· Technical

Lipid Structures

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ABSTRACT

Much of the function of lipids, as in shortenings, confections, biological membranes, etc., depends on the structures they exhibit, i.e., their crystalline and mesomorphic states. Triglycerides may serve as a point of departure for considering the crystal state of lipids. The three principle cross-sectional arrangements of long chains–α, β' and β–in which there is kinship to hydrocarbons, offer a major basis for classification. Different crystal forms are rheologically different. Complications in the chain length direction lead to stepped configurations in the methyl planes and to double and triple chain length structures. A detailed consideration of the time-honored melting point alternation of homologs sheds light on the lipid crystal picture. A startling feature is the catalysis of isomerization by the solid state of diglycerides, with a consequent shift in equilibrium far toward 100% 1,3-diglyceride. Stepwise reversible transformations, as in hydrocarbons, are documented for high molecular weight 1-monoglycerides. A common feature, the sharp drop with mixture of stable form melting points, to "expose" metastable forms as stable forms for intermediate compositions is strikingly exhibited by fatty alcohols. The two bases for mesomorphism, or liquid crystal formation, among lipids are discussed: (1) dichotomy between molecular moieties in degree of polarity, as in phospholipids; and (2) dichotomy in molecular geometry as in cholesteryl esters. The former type is associated with three main basic arrangements–smectic or lamellar, middle or hexagonal (normal and reversed), and viscous isotropic or cubic (normal and reversed). The latter is associated with two main arrangements–cholesteric (essentially limited to cholesteryl compounds) and smectic. The importance of mesomorphism in consideration of membranes and emulsions is emphasized. Developments in understanding the structures of interfacial lipid states (including monomolecular surface films) and the correspondence of interfacial with bulk states is a matter of great continuing interest.

PREFACE

I am most grateful to the Society for the Award, and to the Applied Science Laboratories, and to the many individuals responsible. It is a notable group of recipients that I follow, and I look with admiration on their achievements. As I do so it is not without a little chauvinism that I see how, among other contributions, they have in recent decades brought lipids up from their status as handmaidens in biochemistry and nutrition. Phospholipids, prostaglandins, acid metabolism, sterol metabolism now occupy a front row in scientific and practical concern.

Though Heywood Hale Broun of the media deplores that predictable pattern for the modern athlete to chant "It was a great team effort," I may be permitted to say that no chemist is an island, either; he has a laboratory and he has colleagues. Among many colleagues I would mention two–for some 25 years, variously my right and left hand, and a large part of my head–Mr. Fred R. Hugenberg and Mr. Clarence B. Stewart.

At this point in time we hear much of the reordering of priorities in technology and research. Clearly some reordering is overdue, with massive public technical problems crying for solution. And I would take my opportunity to say this: that there can be a splendid interaction between the basic and the practical.

And yet the best progress–however defined–calls for each investigator, each type of investigator, to do largely "his thing." A goose, by way of illustration, may be good at laying eggs–and golden or no, they cannot be laid square nor seven inches in diameter on demand. Before I proceed, I urge you to defend the goose, lest it turn into a passenger pigeon.

INTRODUCTION

I would talk with you of Fatty Structures, not in a molecular sense–the molecules I speak of being all familiar or of familiar type–but rather in a physico-chemical sense.

There has been much and widely scattered talk of such structures, but not enough, perhaps, in the abbreviated but generalized and comprehensive form which I would attempt to present.

STRUCTURE

I would talk of structure, then, in the sense of crystalline vs. liquid structure. Even the gaseous state, essentially without order, may show molecular association as evidenced by the dimerization of acetic acid and by the Van der Waals equation. The crystalline state with an obviously high degree of order, nevertheless, in the case of nearly all real crystals, contains many imperfections and dislocations. These facts of nature complicate our considerations. The character of the intermediate liquid state, to which for sufficient reason we shall return at a later point, is still a subject, perhaps increasingly, of dispute by sophisticated theoreticians.

First let us consider in some detail the crystalline state as it is manifested by lipid matter in butter, in ice cream, in shortenings, in peanut butter, in candy, on certain pond surfaces, in candles, in cosmetic creams, in shoe and furniture waxes, in gallstones, in atheromas, in body fat depots, and perhaps, in cell membranes.

While much useful and still valuable structural information on lipids was developed earlier, rapidly advancing and well-defined understanding of lipid structure dates from the application of x-ray techniques by Alex Müller and colleagues beginning about 1923(1). X-ray diffraction *remains* the tool per excellence for crystal structure study, though microscopy, dilatometry, calorimetry, differential thermal analysis, dielectric measurement, nuclear magnetic resonance, IR spectroscopy has each made and will continue to make its contribution, and of course the several techniques are supplementary.

Müller recognized three different parallel packings of hydrocarbon chains(2) which determine the three different cross-sectional structures of Figure 1. These occur widely among long chain compounds. There is indeed a problem of nomenclature in long chain polymorphism. But two points give me comfort: (1) while good progress toward a general scheme has been made, we are so far from a final solution

[1]E.S. Lutton received the 1971 AOCS Award in Lipid Chemistry at the AOCS Meeting, Atlantic City, N.J., October 1971. The following is his Award Address, presented at the Plenary Session.

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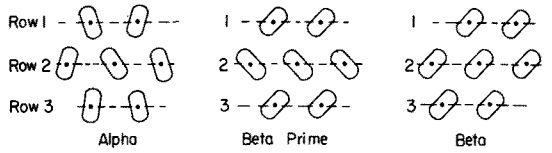

FIG. 1. Cross-sectional structures of long chain compounds.

that it is premature to try for one; and (2) within the limited area of most specific problems, workable nomenclatures have been or can be readily established. The cross-sectional patterns of Figure 1 are given names associated with their occurrence in triglyceride polymorphism, i.e., α, β' and β. The silhouette of the end view of a zig-zag hydrocarbon chain in a crystal is actually an elongated four leaf clover, here depicted as an ellipse.

β' is the most common packing pattern here alternate rows are oppositely oriented; a more sophisticated nomenclature of von Sydow(3) designates this as $0 \perp$ (orthorhombic $\perp$). β has all chain axes oriented in one way; it is T $\parallel$ (or triclinic parallel) in von Sydow's nomenclature. In α the chain axes are randomly oriented. It has hexagonal symmetry and has therefore been called H (for hexagonal).

As polarity of the molecule increases, there is departure from the simple α, β' and β packing, but we cover many cases without much departure from these three.

