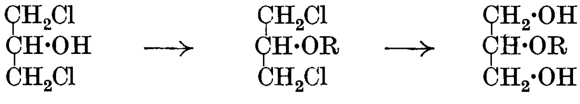
LI.—*The Partial Esterification of Polyhydric Alcohols. Part X. The Discovery of the First True β-Glyceride, and the Untrustworthiness of the Supposed Structures of Certain Diglycerides.*

By Arthur Fairbourne.

The following method of synthesising β-derivatives of glycerol has formerly been regarded as trustworthy for β-esters (Grün, *Ber.*, 1910, **43**, 1288), although untrustworthy for β-ethers (Gilchrist and Purves, J., 1925, **127**, 2735) :



$$\begin{array}{l} CH_2Cl \\ | \\ CH{\cdot}OH \\ | \\ CH_2Cl \end{array} \longrightarrow \begin{array}{l} CH_2Cl \\ | \\ CH{\cdot}OR \\ | \\ CH_2Cl \end{array} \longrightarrow \begin{array}{l} CH_2{\cdot}OH \\ | \\ CH{\cdot}OR \\ | \\ CH_2{\cdot}OH \end{array}$$

In Part V (J., 1926, 3148), however, it was shown to produce α- instead of β-esters, and the publication of this result was followed by claims of the discoveries of the first true β-ester of glycerol (Helferich and Sieber, *Z. physiol. Chem.*, 1927, **170**, 31; 1928, **175**, 311) and also of the first true β-ether (Hill, Whelen, and Hibbert, *J. Amer. Chem. Soc.*, 1928, **50**, 2235; Hibbert, Whelen, and Carter, *ibid.*, 1929, **51**, 302).

In Part IX (J., 1929, 2232) it was shown, on the other hand, that the method was trustworthy for the preparation of the β-ethers, thus precisely reversing the relative values assigned to the reaction in the literature; and it was incidentally realised that the credit of synthesising the first true β-ether of glycerol is apparently due to Gilchrist and Purves (*loc. cit.*), who, however, mistakenly recorded their experiment as a failure instead of as a success.

An almost parallel re-investigation of this synthesis has now been independently carried out by Hibbert and Whelen (*J. Amer. Chem. Soc.*, 1929, **51**, 1943), who, reasoning from the evidence considered in Part VII of this series, studied the same reactions and reached identical conclusions. These authors, however, effected their final hydrolysis by a modified process which involved a treatment with acid. Since alkaline conditions frequently favour migratory changes, it is very doubtful whether acidic conditions ought thus to be substituted for them, in seeking to prove that migrations could not have occurred in Gilchrist and Purves's work. On the other hand, the introduction of acid has greatly improved the yield obtainable from these reactions, which therefore now constitute a trustworthy process for preparing true β-ethers of glycerol without the formation of their α-isomerides.

If the conclusion reached in Part V (*loc. cit.*) is correct, that all the preparations of supposed " β "-monoglycerides known in 1926 were illusory, Helferich and Sieber would appear to be justified (*loc. cit.*) in claiming that they have now isolated the first true β-glyceride ever obtained.

It is clearly desirable, for this and other reasons, that all supposed esterifications in the β-position of glycerol should be subjected to careful scrutiny, and the present paper consists of an inquiry into some of these cases.

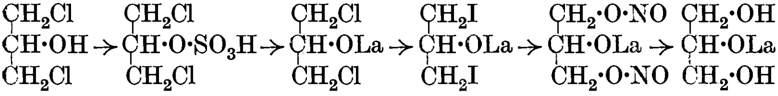
Esters of inorganic acids, such as the nitrates and phosphates, have not normally been contemplated in connexion with the general statements referring to " β "-monoglycerides and " β "-mono-esters made in this series of papers, but " β "-monochlorohydrin has necessarily been taken into consideration, to some extent, as an intermediate product in one of the suggested syntheses investigated in Part V (*loc. cit.*). Prepared by the method of Hanriot (*Ann. Chim.*, 1879, **17**, 76), the particular specimen employed in that investigation was proved by its *p*-nitrobenzoate to consist almost entirely of the unwanted α-isomeride. Henry (*Bull. Acad. roy. Belg.*, 1897, **33**, 110), however, apparently succeeded in differentiating between samples of these isomerides by reducing them to propylene glycol and trimethylene glycol, respectively. Read and Hurst (J., 1922, **121**, 989) also describe a preparation of the " β "-monochlorohydrin, but give no satisfactory proof of the structure of their product. Smith and Samuelsson (*Z. physikal. Chem.*, 1918, **92**, 717; 1920, **94**, 691, 723) have shown that the proportion of the isomerides which are produced when glycerol and hydrogen chloride react upon one another varies with the conditions adopted.

