Similar study by Baliga of accumulated fractions of the nature of nos. 14—17 in Table IX, by means of somewhat tedious concentration of the diene acid by low-temperature crystallisation from acetone or ether, eventually led us to an acid with iodine value 130 (calc., 151·2) which was a mixture of about two-thirds of the dienoic acid with one-third of erucic acid. Scission-oxidation of the methyl esters from the concentrate of the acid yielded brassylic and hexoic acids, thus establishing its structure as docosa-13 : 16-dienoic acid. The acid yielded a crystalline tetrabromobehenic acid which melted at 106—107°.

The group of homologous unsaturated fatty acids containing 18, 20, and 22 carbon atoms in rape- and mustard-seed oils (and probably in most other Cruciferæ seed fats) thus presents the interesting relationships shown in Table X. It will be seen at once that in each the unsaturated groups are situated at the end of the molecule remote from the carboxyl group, *i.e.*, they are all structurally derived from the system $CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot$. (The structure of the hexadecenoic acid in rape-seed oil, as in other seed fats, has been found to be the same as that of the acid in fats from other classes of fauna and flora, namely, hexadec-9-enoic acid.)

TABLE X.

Unsaturated C_{18}, C_{20}, and C_{22} acids in Cruciferæ seed fats.

$C_{18}H_{30}O_2$	Linolenic	$CH_3\cdot CH_2\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$
$C_{18}H_{32}O_2$	Linoleic	$CH_3\cdot[CH_2]_4\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$
$C_{18}H_{34}O_2$	Oleic	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$
$C_{20}H_{38}O_2$	Eicosenoic	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_9\cdot CO_2H$
$C_{22}H_{42}O_2$	Erucic	$CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot[CH_2]_{11}\cdot CO_2H$
$C_{22}H_{40}O_2$	Docosadienoic	$CH_3\cdot[CH_2]_4\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot[CH_2]_{11}\cdot CO_2H$

The Origins of Oleic and Linoleic Glycerides in Seed Fats. Some Facts and a Few Speculations.

One is reluctant to conclude without brief reference to the fascinating topic of biosynthesis of fatty glycerides in the ripening seed. Such reference may be profitably mainly restricted to the experimentally ascertained facts at present available, since these are still insufficient to warrant any attempt at even partial explanation of the chemical processes involved.

That seed fats are built up from pre-formed sugars—probably mainly hexoses—is well established; some data from one of the classical studies of du Sablon (*Rev. gén. Bot.*, **1897**, **9**, **313**) are reproduced (Table XI) to illustrate this.

TABLE XI.

Carbohydrate and fat contents in almonds during ripening.

	June 9.	July 4.	August 1.	September 1.	October 4.
Glucose, %	6·0	4·2	0	0	0
Sucrose, %	6·7	4·9	2·8	2·6	2·5
Starch, %	21·6	14·1	6·2	5·4	5·3
Fat, %	2·0	10·0	37·0	44·0	46·0

No intermediate products between sugar and fatty acids having yet been isolated, the many attempts which have been made to explain the mechanism involved are largely conjectural. It is perhaps fair to say that, on the whole, it seems likely that initial breakdown of hexose *via* pyruvic acid to an acetaldehyde-like nucleus, followed by condensation of this to give aldol-like rather than polyene aldehyde products, forms the basis of the process. The reasons for, on the one hand, the frequent tendency to form the C_{18} chain, and, on the other hand, the production of chains (notably C_{16}, but also C_{12}, C_{14}, C_{20}, or C_{22} in specific biological groups) of carbon content other than C_{18}, are at present obscure, as also are those for the peculiarly definite groupings in the unsaturated fatty acids which have formed the main topic of this discussion.