Without proceeding through Malkin's development(4) we can remember here that he associated α with vertical chain orientation (an association now known to be widely but not universally correct). Melting point alternation between odd and even members of homologous series is not observed when the compounds are α at the melting point. Malkin showed by simple geometrical diagrams how alternation was unlikely for vertical but likely for tilted chains; Larsson, however has since shown that under special circumstances tilted chains need *not* show alternation (5).

TRIGLYCERIDES

The triglycerides being quite nonpolar take on many features of the linear hydrocarbons; they exhibit with rare exceptions only the three cross-sectional structures we have just seen—α, β' and β. But with these more complicated molecules, other types of structure complication arise.

Among saturated triglycerides, tristearin (SSS) is the compound of reference. Its behavior is indicated in Table I.

A more stable form is readily obtained from one less stable, thus $\alpha \rightarrow \beta' \rightarrow \beta$. The three melting points have more than 100 years' history. In 1934 Clarkson and Malkin(9), by diffraction studies, showed them to be based on crystal structure difference. Their proper association with diffraction patterns, sometime in dispute, is now well established and agreed upon.

For the homologous series tricaprin through tristearin, etc.(6), it was early observed that β melting points alternate between odd and even glycerides, but α and β' do not. The nonalternation of tilted β' plus an unexpected but very real variation of melting point for given polymorph resulted in proposal of a fourth (intermediate melting) tristearin form, since discarded. The analysis of Larsson (5) showing how β'

TABLE I

Melting Points of SSS (6), SPS (7) and PSP (8)[a]

Form	SSS	SPS	PSP
α	54.7	51.8	47[b]
β'	64.0	(69.0)[c]	69.0
β	73.3	68.5	(65.5)[c]

[a]SSS = tristearin; SPS = 2-palmitoyl distearin; PSP = 2-stearoyl dipalmitin.

[b]Softening Point.

[c]Obtained with difficulty.

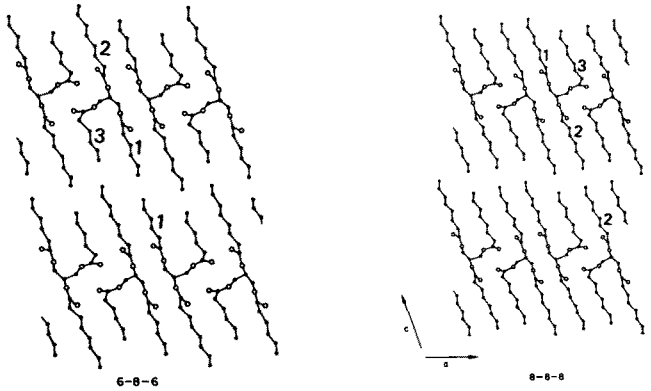

FIG. 2. Comparison of postulated 8-8-8 and 6-8-6 triglyceride structures.

could be tilted yet nonalternating should have resolved any lingering doubts about the polymorphism of tristearin.

With the mixed glyceride (PSP), β, actually lower melting than β', is difficulty obtained—so far only by low temperature crystallization from solvent, preferably with heterogeneous seeding as with succinic acid.

With SPS, β' is difficulty obtained—so for only by long time storage of β crystals in solvent. Again β' is higher melting. The writer, addicted to Ockham's razor, is not persuaded of the occurrence of intermediate forms for mixed C_{16}-C_{18} saturated triglycerides.

Among palmitic-stearic (P-S) triglycerides, and lower homologs as well, it is observed that β-tending compounds, e.g., SSS, crystallizing in volumes of several cc and more, develop an expanded, sometimes almost snow-like structure of quite low bulk density, in striking contrast to the normal solid mass of β'-tending compounds, e.g., PSP. Correlated with this contrast in bulk crystallization behavior there is a difference in stiffening power in oil, β being commonly much less stiffening than β' (10,11).

Larsson has reported (12) and Webb of our laboratory has confirmed (private communication) a herringbone arrangement of the long chains in β' phase. Larsson points out that the process of transformation to β' from vertical-chained α may involve simple collapse, as with an accordian, perpendicular to the methyl planes, while transformation to β with its altogether parallel long chains may involve more cataclysmic chain shifts. It may well be that some such considerations permit the compact β' structures grown from melt or via α, as opposed to the expanded β structures grown via α, although β may be quite compact if developed very slowly from melt or other crystalline states.

In shortening processing, a hardstock, essentially a mixture of fully saturated hydrogenated triglycerides, is present to give heat resistance, i.e., stability at warm temperatures. β-tending SSS, as in soybean hardstock, is the preferred component of hardstock for a family of solid-containing but pumpable shortenings; β'-tending PSP, as in cottonseed hardstock, is a preferred component of hardstock for plastic shortening.

It was early recognized by a combination of physical studies on disaturated components and hydrogenated fractions therefrom that several vegetable oils strongly tend to have saturated acids in the 1 or 1 and 3 positions (13,14) while lard, in striking contrast, has saturated acid, specifically palmitic, in the 2 position (15,16). Such observations immediately negated any principle of random or only slightly modified random distribution of fatty acids in natural fats and pointed directly to some sort of specific distribution, indeed to more than one sort of specific distribution. Enzymatic analysis by the methods of Mattson, Desnuelle and Brockerhoff have greatly extended and quantitated these findings.

The detailed crystal structure of tristearin has not been

TABLE II

Characterization of β Forms of 16-18 Triglycerides

Glyceride	Unchanging chain no.[a]	Slope (up) of triads of methyl groups[b]	Main short spacings
18-18-18	2-2	R	4.61, 3.84, 3.68
18-16-18	3-3	L	4.57, 3.81, 3.72
16-18-16	1-1	L	4.59, 3.82, 3.73
16-18-16	3-3	R	4.61, 3.87, 3.67
16-16-18	1-1	R	4.61, 3.85, 3.67
16-16-16	2-2	R	4.61, 3.84, 3.68

[a]In straight line from tier to tier.
[b]Right or left.

studied because of difficulty in growing crystals of adequate size. But structures have been determined for the lower homolog, e.g., tricaprin in the β phase (17).

A further development with β follows from an effort to explore β' by Doyne and Gordon (18) with 2-11-bromoundecanoyl-1,3-dicaprin. This is essentially a lower homolog of β'-tending PSP with the end methyl of the middle chain ω-substituted by heavy element bromine, helpful in getting diffraction data. Doyne and Gordon's glyceride gave not β' but β and a structure like tricaprin but with a difference. From this difference one can speculate as to the whole array of mixed P-S triglycerides (19). The essence of this speculation is in Figure 2.