No record has been found of any attempt to prepare a β-monoglyceride from a veritable specimen of β-monochlorohydrin by the method Grün suggested (*loc. cit.*), although Delaby and Dubois recently contemplated this synthesis (*Compt. rend.*, 1928, **187**, 949) in connexion with their belief that the β-mono-ester predominates when glycerol and formic acid react; nor is it thought likely that such an attempt will succeed, since a preferential production of α-mono-esters is usual whenever intermediate αβ-rings can occur (compare Part V, *loc. cit.*; Part VII, J., 1929, 129; Part IX, *loc. cit.*).

Grün considered, however, that the trustworthiness of his alternative process for preparing β-monoglycerides, based on the reactions discussed at the beginning of this paper, had been experimentally confirmed (*loc. cit.*) by his resulting " β "-monolaurin reacting with phenylcarbimide, and by his " α "-monolaurin not doing so.

This reaction has therefore been re-investigated: it is found that both the α- and the " β "-monolaurin prepared by his method can yield diphenylurethanes, which are identical, since no depression of melting point is caused when they are mixed.

Thieme also synthesised a " β "-monolaurin by a modification of Grün's process (*J. pr. Chem.*, 1912, **85**, 284):



$$\begin{array}{lllllllllll} CH_2Cl & & CH_2Cl & & CH_2Cl & & CH_2I & & CH_2{\cdot}O{\cdot}NO & & CH_2{\cdot}OH \\ CH{\cdot}OH & \rightarrow & CH{\cdot}O{\cdot}SO_3H & \rightarrow & CH{\cdot}OLa & \rightarrow & CH{\cdot}OLa & \rightarrow & CH{\cdot}OLa & \rightarrow & CH{\cdot}OLa \\ CH_2Cl & & CH_2Cl & & CH_2Cl & & CH_2I & & CH_2{\cdot}O{\cdot}NO & & CH_2{\cdot}OH \end{array}$$

$[La = CO{\cdot}C_{11}H_{23}]$

Comparison of his product with an authentic specimen of α-monolaurin led him to believe that they were different substances; he consequently extended his researches to include the corresponding " αβ "- and " αγ "-dilaurins, which, again, he found to be different from each other. Finally (*loc. cit.*) he investigated the disintegration of trilaurin by sulphuric acid, and estimated the proportions of the various partly esterified laurins produced in that reaction.

The whole of this work is shown in the following experimental portion to rest on a double fallacy, since the " β "-monolaurin obtainable by his method is undoubtedly identical with α-monolaurin, when pure, and the supposedly isomeric " αβ "- and " αγ "-dilaurins are identical with each other also.

The controversy which arose between Grün and Thieme (*Ber.*, 1912, **45**, 3691; 1913, **46**, 1653, 2198) is thus largely explained: both authors correctly recognised the same material as the one they had synthesised, and each insisted on the structure which his own preparation appeared to support.

To make the evidence of identity more definite, Thieme's intermediate αγ-di-iodohydrin β-monolaurate has now been synthesised in another way, and obtained for the first time as a solid. This was hydrolysed, like the crude material, to α-monolaurin, which was again identified by a mixed melting point.

Another supposed β-monoglyceride is "β"-monomyristin, isolated by Grün, Schreyer, and Weyrauch (*Ber.*, 1912, **45**, 3420). Their preparation has therefore been repeated, and the product compared with an authentic specimen of α-monomyristin obtained by the method of Fischer, Bergmann, Bärwind, and Pfähler (*Ber.*, 1920, **53**, 1589, 1606, 1621). Both are identical.

