

Classification of Glyceride Crystal Forms

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The earlier nomenclature used to describe glyceride crystal forms are discussed on the basis of recent results on molecular arrangements from single-crystal structure analyses. The principles of nomenclature used by Lutton are very convenient, specifying direct relations between names used and characteristic chain packing properties. This scheme is, however, incomplete as all possible alternatives of chain packing have not been taken into account. It is furthermore shown in this paper that Lutton's term sub- α is irrelevant in the scheme. An improved classification is suggested based on criterions which define three types of crystal forms (α , β , and β') according to X-ray powder diffraction and infrared absorption data. The crystal form termed "intermediate" which occurs in complex triglycerides is related to our knowledge of chain packing and chain sorting of saturated and unsaturated chains into different layers. More detailed classification in order to describe the structure, which must be based on single crystal data, is also discussed.

In connection with an investigation of the phase behaviour of glycerides¹ the present author was faced with the problem of terming new crystal forms. Two schemes of nomenclature, *viz.* Malkin's and Lutton's were used in the earlier literature. Malkin² introduced the terms α , β' , and β to denote the crystal forms of triglycerides in the order of increasing melting points. The melting points of forms with closely related crystal structures, however, may coincide or differ only slightly. Furthermore, this nomenclature gives no information regarding the crystal structure and there are in fact members of a series of glycerides with homologously isomorphous crystal structures, which should have different names according to Malkin's terminology.¹ Lutton³ was later able to characterize the crystal forms by their X-ray short-spacing data. The dominating short-spacing lines in the X-ray diffraction pattern of a longchain compound are due to the lateral packing of the hydrocarbon chain. The use of X-ray short-spacing data as a basis of nomenclature is therefore more convenient as they are related to the actual crystal structure. The short-spacing data given by Lutton for identification of the forms β , β' , and α correspond to the triclinic chain packing $T//$,⁴ the common orthorhombic chain packing O_{\perp} ,⁵ and the hexagonal chain packing H ,⁶ respectively. Later,

however, four other chain packings have been described: O'_{\perp} ,⁷ $O//$,⁸ $O'//$,⁹ and $M//$.¹⁰ One of these more unusual chain packings occurs in glycerides.¹¹

Quite recently Gunstone¹² proposed a new nomenclature of glyceride forms based on their long-spacing values. The long-spacing data, however, provide rather poor structural information. Furthermore, complications in the applications may arise due to the possibility of the occurrence of two crystal forms of a compound with the same or very similar long-spacing values (*e.g.* racemic 1-monoglycerides).

It is thus obvious that there is a need for a new scheme of nomenclature with precise definitions to be able to term new polymorphs uniformly.

A NEW NOMENCLATURE

For description of the polymorphism of glycerides¹ the present author used a nomenclature in which Lutton's scheme was included. It was then possible to term new forms unambiguously whereas names of earlier described forms remained unchanged. This new nomenclature has earlier been described briefly (Ref. 1), and complete definitions with new data that support this system, will be given below. Some general applications on complex glycerides will also be presented here.

Lutton characterized the form sub- α by transition relations and the possibility to use an alternative name for sub- α is of course a complication. Two crystal forms called sub- α (according to Lutton's terminology) occurring in simple glycerides have been described, one in triglycerides and one in racemic 1-monoglycerides. In the case of triglycerides the transition α to sub- α is a second-order one,¹ *i.e.* the changes in the lattice take place continuously as opposed to all other phase transitions in simple glycerides which are first-order ones with discontinuous lattice changes. A β' -form (according to Lutton's terminology) has been obtained of the racemic 1-monoglyceride of 11-bromoundecanoic acid,¹ which according to X-ray data and infrared absorption data is isomorphous with the form of racemic 1-monolaurin that earlier was called sub- α . These inconsistencies provide strong reasons to eliminate the term sub- α .