Instead of tristearin the 10-carbon shorter glyceride trioctanoin is drawn to correspond as closely as possible to the published tricaprin structure. This substitution does not change the geometric argument. Similarly, 6-8-6 is drawn instead of 16-18-16 or PSP. As Doyne and Gordon have shown in their study, there must be a shift of molecules for 6-8-6 to permit close packing of methyl groups.

The nature of the necessary shifts can be described by focusing on the individual acyl chain which is duplicated in the molecular row immediately below. This requires a recognition of distinction among the three chains, here labeled 1,2 and 3 with 1 and 3 side by side, 1 and 2 in line.

It is the 2 chains which are continuous in the 8-8-8 structure, but the 1 chains in the 6-8-6 structure. Another thing to note is that in the 8-8-8 structure there is a group of three methyls which slopes upward to the right, but in 6-8-6 the slope is upwards to the left.

In Table II are tabulated the variations for all 6-8 or rather 16-18 triglycerides.

In this table the main feature to note is that the methyl group alignment, upward to the right or left, is correlated with a small but definite short spacing variation. Moreover in binary systems with tristearin, it is observed that with like methyl arrangement there is less melting point depression than with unlike methyl arrangement. By such slender reeds, as well as by Doyne and Gordon's structure determination, the speculation is supported; and we await a test of the detailed β crystal structure of a normal mixed triglyceride.

We have not yet encountered all the vagaries of triglyceride structure, for if chain lengths differ sufficiently a new complication creeps in (see Fig. 3). Thus if the middle chain is shorter or, indeed, longer than the other chains, generally by as much as 4 carbons, then there may be a segregation of chains to form triple structures (20).

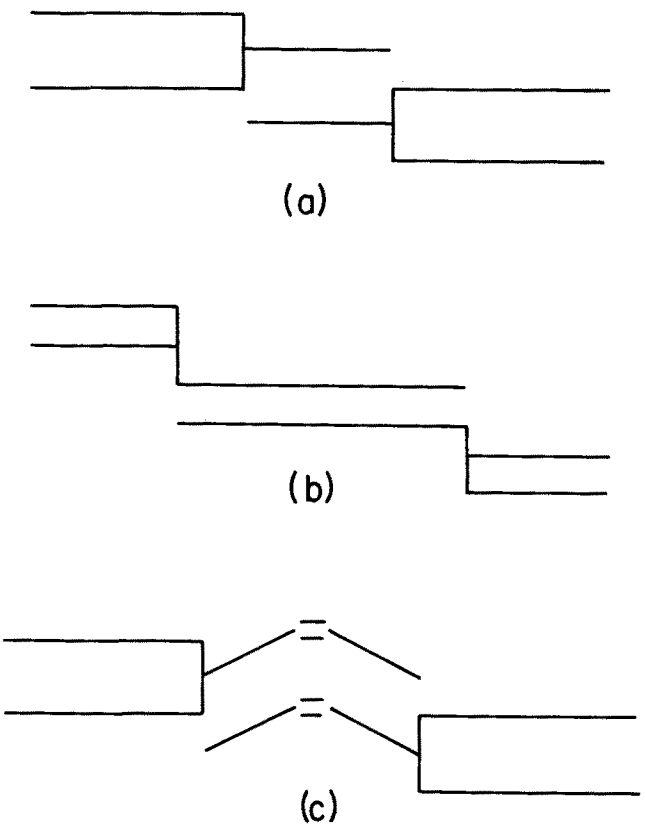

FIG. 3. Triple chain length structures of triglycerides.

TABLE III

Polymorphism of Distearin (23)

1,3-Distearin		1,2-Distearin	
Form	Melting point	Form	Melting point
β-a	77.7	α	59.5
β-b	78.2	β′	71

The same is true if the different chain is in the 1 rather than the 2 position.

These triple structures are of particular interest in the unsaturated case, specifically in the cocoa butter problem. The two main glycerides of cocoa butter are 2-oleoyl distearin (SOS), and (POS). The unsaturated chains segregate like chains of differing length so that SOS and POS and their mixtures, as in cocoa butter, crystallize in a triple chain length stable form, of β cross-sectional type, which has been called β-3 (2). The predominant metastable form of cocoa butter, among several, is a double chain length β′ form (22), and the difficulties in crystallizing cocoa butter may well arise from the profound structural difference between β′-2 and β-3. Certainly the key to finding a compatible extender for cocoa butter is locating another β-3 tending fat of similar melting behavior.

Enrobing materials from coconut oil or palm kernel oil, are almost universally of β′-2 structure and definitely incompatible with cocoa butter. The same is true of randomly esterified C_{16}-C_{18} fats. Only naturally occurring vegetable disaturated or proper synthetic glycerides lead to cocoa butter-compatible alternatives.

DIGLYCERIDES

With the diglycerides we need not linger long, but some interesting points appear. In Table III we see no α for symmetrical diglycerides but a relatively stable α for unsymmetrical, two β-type phases for symmetrical, and one β′ phase for unsymmetrical. Although symmetrical distearin does not form α when pure, with 30% 1-monostearin it forms a vertical-chained metastable α phase with long spacings longer than those of any phase of either component.

One wonders of course whether the two chains of a diglyceride crystallize side by side or extend more or less in opposite directions. Detailed structure study of thio- and brominated symmetrical diglycerides by Larsson (24) and by Hybl and Dorset (25) indicate herringbone type structures, observed before the aforementioned herringbone type β′ triglyceride structures.

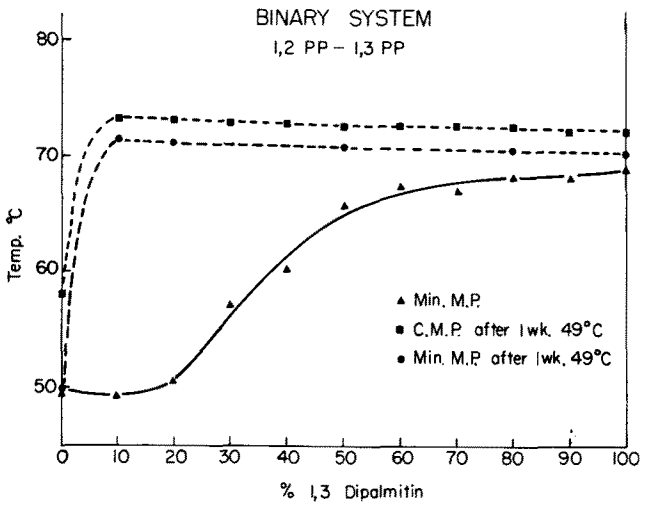

FIG. 4. Conversion of 1,2- to 1,3-dipalmitin in crystalline state.