Two aspects of the elaboration of seed-fat glycerides are, however, quite clearly established by experimental observation : (*a*) in the early stages of ripening, free fatty acids predominate, and the final fat consisting of neutral triglycerides is only fully developed at a comparatively late stage of maturity, and (*b*) the mean unsaturation of a seed fat (which at maturity is relatively highly unsaturated) usually at first only slightly exceeds that of monoethenoid glycerides, rapid increases in unsaturation occurring at a late stage in the ripening of the seed. These facts were first noted by Ivanow (*Beihefte bot. Zent.*, 1912, **28**, 159) in the ripening seeds of rape, hemp, poppy, and flax, and the final rapid increase in unsaturation is illustrated in Table XI by some figures from subsequent work by Vargas Eyre (*J. Agric. Sci.*, 1915, **7**, 120; *Biochem. J.*, 1931, **25**, 1902) on ripening linseed.

TABLE XI.

Development of fatty oil, and of its unsaturation, in ripening flax seed.

Days after flowering.	Oil (dry seeds), %.	Iodine value.
10	2·5	114
14	15·1	119
17	31·1	127
23	37·0	143
28	36·9	170
35	36·8	180
51	36·3	190

Exactly similar sequences of changes have since been observed during ripening of cottonseed (Caskey and Gallup, *J. Agric. Res.*, 1931, **42**, 671; Lonzinger and Raskina, *Maslob. Shir. Delo*, 1931, Nos. 2—3, 57), niger seed (Sahasrabuddhe, *Indian J. Agric. Sci.*, 1932, **3**, 57), soya bean (Rewald and Riede, *Biochem. Z.*, 1933, **260**, 147), and lupins (Neumann, *ibid.*, 1941, **308**, 141). Clearly, the ultimate production of a mixture of unsaturated fatty acids in which more linoleic acid than oleic acid is present than at earlier stages can arise in one of two ways : (*a*) desaturation of pre-formed oleic glycerides, or (*b*) preferential synthesis in the later stages of linoleic rather than oleic acid. Unfortunately, results so far published are expressed on a percentage basis, whereas an attempt to assess the total amount of these fatty acids produced at different stages (*e.g.*, per 100 or per 1000 fruits) might have enabled this important point to be settled. Perhaps it is permissible to feel, in the absence of direct evidence, that the synthesis from the products of sugar metabolism is more likely to lead to different fatty acids at different stages of seed maturity than that a dehydrogenation of pre-formed oleic acid is involved. It is also perhaps pertinent here to refer to recent work by E. H. Farmer and others which has defined the special characteristics of the pentadiene grouping, $\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot$, with its central " reactive " methylene group, and to suggest that, just as this system behaves specifically in its reactivity with oxygen or with hydrogen, so also it may on occasion serve as a specific halting point in the biosynthesis of unsaturated fats : it certainly appears with great frequency in these compounds.

A more practical point is that, under different conditions, seeds of a given species may yield fats in which the proportions of oleic and linoleic acid vary somewhat widely. It is possible to illustrate this from the results of many component acid analyses of seed fats, a selection of which is given in Table XII. The causes of the variation are not clearly differentiated, but the instances given in Table XII show that (*a*) the specific variety of a plant species, (*b*) the climatic (especially temperature and humidity) conditions of growth, and (*c*) the nature of the soil and probably other factors can all influence the composition of the seed fat.

TABLE XII.*

Variation in oleic and linoleic acid contents of some seed oils from different sources.

	Iodine value.	Component acids, %. Satd.	Oleic.	Linoleic.	Linolenic.
Groundnut oil (Leguminosæ) :					
India	93	23	46	31	—
Nigeria	86	19	61	20	—
Argentina	100	25	42	33	—
Soya bean oil (Leguminosæ) :					
" Dunfield " var., Missouri 1936	103	12	59	28	1
,, ,, 1937	124	13	33	51	3
,, Indiana 1937	127	13	31	53	3
Linseed oil (Linaceæ) :					
" Bison " var., Minnesota	163	11	30	18	40
,, Saskatchewan	187	9	22	15	54
" Redwing " var., Minnesota	182	10	23	15	52
,, Saskatchewan	195	8	16	18	57
Niger-seed oil (Compositæ) :					
West Africa	136	12	16	72	—
India	129	9	39	52	—
Safflower-seed oil (Compositæ) :					
Carthamus tinctorius, U.S.A.	149	7	26	67	—
,, India	136	6	33	61	—
C. oxyacantha, India	112	7	56	37	—
Sunflower-seed oil (Compositæ) :					
Europe	136	11	22	67	—
U.S.A.	131	7	34	59	—
India	112	10	49	41	—