The subcell dimensions, which characterize the actual chain packing, may vary considerably with corresponding variations in the short-spacing data as a consequence. Additional experimental evidence would therefore be valuable for the identification of the chain packing. Chapman¹³ found that the appearance of the infrared absorption bands due to the CH_2 rocking vibration near 720 cm^{-1} can be used in the determination of chain packing. A single peak there should thus correspond to parallel chain planes, while two peaks of almost equal intensity correspond to a packing in which the plane of every second chain is perpendicular to the planes of the other. Deviations from this ideal behaviour have been discussed by Abrahamsson and Fischmeister.¹⁴ If X-ray short-spacing data are correlated with infrared absorption data the case when all chain planes are parallel can certainly be distinguished from the case when every second chain plane is perpendicular to the planes of the rest. The hexagonal chain packing, where the details of the

arrangement are still unknown (*cf.* Ref. 1), can always be recognized from its characteristic simplicity in the X-ray short-spacing region. These three types of chain packing correspond to the crystal forms α , β , and β' defined according to the following criteria:

1. A form which gives only one strong short-spacing line near 4.15 Å is termed α .
2. A form showing two strong short-spacing lines near 4.20 and 3.80 Å or three strong lines near 4.27, 3.97, and 3.71 Å, and which also exhibits a doublet in the 720 cm^{-1} region of the infrared absorption spectrum, is called β' .
3. A form which does not satisfy criteria 1 or 2 is called β .

When two or more crystal forms of a compound receive the same name they should be distinguished by subscripts, *e.g.* β_1 , β_2 , and it is recommended that they are numbered in the order of decreasing melting-points.

It is always possible to apply these criteria by the use of routine methods. This nomenclature can be described as a classification of chain packings in terms of arrangement of the chain planes. All chain planes are parallel in the β -form, whereas two perpendicular orientations occur in the β' -form. Different modes of thermal movement in the α -form have been discussed (*cf.* Ref. 1), and in any instance one can definitely conclude that there is no ordered arrangement of the chain planes. A presumption made here is that all chain axes of a hydrocarbon chain layer are parallel, which is quite reasonable as crossed chain arrays have been found only in compounds with very strong polar or ionic interaction between end groups. It may seem curious that criterion 3 above is a negative one, but the reason for this is simply that the different packing modes of parallel hydrocarbon chains cannot be defined unambiguously by their X-ray short-spacing data.

The β' -forms of all examined glycerides show the common orthorhombic chain packing $O\perp$ (short-spacing lines 4.20 and 3.80 Å) but a glyceride crystal form with the closely related chain packing $O'\perp$ (short-spacing lines at 4.27, 3.97, and 3.71 Å) is quite possible and should also be called β' .

It should finally be emphasized that the nomenclature suggested above is merely a modification of that of Lutton according to later results from detailed single crystal analyses of glycerides.

THE "INTERMEDIATE" FORM AND COMPLEX GLYCERIDE MIXTURES

There is no doubt about the existence of a fourth crystal form in complex mixtures of triglycerides. According to thermal and X-ray data the crystal form β' of triglycerides described by Malkin seems to be the same form, and was probably formed due to the presence of impurities. Hoerr¹⁶ has termed this form "intermediate" as the melting point is between those of β' and β . Hoerr reported that except for a strong short-spacing in the neighbourhood of 4.6 Å there are two other strong spacings at 4.15 and 3.75 Å. These short-spacing values are roughly the same as those from equal amounts of the two common chain packings $T//$ and $O\perp$, and it is therefore not surprising that the existence of this form has been doubted for a long time. Somewhat different

values have recently been found in the "intermediate" form of beef tallow:¹⁷ 4.60 Å, 4.46 Å, 4.32 Å, and 3.83 Å, all of about the same intensity. Short-spacing values for three chain packings which are uncommon in simple long-chain compounds are given in Table 1. They represent together with the

Table 1. Short-spacing diffraction data characteristic for the three uncommon chain packings with parallel chains.