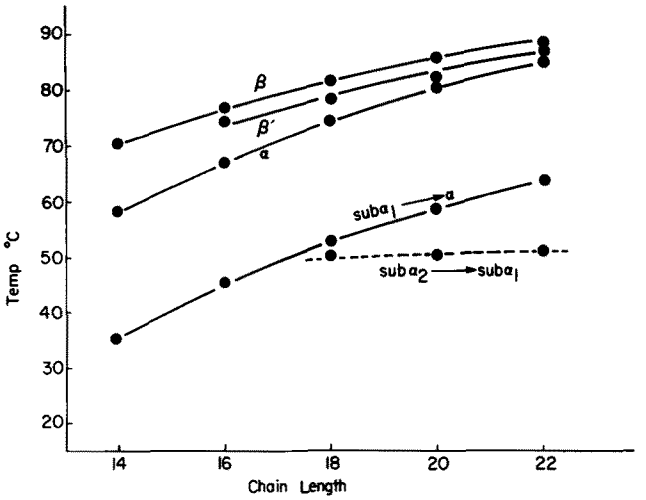

FIG. 5. Polymorphism of 1-monoglycerides.

There is an equilibrium in the liquid state involving primary esterification and secondary esterification. A consequence is a 90:10 1-monoglyceride:2-monoglyceride ratio and a corresponding 60:40 1,3-diglyceride:1,2-diglyceride ratio. There is no *a priori* reason why this equilibrium should remain the same in the solid state and it does not, as some hitherto unreported binary studies of 1,3-dipalmitin–1,2-dipalmitin attest (see Fig. 4).

There seems no other explanation for the flat melting curve at 1,3-dipalmitin melting level than that the presence of 1,3 in the crystalline state with 1,2-dipalmitin catalyzes molecular rearrangement from 1,2 to substantially pure 1,3. The mechanism of this process would seem to deserve exploration.

MONOGLYCERIDES

Monoglycerides with significant polarity show significant new features (26) (see Fig. 5). Again we encounter α, but it is only with some strains that the β and β′ designations can be related to those for triglycerides and hydrocarbons. Important points are the reversible solid-solid α to sub α transformation among glycerides, a startling constancy of long spacings, approximately 50 Å, among the polymorphs, and obviously tilted α chains since the long spacings are obviously shorter than (twice) the molecular length. The bulky end grouping with its two hydroxyls requires the tilting of the chain for reasons of space-filling, even in the α form. The nonalternation of melting points for tilted α seems quite in accord with Larsson's views on alternation. Larsson recognized, from x-ray studies, two β-type forms (27) one of simple herringbone type and one of modified herringbone type. His interesting deduction that the β′ form of racemic 1-monoglycerides corresponds to the stable form of enantiomeric 1-monoglycerides, hence must be a 1:1 mixture of enantiomeric crystals, deserves further exploration.

There are indeed two so-called sub α forms. The two reversible transformations are unexplained structurally, but, in what are probably related cases of vertical chain α, successive stages of increased chain axis disorientation have indeed been observed, and related phenomena have been seen in surface films.

The higher transformation point rises in temperature with chain length, the lower is essentially constant and disappears for C_{16}.

As Larsson has emphasized, the term "sub α" is in some ways objectionable. I use it here with minimal defense. It is operationally useful, referring as it does simply to a lower temperature form (or group of forms) reversibly transformable to α.

TABLE IV

Polymorphisim of Stearyl Alcohol (28)

Form Form	Melting point (or transformation point) C
Sub α	44
α	49
$\beta'(\beta)$[a]	50

[a] β' by the nomenclature of Figure 1; β in most literature.

FATTY ALCOHOLS

Fatty alcohols have a polymorphism even more readily related to that of the hydrocarbons than do the triglycerides, as indicated in Table IV.

Of particular interest is the binary system behavior for C_{16}-C_{18} alcohols (29), which illustrates a number of features (see Fig. 6).

There is a strong tendency for stable forms of long chain compounds to follow the ideal solubility law, i.e., to drop in melting point in predictable fashion with addition of a second component. Such behavior is obscured here by the closeness of α and β' melting points. What is evident is a striking example of continuous solid solution formation and a nearly linear melting point relation for α so that it actually becomes the stable phase at the melting point of intermediate compositions, a phenomenon seen in a number of long chain mixtures. Striking, too, is the remarkable drop in sub α to α transformation point with mixture. It is these mixed compositions with α stability and wide temperature range of α stability that are most effective in evaporation suppression on ponds. There is almost certainly a necessary relationship between this stable bulk α phase, generally more plastic than β' or β, and the flexible self-healing film of the pond surface treated with mixed C_{16}-C_{18} alcohols.

FATTY ACIDS

Departure from the α, β', β chain packing pattern increases with polarity and with unsaturation. Saturated acids exhibit β' and β patterns, but not α. More departure is shown by unsaturated acids, the isooleic acids among them, and still more by dihydroxy acids made from the isooleics.

ISOOLEIC ACIDS

Isooleic acids, the isomeric octadecenoics, have long been recognized products of hydrogenation; in 1947, vaccenic was erroneously, as it turned out, reported to have special growth-promiting activity and received much attention.

A series of isooleics, both *cis* and *trans* monooctadecenoic acid from 6:7-12:13, was synthesized by Huber (30). Both *cis* and *trans* series were found to have alternating melting points, with dimorphism of elaidic since reported by Harris et al. (31). For *trans* acids, the principal contributors to so-called isoleic, alternating diffraction patterns were reported (32).

The dihydroxy stearic acids made from isooleic acids by performic acid treatment were subjected to detailed study (33). An alternation in melting point, and an alternation in long spacings separated "odd," i.e., 7,8-dihydroxy, etc., from "even," i.e., 8,9, etc., but intensity analysis of x-ray diffraction lines was employed to distinguish individual "odd" and individual "even" acids. The several orders of long spacing lines had characteristic and calculable relative intensities according to hydroxyl position on the acids.