Further, the corresponding "αβ"- and "αγ"-dimyristins described by Grün and Theimer (*Ber.*, 1907, **40**, 1792) have now been prepared by the recommended processes, and the samples obtained are again identical with each other.

A precisely similar case to the laurins and the myristins is that of the margarins, all five of which have recently been described by Thomson (*Trans. Roy. Soc. Canada*, 1926, **20**, III, 445):

I.	α-Monomargarin	m. p. 76°, $n_D^{80°}$ 1·441.
II.	"β"-Monomargarin	
III.	"αβ"-Dimargarin	m. p. 70—72°, $n_D^{80°}$ 1·439.
IV.	αγ-Dimargarin	
V.	αβγ-Trimargarin.	

By analogy with the cases just cited, and also from a consideration of the methods of preparation adopted for these glycerides, it is very probable (see Part V) that (I) and (II) should be identical, and (see Parts VII and VIII) that (III) and (IV) should be identical with each other also.

The eight recorded determinations of physical constants summarised in the above table appear to establish these identities, and make it clear that only two out of the four possible partly esterified margarins have really been isolated. (Mixed melting points would, however, still be desirable in confirmation of these identities.)

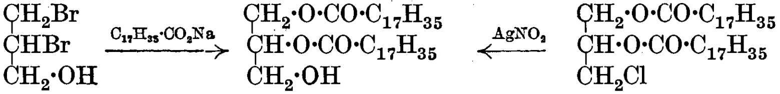
Among other similar cases of supposed isomerism, believed to be due to esterification in the β-position, may be mentioned the "αβ"- and "αγ"-dipalmitins and the "αβ"- and "αγ"-distearins.

The "αβ"- and "αγ"-structures are still separately assigned to these diglycerides in authoritative modern works of reference (*e.g.*, Ubbelohde's "Handbuch der Öle und Fette," 1929, vol. I, pp. 174—176), and the reactions concerned in their preparations are still often relied upon as satisfactory evidence of constitution (see

Thomson, 1928, *loc. cit.*; Delaby and Dubois, *Compt. rend.*, 1928, **187**, 767, who now record the syntheses of " αβ "- and " αγ "-diformates in these ways; also the work of Grün and Limpächer described below; and the applications of these reactions to the preparations of " symmetrical " and " unsymmetrical " mixed triglycerides by Whitby, J., 1926, 1458, by Humnicki and Lunkiewicz, *Bull. Soc. chim.*, 1929, **45**, 422, and by Weizmann and Haskelberg, *Compt. rend.*, 1929, **189**, 104).

Their syntheses have therefore been re-investigated, and the expected identities experimentally proved.

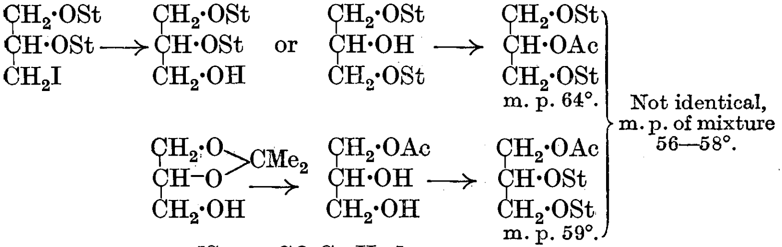
Thus, in the typical case of the distearins, the " αβ "-isomeride is described as having been synthesised both from αβ-dibromohydrin by Guth (*Z. Biol.*, 1903, **44**, 78) and by Renshaw (*J. Amer. Chem. Soc.*, 1914, **36**, 537), and also from the αβ-distearate of monochlorohydrin by Grün and Theimer (*Ber.*, 1907, **40**, 1792) :



$$\begin{array}{l} CH_2Br\\ CHBr\\ CH_2{\cdot}OH\end{array} \xrightarrow{C_{17}H_{35}{\cdot}CO_2Na} \begin{array}{l} CH_2{\cdot}O{\cdot}CO{\cdot}C_{17}H_{35}\\ CH{\cdot}O{\cdot}CO{\cdot}C_{17}H_{35}\\ CH_2{\cdot}OH\end{array} \xleftarrow{AgNO_3} \begin{array}{l} CH_2{\cdot}O{\cdot}CO{\cdot}C_{17}H_{35}\\ CH{\cdot}O{\cdot}CO{\cdot}C_{17}H_{35}\\ CH_2Cl\end{array}$$

Repetition of these two processes has now produced specimens of the supposed " αβ "-distearin, melting, alone or mixed, at 78—79°; but the αβ-structure cannot be regarded as confirmed by this agreement (compare Part VII), since the same distearin, again causing no change in mixed melting point, has also been obtained from αγ-dichlorohydrin by a repetition of the synthesis of " αγ "-distearin described by Guth (*loc. cit.*).