$M//$ (β_1 -(\pm)-1-monglycerides ¹)	$O//$ ((-)-2-methyl-2-ethylicosanoic acid ⁸)	$O'//$ (oleic acid ⁹)
4.57 s.	4.61 v.s.	4.71 v.s.
4.35 s.	4.12 s.	4.05 m.
3.85 s.	3.75 v.s.	3.78 v.s.

common triclinic chain packing $T//$ all packing modes of parallel hydrocarbon chains hitherto found. It can be seen that the values given by Hoerr are in good agreement with those corresponding to $O//$, whereas the values from the tallow "intermediate" form cannot unambiguously be assigned to any known chain packing. It should be noticed in this connection that two different chain packings may occur in non-equivalent chain layers in a crystal form of a triglyceride mixture. When we are dealing with glycerides containing both saturated and unsaturated hydrocarbon chains this is in fact the most probable situation as there is a tendency for chain sorting so that only saturated chains occur in one set of layers and only unsaturated in another. We might even expect to find the chain packing $O'//$ in the *cis*-unsaturated layers, as the *cis*-double bonds can be accommodated in this packing with very small distortions.⁹

It is evident that the "intermediate" form does not fit into the classification defined above as it is characterized by thermodynamic stability relations. It is quite possible that triglyceride systems exist which exhibit two or more forms which are "intermediate" in relation to β and β' and it is even possible that such a form can possess the same packing (and hence short-spacing values) as β or β' . It is therefore recommended that the nomenclature proposed here is used also for this fourth form, and when it shows the short-spacing values given above it should consequently be termed β_2 . Thus we can conclude that a large categorie of complex triglyceride mixtures (*e.g.* margarine) can show four crystal forms which are α , β' , β_2 , and β_1 in the order of increasing stability. There is much evidence for assuming that the tuning fork conformation is maintained during the polymorphous transitions. The vertical α -form with hexagonal chain packing separates from the melt and during the following phase transformations the layer arrangement is preserved with changes of lateral chain packing and chain tilt only. The stability of the β' -form of such mixtures is explained from its specific methyl end group packing¹⁵ which is very insensitive for variations of the fatty acid chain lengths.

Table 2. Arrangement in layers for crystal form β and β' of glycerides.

	β'	β
Racemic 1-monoglycerides	(sub- α) $O_{\perp}(021)$	β_1 and β_2 : $M//(\bar{1}\bar{1}1)$
Optically active 1-monoglycerides	β_1 : $O_{\perp}(021)$ β_2 : $O_{\perp}(111)$	$M//$ *
2-Monoglycerides	—	$T//(\bar{1}\bar{1}1)$
1,3-Diglycerides	—	β_1 : $T//(\bar{0}01)$ β_2 : $T//(\bar{0}11)$
Triglycerides	$O_{\perp}(111)$	$T//(\frac{1}{3}01)$

* form crystallizing from the melt only, no single crystal data available. The probable chain packing according to X-ray powder data is therefore given.

FURTHER CLASSIFICATION BASED ON X-RAY SINGLE CRYSTAL DATA

A deeper insight into the phase behaviour of glycerides requires detailed knowledge of the molecular arrangement, which can be obtained from analysis of X-ray single crystal data. Replacement of the terminating methyl groups in the acyl chains by bromine or iodine atoms offers good possibilities for complete structure determination.¹ Even in cases where this technique is not successful it is often possible to reveal the main features of the molecular arrangement from the single crystal data, (*cf.* Ref. 11). It is also always possible to determine the packing of the hydrocarbon chains from an analysis of the subcell reflexions.⁴ The chain arrangement in layers provides a possibility of further classification. It can be defined by giving the indices of the end group planes in terms of the subcell of the chain packing (*cf.* Ref. 15). The end group planes occurring in different glyceride crystal forms are given as an example in Table 2. This classification also defines the tilt of the hydrocarbon chain towards the end group planes and illustrates other structural properties, *e.g.* the occurrence of terraces of methyl end groups in the β -form of triglycerides. It is also possible to predict from this information whether the corresponding homologically related isomorphous series show alternation in the physical properties or not.¹⁵ Additional information is available from X-ray single