Employing the intensity feature to explore the composition of hydrogenation octadecenoics met with only moderate success, but sufficient to show that there was not simply 9-octadecenoic and 12-octadecenoic, as to be expected from hydrogenated linoleic acid, but a wide mixture of at least most of the acids from about 7-13 octadecenoic, a conclusion since confirmed by ozonization and by chromatography (34).

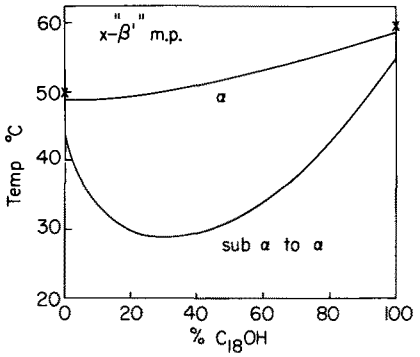

FIG. 6. Binary system of C_{16}-C_{18} alcohols.

MESOMORPHIC STATE

And now we turn from crystalline to other ordered lipid states, often called liquid crystalline, the first report of which was that of Reinitzer (35) some 83 years ago. A better term is mesomorphic (for intermediate in form between crystalline and liquid). It may or may not be quite correct to regard the ultimate element of these states as a combination of a crystal-like portion and a liquid-like portion, but almost certainly a region of the structure is characterized by strong forces as in a crystal and a region, generally much the larger, by weaker forces as in a liquid. We have recognized the high degree of order in a crystal but have had little to say about liquids. There has been a fashion, supported by some theoretical development, to regard the liquid state as essentially composed of micro crystals; by another view, liquids are truly noncrystalline, exhibiting a close-packed disorder which is not, however, without forces between molecules and parts of molecules. I prefer the latter view for liquids and for that generally larger portion of mesomorphic states which is characterized by weaker forces.

Lipid chemistry must recognize two different bases for mesomorphic state formation. The first and more familiar type involves a contrast in ionic or polar character of portions of the molecule as in the case of soaps. Phospholipids, also of ionic character, have received much attention in the last decade, with great clarification of some mesomorphic aspects by Luzzati, Chapman and Small, among others.

There are apparently many mesomorphic structural types which can appear for polar lipids. One generally needs to consider only five, among which are two pairs, hence but three major basic schemes of arrangement (see Fig. 7).

It is smectic or layered structure or neat phase which is clearly the most important and widely occurring. It is a slice of such a phospholipid-based structure which, with some modification, corresponds beyond reasonable doubt to the biological bilayer membrane. The disposition of

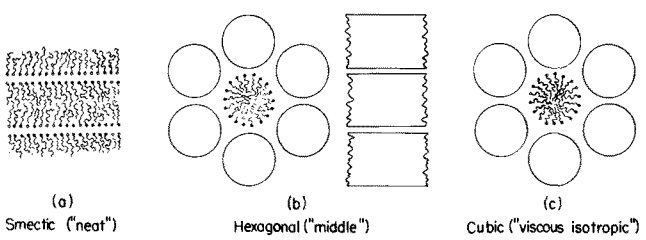

FIG. 7. Some proposed mesomorphic structures of polar lipids.

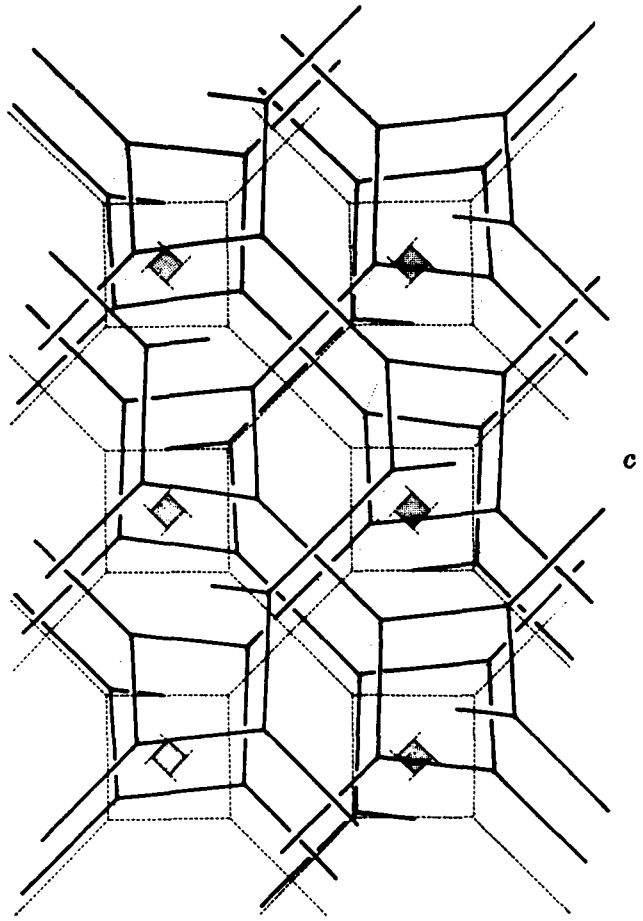

FIG. 8. Proposed viscous isotropic structure.

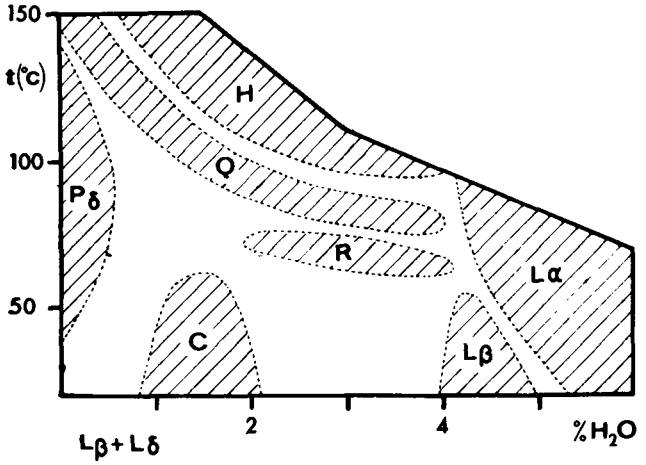

FIG. 9. Phase behavior of aqueous egg lecithin system.

cholesterol, for instance, in such a structure is a problem; surely it is there in considerable disorder as though dissolved but perhaps with hydroxyl group in the polar portion. More difficult is the disposition of protein; it, too, is probably present in some disorder, with polar portions attracted to the aqueous region and nonpolar portions attracted to the hydrocarbon region. The geometry of membrane-lipid-requiring enzymes is a part of protein chemistry which still needs much study.