Fischer (*Ber.*, 1920, **53**, 1621) employed the αβ-distearate of monoiodohydrin, instead of that of monochlorohydrin, in a reaction which is very similar to one of the three just mentioned, but he diagnosed the unexpected " αγ "-structure of his product indirectly from the difference in physical properties of its acetate and of α-acetoxy-βγ-distearin synthesised in another way :



$$\begin{array}{l} CH_2{\cdot}OSt\\ CH{\cdot}OSt\\ CH_2I\end{array} \longrightarrow \begin{array}{l} CH_2{\cdot}OSt\\ CH{\cdot}OSt\\ CH_2{\cdot}OH\end{array} \text{ or } \begin{array}{l} CH_2{\cdot}OSt\\ CH{\cdot}OH\\ CH_2{\cdot}OSt\end{array} \longrightarrow \begin{array}{l} CH_2{\cdot}OSt\\ CH{\cdot}OAc\\ CH_2{\cdot}OSt\\ \text{m. p. } 64^\circ.\end{array}$$

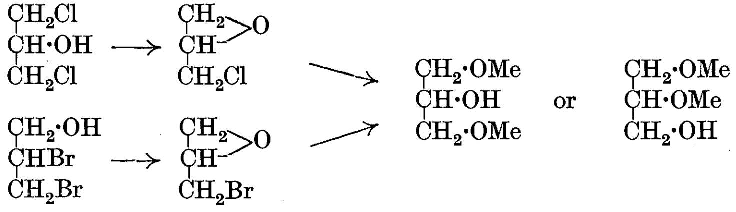
$$\begin{array}{l} CH_2{\cdot}O\\ CH{-}O\\ CH_2{\cdot}OH\end{array}\!\!>CMe_2 \longrightarrow \begin{array}{l} CH_2{\cdot}OAc\\ CH{\cdot}OH\\ CH_2{\cdot}OH\end{array} \longrightarrow \begin{array}{l} CH_2{\cdot}OAc\\ CH{\cdot}OSt\\ CH_2{\cdot}OSt\\ \text{m. p. } 59^\circ.\end{array}$$

$[St = {\cdot}CO{\cdot}C_{17}H_{35}]$

The identity of the samples of the " αβ "- and " αγ "-distearins now obtained is thus fully in accord with Fischer's interpretation of his experiment, and with his prophecy that the "αβ" mixed diglycerides of Grün and Schreyer (*Ber.*, 1912, **45**, 3420) will probably be found to have the αγ-structure; moreover, it explains Renshaw's confidence (*loc. cit.*) that Hundeshagen (*J. pr. Chem.*, 1883, **28**, 219) must have isolated at least a small quantity of the "αβ"-isomeride from his direct esterification of glycerol with stearic acid; it explains the similar claim of Kreis and Hafner (*Ber.*, 1903, **36**, 1123); but it discredits, for example, the constitution of the glyceride phosphate recorded by Renshaw and Stephens (*J. Amer. Chem. Soc.*, 1914, **36**, 1770).

No suggestion is now made that both possible isomerides may not be present to some extent in the crude products obtained from any, or indeed from all, of these reactions; all that is claimed in this connexion is that various processes separately recommended for the preparations of the "αβ"- and "αγ"-dilaurins, -dimyristins, -dipalmitins, and -distearins have produced specimens which, when purified, are identical with their supposed isomerides in every case.