* The data in Table XII are due to the following authors : soya bean oils, Dollear, Krauczunas, and Markley (*Oil and Soap*, 1938, **15**, 263); linseed oils, Painter and Nesbitt (*ibid.*, 1943, **20**, 208); niger seed oil (India), Vidyarthi and Mallya (*J. Indian Chem. Soc.*, 1940, **17**, 87); safflower (India, *C. tinctorius*), Vidyarthi (*ibid.*, 1943, **20**, 45); (U.S.A.) Jamieson and Gertler (*Oil and Fat Ind.*, 1929, **6**, No. 4, 11); sunflower (U.S.A.), Baughman and Jamieson (*J. Amer. Chem. Soc.*, 1922, **44**, 2952); sunflower and *C. oxyacantha* (India), Kumar (Thesis, University of Allahabad, 1947). The figures for the groundnut oils, niger-seed (West Africa), and sunflower seed (Europe) oils are from work in the Department of Industrial Chemistry, University of Liverpool.

Variations due to botanical variety may possibly operate in the group of groundnut oils, and almost certainly do so in the two nearly-related species of *Carthamus* (Indian safflower-seed oils); the clearest illustration of this influence in Table XII is, however, the different composition of oils from " Bison " and " Redwing " varieties of *Linum usitatissimum* when grown in the same locality (*e.g.*, Minnesota).

It has become recognised that seed of the same variety grown in climates in which the mean temperature is markedly different yields a more unsaturated fatty oil in the colder regions; this is well illustrated by the increased linolenic and diminished oleic acid contents of the two varieties of linseed grown in Saskatchewan as contrasted with those from Minnesota. Temperature is not, however, the only factor involved : thus the " Dunfield " variety of soya bean grown in Missouri in two successive seasons yielded oils widely different in their oleic and linoleic contents. In 1936 the season was not only abnormally hot but also abnormally dry, and the unusually low unsaturation of the oil from the 1936 crop is attributed by Dollear *et al.* (*loc. cit.*) to other environmental factors as well as to temperature.

The data for the three *Compositæ* seed fats in Table XII emphasise these points in three oils which have some technical interest as " drying oils ", thus suggesting that the choice of site and cultivation of such crops must be carefully considered from the standpoint of the component acids produced in the seed oils. The Indian sunflower-seed oil quoted is exceptionally interesting in this respect, since Kumar states that the seed was of known origin—a strain originally brought from Russia to the United States, where it was grown for four generations (which there yielded typical American oil of higher linoleic and lower oleic content) before seed from the fourth generation was used in India and furnished oil with only 41% of linoleic acid in its component acids.

In conclusion, attention may be directed to the importance of detailed analyses of the unsaturated acids in oils thus grown for technical purposes, and also to the possibility of undertaking further studies of the development of the fatty components as the seeds ripen, in order to obtain much needed further information as to what takes place. In the United States, work of this kind is being undertaken at research centres within reach of the crops, and it should be stressed that such studies should be carried on near the areas of cultivation of the oilseed crops. It appears important that, where large-scale cultivation of different oil-bearing seeds is contemplated or in progress in tropical or sub-tropical parts of the British Commonwealth, local research stations should not only be concerned with the cultivation problems immediately involved, but should include one or more chemists skilled in the modern techniques of component fatty acid and mixed glyceride determinations, and have facilities to make use of them. Progress can only be slow and uncertain if specimens of oil have to be sent to this country for study, and in the investigation of fat production at progressive stages of the ripening seed it is useless to expect much progress until the experimental chemical work can be carried on close to where the seed is being grown. Since such studies would undoubtedly contribute largely to fundamental knowledge of fatty synthesis in the plant and of the manner in which the many different natural fatty acids—saturated as well as unsaturated—may arise, it is not inappropriate to conclude this lecture by a reference to this important practical point.