Next in order of prevalence among mesomorphic states is hexagonal or middle. Its structure as proposed by Luzzati et al. (36) and now widely accepted is here depicted. The middle phase of soap is of this sort, with hydrocarbon interiors and aqueous exteriors to the close-packed cylinders which are not rigid but must exist like close-packed snakes essentially everywhere parallel throughout the structure.

An inverted structure, reversed hexagonal or reversed middle, must be recognized with polar interiors and hydrocarbon exteriors to its cylindrical elements. (We deal here, of course, with a situation like the micelles of detergents in water with their hydrocarbon interiors, as opposed to the micelles of polar compounds in organic solvents with their polar interiors. In general the interior regions of the structured element are present in lesser proportions.)

Unnecessary as it may be, it seems well to remove any possible confusion between hexagonally packed crystalline α and hexagonal mesomorphic middle. The close-packed rods of α are individually long hydrocarbon chains of about 4 Å diameter. The close packed rods or cylinders of middle phase are columns of many chains, the columns being some 40 Å in diameter.

A remarkable state not finally characterized as to structure is the viscous isotropic phase encountered with many polar long chain compounds. It is easy to suppose that this state involves cubic structure as of close packed spherical micelles, and here, too, one must recognize two cases, one with nonpolar and one with polar interiors.

There is experimental support for this close packing of spheres, but the best such evidence I know involves "worked" or manipulated specimens which may not indicate fully the basic structural tendency.

I am drawn to Luzzati and Spegt's somewhat different proposal (37), complicated though it may be, of two interpenetrating networks, each network built of triply connected short cylinders like portions of hexagonal phase cylinders, the whole being of cubic symmetry, hence isotropic (see Fig. 8).

What appeals to me in this proposal for viscous isotropic, which often occurs in a phase diagram between smectic and hexagonal, is that it permits the same double continuity of both polar and nonpolar regions, as is clearly recognizable in smectic and hexagonal structures, but as cannot exist in the packing of spheres.

PHOSPHOLIPIDS

What phases, then, do phospholipids show? We shall give only limited consideration to their complex behavior as indicated in Figure 9.

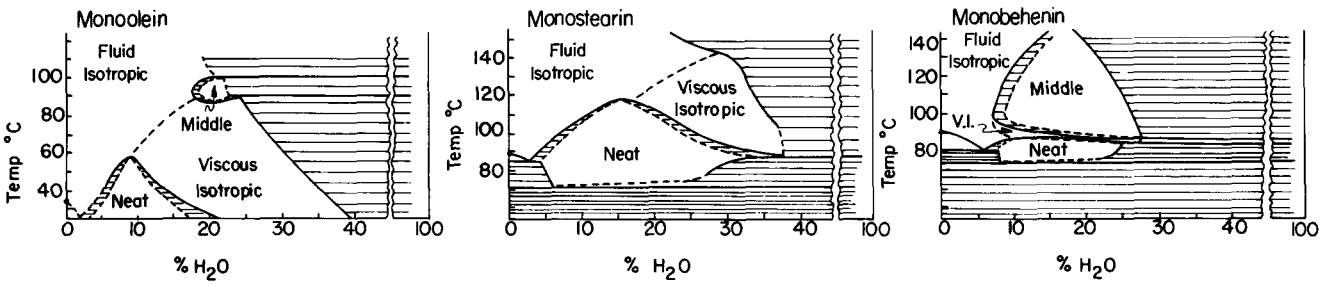

FIG. 10. Phase behavior of aqueous monoglycerides.

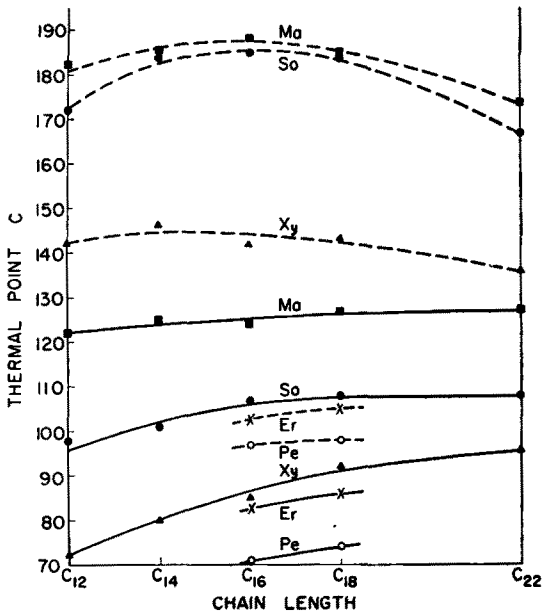

FIG. 11. Melting points of anhydrous polyol monoesters.

According to Luzzati et al. (38), we contend with a plethora of phases at low H_2O contents, in the egg lecithin-H_2O system. Among these phases, C is ordinary crystal of some sort, $L\beta$ is α as we have considered it herein, and P and R are of exotic mesomorphic character; but H, Q and $L\alpha$ are our three familiar mesomorphic types—hexagonal or middle, cubic or viscous isotropic, and lamellar or smectic. Clearly there is no haven of simplicity among the phospholipids.

Somewhat similar behavior is shown by egg phosphatidyl ethanolamine but with less H_2O uptake than by egg lecithin. Phosphatidyl choline and ethanolamine are present in membranes for a purpose, and who can doubt that part of the purpose lies in regulating the membrane for water association, indeed for structure potential in manner somehow relating to the attributes of bulk structure?

HYDROXYL COMPOUNDS

Now to something simpler—hydroxy lipid compounds, e.g., monoglycerides, sorbitol esters, etc. First, a few generalizations as matters now appear reveal that: Thus far no monohydroxy compound has alone, or with H_2O only, been observed to form a mesomorphic state. No dihydroxy compound (with the exception of short chain monoglycerides) has been found to form meso states alone, but with H_2O such states are typical. Trihydroxy compounds, at least with hydroxyls close together as in erythritol monoester, do form mesomorphic states, even if anhydrous.

MONOGLYCERIDES

The monoglycerides are, of course, interesting for physiological and industrial reasons. To make an acquaintance out of a friend, I would suggest having him taste melted monoolein; his mouth will immediately feel like a bathtubful of gelatin due to formation of the viscous isotropic phase. By the same mechanism a number of innocent rats have been assassinated by intubing with pure monolein and consequent plugging of their small unsuspecting bellies.