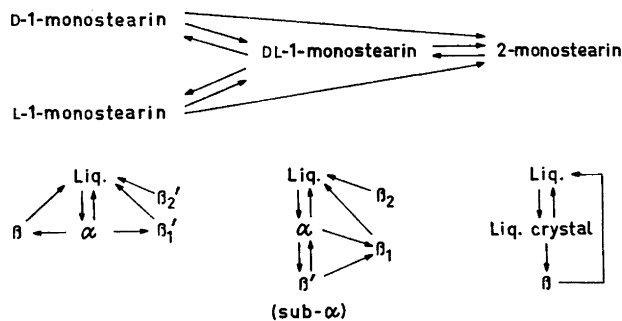


Fig. 1. Schematic illustration of phase transitions in monostearin.

crystal data even if the complete structure cannot be determined, *e.g.* whether all chains are parallel or if alternation of the chain tilt occurs.

Single crystal data are sometimes necessary if the polymorphism is to be described correctly. The monoglycerides represent a case in point. The complicated phase behaviour of monostearin¹ is shown schematically in Fig. 1. The identity of the sample has to be checked during the investigation to exclude the possibility of isomerization by acyl migration. Separation into antipode crystals occur when a sample of a racemic 1-monoglyceride is crystallized rapidly from solvents. The antipode crystals obtained in that way have been identified from the single crystal data as β_1' . They have earlier been erroneously described as the β' -form of racemic 1-monoglycerides. X-Ray single crystal data were also necessary for identification of the β_2 -form of racemic 1-monoglycerides, a form which is remarkable as it has revealed a new type of polymorphism in long-chain compounds involving alternate stacking of layers.¹¹

In mono- and diglycerides there are many possibilities of inter- and intramolecular hydrogen bonding and alternative molecular conformation of di- and triglycerides (the directions of the acyl chains with respect to the glycerol residue) have been discussed for a long time. Single crystal structure studies have shown, however, that the polymorphism is mainly due to the possibility of alternative packing modes of the hydrocarbon chains. This is a strong argument for the use of the nomenclature system suggested here.

The nomenclature given here can of course be applied to any type of long-chain compound. It should in fact be most valuable for discussions of polymorphism on complex lipid systems (*e.g.* glycerides-phosphatides-cholesterol esters) if the same terminology is used for the crystal forms of different mixtures as well as for those of the pure components.

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REFERENCES

1. Larsson, K. *Arkiv Kemi* **23** (1964) 35.
2. Malkin, T. and Meara, M. L. *J. Chem. Soc.* **1939** 103.
3. Lutton, E. S. *J. Am. Oil Chemists' Soc.* **27** (1950) 276.
4. Vand, V. and Bell, I. P. *Acta Cryst.* **4** (1951) 465.
5. Bunn, C. W. *Trans. Faraday Soc.* **35** (1939) 482.
6. Müller, A. *Proc. Roy. Soc. A* **127** (1930) 417.
7. Abrahamsson, S. *Acta Cryst.* **12** (1959) 304.
8. von Sydow, E. *Acta Chem. Scand.* **12** (1958) 777.
9. Abrahamsson, S. and Ryderstedt-Nähringbauer, I. *Acta Cryst.* **15** (1962) 1261.
10. Abrahamsson, S. and Westerdahl, A. *Acta Cryst.* **16** (1963) 404.
11. Larsson, K. *Arkiv Kemi* **23** (1964) 29.
12. Gunstone, F. D. *Chem. Ind. (London)* **1964** 84.
13. Chapman, D. *J. Chem. Soc.* **1957** 4489.
14. Abrahamsson, S. and Fischmeister, I. *Arkiv Kemi* **14** (1959) 57.
15. Larsson, K. *J. Am. Oil Chemists' Soc.* *In press*.
16. Hoerr, C. W. *J. Am. Oil Chemists' Soc.* **41** (1964) (7), pp. 4, 22, 32, 34.
17. Sumi, K. and Abe, Y. *J. Japan Oil Chemists' Soc.* **11** (1965) 606.

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