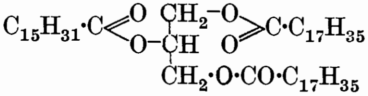
Two of the reactions now under consideration can also give rise to identical glycerol di-ethers (Part VIII, J., 1929, 1151; Gilchrist and Purves, J., 1925, **127**, 2735). Since, in this case, no subsequent wandering of acyl groups can occur, these identical products must result directly from the syntheses themselves, and the explanation would consequently seem limited to the assumption than an αβ-oxide is formed (Part IX, *loc. cit.*),



an assumption which is strengthened by the experimental proof that initial substitution of its αβ-oxide, epichlorohydrin, for the dichlorohydrin does not affect the identity of the product obtained (Part VIII).

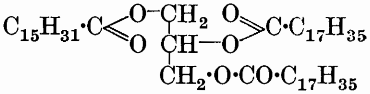
The formation of these intermediate αβ-oxides can doubtless occur also during the similar preparations of the glycerol esters. In addition, however, interchanges of acid radicals, with one another and also with different radicals, take place so easily (see Part VII) that an explanation of these changes, not involving a large or difficult movement of heavy radicals such as the stearyl and palmityl groups, is much needed.

If the tendency towards the formation of ortho-esters is taken into consideration (see Parts VII and IX), these changes can readily be represented merely by a rearrangement of valencies in which little or no actual migration or relative movement of the atoms themselves has to be presumed.



$$\begin{array}{l} C_{15}H_{31}\cdot C{<}\begin{matrix}O & CH_2-O\\ O- & CH\quad O\end{matrix}{>}C\cdot C_{17}H_{35} \\ \qquad\qquad\quad CH_2\cdot O\cdot CO\cdot C_{17}H_{35}\end{array}$$

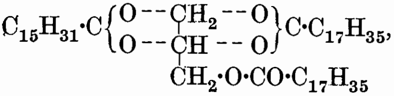
αγ-Distearin-β-palmitate.



$$\begin{array}{l} C_{15}H_{31}\cdot C{<}\begin{matrix}O- & CH_2\quad O\\ O & CH-O\end{matrix}{>}C\cdot C_{17}H_{35} \\ \qquad\qquad\quad CH_2\cdot O\cdot CO\cdot C_{17}H_{35}\end{array}$$

βγ-Distearin-α-palmitate.

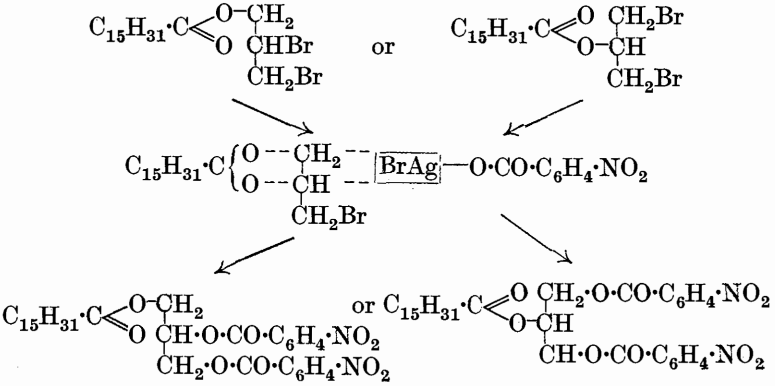
If conditions can exist in which the Hantzsch type of carboxyl group (*Ber.*, 1917, **50**, 1422; Part VII, *loc. cit.*) actually occurs, the above two formulæ may even become identical,



$$\begin{array}{l} C_{15}H_{31}\cdot C\left\{\begin{matrix}O\,--\,CH_2\,--\,O\\ O\,--\,CH\,--\,O\end{matrix}\right\}C\cdot C_{17}H_{35}, \\ \qquad\qquad\qquad CH_2\cdot O\cdot CO\cdot C_{17}H_{35}\end{array}$$

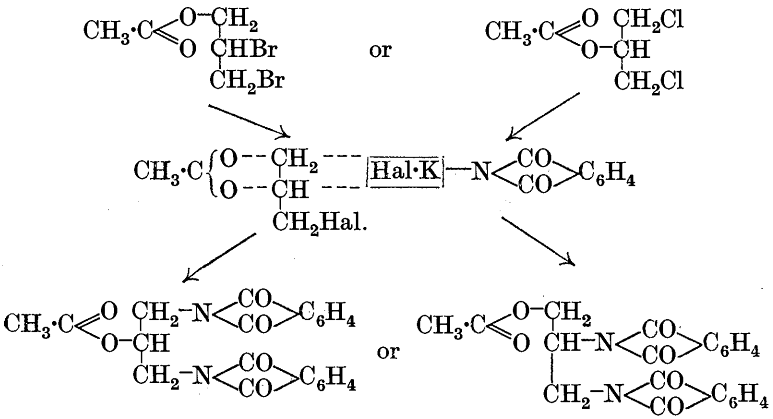
and, in any case, a tendency towards the transitory formation of such αβ-oxidic rings would seem very probable.