With monoolein we encounter in Figure 10 the three most common types of mesomorphic states—smectic, hexagonal, viscous isotropic (39). The latter two are probably reversed, i.e., with polar interiors (an aspect not always easy to determine).

It has been found that the state of a monoglyceride used as an emulsifier or cake promoter is important to its function. It is important that it be in the smectic state during preparation of aqueous dispersions for subsequent culinary applications (40).

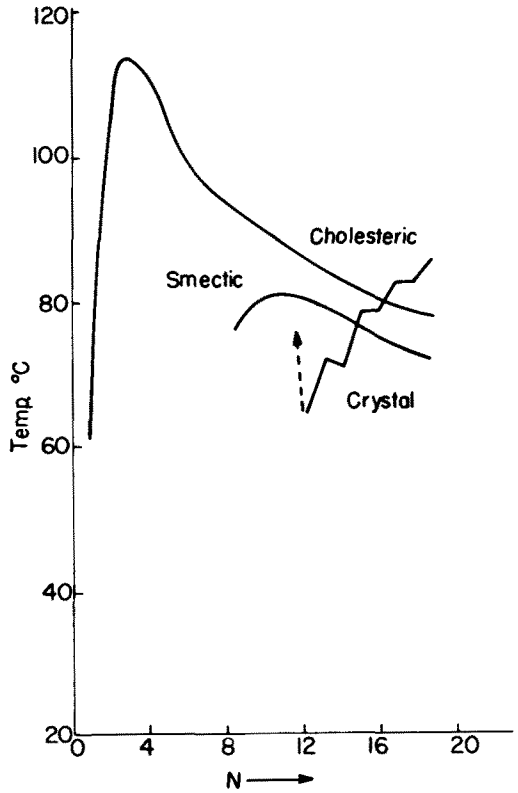

FIG. 12. Melting points of saturated cholesteryl esters.

With saturated compounds we see marked contrast between chain lengths. It is plain that middle or hexagonal phase is absent in monostearin and yet occupies a large region of the phase diagram for monobehenin with its longer hydrocarbon chain. The precise basis for the difference is obscure, but monostearin can be caused to exhibit middle phase by addition of more nonpolar material in the form of triglyceride or diglyceride.

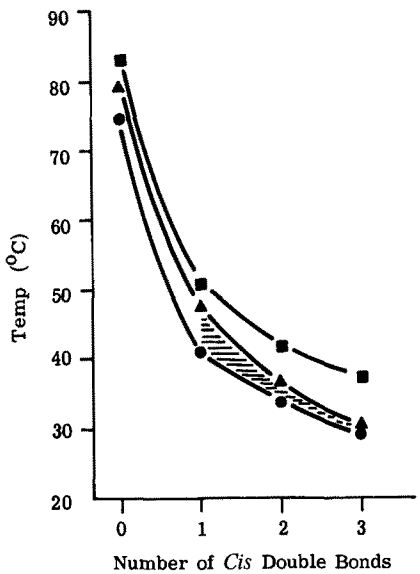

FIG. 13. Melting points of C_{18} cholesteryl esters. Transition temperature vs. the number of *cis* double bonds in C_{18} fatty acids esterified with cholesterol: ■ the crystal (C_1)⇔isotropic transition; ▲ the cholesteric ⇔ isotropic transition; ● the smectic ⇔ cholesteric transition. Shaded area refers to the temperature domain of the cholesteric mesophase.

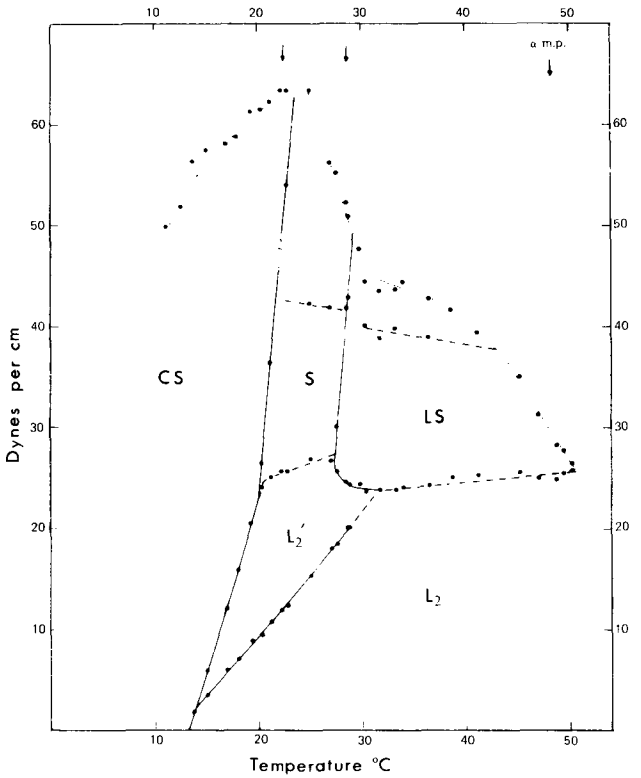

FIG. 14. Phases of surface films of dodecyl acetate.

POLYOL MONOESTERS

Behavior of a series of anhydrous polyol monoesters with three or more hydroxyls in the ester (41) is exhibited in Figure 11. These are randomly esterified, hence not pure isomers, but with esterification in primary position probably predominant.

Polymorphism in the crystal state is quite complicated. Mesomorphic mp increases with polyol length and passes through a low maximum at intermediate acyl chain lengths. There is a further interesting feature—behenates crystallized from solvent, on heating, form smectic states; upon mesomorphic melting they transform into hexagonal states of some 5 C higher melting level. The latter states on cooling and crystallizing (into a different crystal state from the original) return on subsequent heating. One pictures here some specific relationship between the solvent-derived and the melt-derived crystal states and the respective mesomorphic state to which they proceed on melting.

STERYL ESTER MESOMORPHISM

The second and different basis for mesomorphism among lipids relates to steryl, especially cholesteryl, esters. There is no polar-nonpolar dichotomy of portions of the molecule. Indeed the sterols themselves, weakly polar, do not exhibit mesomorphism, although they do participate with other compounds. It is the steryl esters which show mesomorphism based on a dichotomy between the high melting tendency of the stiff essentially planar polycyclic portion and the lower melting tendency of the two chain-paraffin portions—the acyl moiety located at the hydroxyl position and the branched alkyl portion of the steryl group.

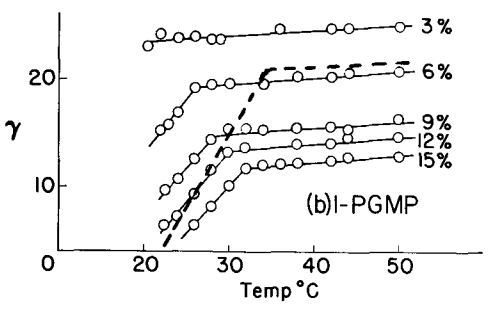

FIG. 15. Interfacial tension of propylene glycol monopalmitate (and stearate).

TABLE V

Steryl Ester Comparisons

A. Melting Point or Transformation Point of Chlorides (45)

Chloride	To crystal[a]	To cholesteric[a]	Melting point
Cholesteryl	50.5	67.3	95.7
Cholestanyl	80.0	---	114.0
Campesteryl	75.5	---	104-105
β-sitosteryl	62.3	---	82.7
Stigmasteryl	70.5	---	94.5

[a]On Cooling

B. Melting Point or Transformation Point of Oleates and Palmitates on Heating

Ester	Smectic	Cholesteric	Crystal
Cholesteryl oleate (44)	41	47.5	51
Palmitate (42)	78.1	82.6	77.5
Stigmasteryl oleate[a]	29	---	39.5
Palmitate[a]	---	---	102

[a]From technical stigmasterol [other values reported (46)].

Two mesomorphic types are recognized: (1) the smectic or planar type, comparable except for lack of polarity with other smectic mesomorphs; and (2) cholesteric, of still uncertain structure but characterized by a lesser degree of order than smectic as attested by enthalpy measurements. Some sort of spiraling arrangement gives rise to a 5000 Å repeat distance which, by interference phenomena, gives rise to the striking color effects of remarkable temperature sensitivity, which are the actual basis for the recent great interest in the cholesteric state.

CHOLESTERYL ESTERS

Saturated

Figure 12, partially summarizing the work of Ennulat (42), Davis et al. (43) and others, shows the interesting mesomorphic and crystalline melting of the series of saturated esters. Differential thermal analysis and microscopy are the tools for studying such compounds.

In the C_{16}-C_{18} region there is a drop in mesomorphic mp with chain length, and the familiar alternating rise in crystal melting makes for quite individual behavior among the homologs. Cholesteric phase continues down to C_2, and smectic stops abruptly at C_9. Crystal melting points for lower chain lengths are quite erratic.

The important C_{18} esters, as reported by Small (44), are mutually consistent in behavior (see Fig. 13).

It is not to be overlooked that mesomorphic states of oleate, the most common of the cholesteryl esters, and of linoleate, melt near body temperature. This fact along with evidence that there are sites in tissues where lipid matter is as high as 95% in cholesteryl esters and these high in oleate, indicates that there is good reason to speculate that the cholesteric phase plays some biological role, perhaps not the phase as such but the special molecular shape essential to that phase.

This speculation is made more intriguing by the failure, up to this point, to observe cholesteric phases for any phytosterol esters; these being little absorbed on ingestion and, moreover, tending to limit cholesterol absorption. A smectic phase has indeed been observed for stigmasterol oleate, but no cholesteric phase. Table V shows the contrast

between cholesteryl and other steryl esters with respect to formation of cholesteric phase.

SURFACE STRUCTURE

Having already touched on the topics of lipid membranes and evaporation prevention by lipids, I should like to consider explicitly the surface structures of lipids. There is a fascinating list of contributors to this topic—the ingenious Agnes Pockels, Lord Rayleigh, Harkins, Langmuir and many another. The occurrence of mono- and multilayers on H_2O is well attested. There is a recognition of several states of monolayers with association sought between specific surface states and familiar bulk states, Harkins, Dervichian and Stenhagen having given particular attention to this matter, and lately Monica Lundquist.

In Figure 14 for docosyl acetate, Lundquist (47) has shown among other striking features, the remarkable identity of α bulk melting level with critical surface melting level of the two dimensional LS or superliquid state of Harkins. A close relationship in structural arrangement seems inescapable. Other bulk-surface film relationships are strongly indicated.

An interesting instance of interfacial structural behavior also involves α-type states. In an oil-H_2O system, with an interfacial additive such as monoglyceride, fatty alcohol or, in the present case, propylene glycol monopalmitate, interfacial tension varies little with temperature down to a point where the rate suddenly increases (see Fig. 5). It has been interpreted (48) that the flat region is that of a liquid monolayer, the steep region that of a solid monolayer, actually an α crystalline monolayer. The amount of slope change is governed by the equation:

$$(\partial\gamma\partial T)_{P,A} = \gamma/T\text{-}1/T\left(\frac{\partial H}{\partial A}\right)_{P,T}$$

A consequence of this behavior is that the plot for a higher molecular weight, higher melting, slightly less polar homolog (here monostearate at a 6% level), which lowers interfacial tension less at high temperatures, crosses the corresponding lower homolog curve and is more interfacially active at low temperature. There are obvious implications for the culinary and cosmetic arts, since many of the emulsifiers employed may pass from liquid to crystalline regions, or vice versa, in process or in use.

It is worthy of note that these slope changes are correlated with significant heat of fusion as in crystal melting. For the equally possible interfacial changes involving development of a mesomorphic state no such slope change is anticipated as the enthalpy change is low.

This is not to say that mesomorphic state development at interfaces is not significant, in particular for emulsion technology. Friberg and Mandell (49), extending the work of Ekwall, are perhaps the chief apostles of the effectiveness of interfacial mesomorphic states in emulsion stability, the increased viscosity of the interface on development of the mesomorphic state being a basis for such opinion.

CONCLUSION

I have led you over a tortuous trail. We have met crystalline enrobing fats, partly crystalline shortenings, α crystalline evaporation controls, mesomorphic biological membranes, mesomorphic and crystalline emulsifiers, smectic and cholesteric steryl esters. In each encounter some feature of lipid structure was involved. But there remain many more unsolved problems in lipid structure than have been solved. A gratifying thing in Lipid Chemistry is that with an immense proliferation of problems, the truly sensational development in methodology has afforded an ever sharper definition of these. And though technology be distressed with each newly recognized ambiguity, research is only the merrier when the ambiguity has technological implications.

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