It is specially noteworthy, moreover, that these "migrations" appear to take place most readily *while other reactions are in progress*: the "migration" of an acyl radical occurring simultaneously with the elimination of a halogen atom from a glycerol molecule, even if the latter does not contain a hydroxyl group, is frequently experienced (Part VII), but could not previously be explained. Such reactions, however, for example, the formation of identical di-*p*-nitrobenzoates from αβ- and αγ-dibromohydrin palmitates (Part VII),



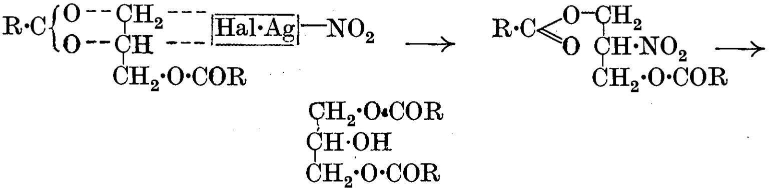
$$\begin{array}{l} C_{15}H_{31}\cdot C{<}\begin{matrix}O- & CH_2\\ O & CHBr\\ & CH_2Br\end{matrix} \quad \text{or} \quad C_{15}H_{31}\cdot C{<}\begin{matrix}O & CH_2Br\\ O- & CH\\ & CH_2Br\end{matrix} \\ \qquad\qquad\searrow \qquad\qquad\qquad\qquad \swarrow \\ C_{15}H_{31}\cdot C\left\{\begin{matrix}O\,--\,CH_2\,--\\ O\,--\,CH\,\ --\\ \quad CH_2Br\end{matrix}\right. \boxed{BrAg}-O\cdot CO\cdot C_6H_4\cdot NO_2 \\ \qquad\qquad\swarrow \qquad\qquad\qquad\qquad \searrow \\ C_{15}H_{31}\cdot C{<}\begin{matrix}O- & CH_2\\ O & CH\cdot O\cdot CO\cdot C_6H_4\cdot NO_2\\ & CH_2\cdot O\cdot CO\cdot C_6H_4\cdot NO_2\end{matrix} \quad \text{or} \quad C_{15}H_{31}\cdot C{<}\begin{matrix}O & CH_2\cdot O\cdot CO\cdot C_6H_4\cdot NO_2\\ O- & CH\\ & CH\cdot O\cdot CO\cdot C_6H_4\cdot NO_2\end{matrix}\end{array}$$

and of identical diphthalimido-compounds from the α- and β-acetates of halogenohydrins (Part VII),

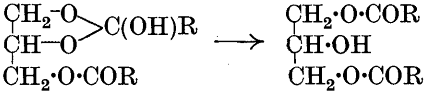


can easily be represented in this way.

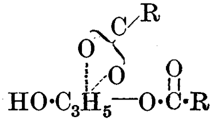
The formation of αγ-diglycerides, by the esterification and subsequent elimination of the halogen atoms of α-monochlorohydrin and α-monoiodohydrin, discussed earlier in this paper, can similarly be explained,



but in such cases, *where a free hydroxyl group is present or is produced*, a somewhat similar explanation has already been put forward tentatively by Fischer (*Ber.*, 1920, **53**, 1621), the hydroxyl group being supposed by him to play an essential part in the mechanism of the change.



It is now clear, however, that these migrations occur whether a hydroxyl group is present or absent, and that a wider explanation is therefore required.

The only attempt to apply broadly the tendency towards the formation of ortho-esters to explain migratory changes in glycerides appears to be that of Grün (*Ber.*, 1921, **54**, 290), whose explanation, however, involves the vague formula  for the diglycerides themselves, instead of the simple mechanism now suggested.

In addition to complications arising (i) from the formation of intermediate glycidic rings, such as that in epichlorohydrin, mentioned earlier in this paper, and (ii) from the migratory effects just considered, there is also, in most syntheses, (iii) the possibility, due to the presence of metallic compounds, that hydrolyses and re-esterifications will take place rapidly (Fischer, Pfähler, and Brauns, *Ber.*, 1920, **53**, 1634; Part III, J., 1925, **127**, 2759). It is therefore thought that the αβ-formula should be accepted as representing the structure of any particular diglyceride only when optical rotation can be demonstrated, or when some other physical difference from the αγ-isomeride, such as the depression of the latter's melting point, can be proved (compare Part VII).

Even in the event of an optical rotation being detected, caution should still be observed: Grün and Limpächer, for example (*Ber.*, 1926, **59**, 1350), synthesised a lecithin from a supposed "αβ"-distearin, m. p. 69°, the sulphuric ester of which had shown some evidence of containing an asymmetric material. The lecithin they obtained was afterwards found to be indistinguishable from that prepared from αγ-distearin (*Ber.*, 1927, **60**, 147). They further synthesised the corresponding kephalins (*ibid.*, p. 151), and were again unable to distinguish between their products.

A preparation of a sample of "αβ"-distearin, with this melting point, and similarly made from its sulphuric ester, is described in detail by these authors in a later paper (*ibid.*, p. 264), but there is nothing in this description to prove that their product was a satisfactory specimen of the true αβ-isomeride as they supposed; it may have consisted, even substantially, of ordinary or αγ-distearin, particularly as they mention that, during its final treatment, crystals were deposited which had the usual melting point of that compound.

The conclusions reached in Part V (*loc. cit.*), that *every supposed isolation of a* β-*monoglyceride then recorded was probably illusory*, and in Parts VII and IX (*locc. cit.*), that "αβ- *and* αγ-*isomerism*" *in diglycerides is frequently accepted on insufficient evidence*, are both thus fully confirmed, so far as the re-examination of "β"-esters has yet been carried.

These conclusions, and the experimental evidence previously put forward in their support, have recently been quoted in several connexions by Hibbert, Whelen, and Carter (*J. Amer. Chem. Soc.*, 1929, **51**, 304, 1602, 1606, 1944, 1945), who stress their importance in reaching an accurate view of the structures of glycerol compounds. It thus becomes increasingly clear that the relative values assigned to the various methods described in the literature for synthesising partly substituted glycerols require to be modified considerably, and a selection has consequently been made below, in accordance with the evidence obtained now and in the previous papers of this series, of what appear to be trustworthy processes for preparing α-, β-, αβ-, αγ-, and αβγ-ethers and esters of definite structure :—

(i) α-*Mono-ethers,* the structures of which were established by Irvine, Macdonald, and Soutar (J., 1915, **107**, 337), are readily produced either by reacting upon monochlorohydrin with alkali and the requisite alcohol (Reboul, *Annalen Suppl.*, 1862, **1**, 238), or by the converse process (Parts I and III,* J., 1921, **119**, 1035; 1925, **127**, 2759; Cross and Jacobs, *J. Soc. Chem. Ind.*, 1926, **45**, 320T) of reacting upon sodium glyceroxide with the requisite halide.

The accidental production of higher ethers (Part III, *loc. cit.*) and of β-ethers (Part IX, *loc. cit.*) as by-products, however, is a complication arising from the use of sodium glyceroxide.

(ii) β-*Mono-ethers* may be prepared, as exemplified in the case of the β-methyl ether, by introducing an ethereal group either into αγ-dichlorohydrin, or into certain other subsequently decomposable αγ-compounds (Part IX, *loc. cit.*; Hibbert, Hill, Whelen, and Carter, *J. Amer. Chem. Soc.*, 1928, **50**, 2235; 1929, **51**, 302, 1943).

(iii) α-*Monoglycerides* may conveniently be prepared from *iso*propylideneglycerol (Fischer, Bergmann, Bärwind, and Pfähler, *Ber.*, 1920, **53**, 1589, 1606, 1621), a synthesis which strongly indicates the α-structure; confirmation being afforded by the rotatory evidence of Abderhalden and Eichwald (*Ber.*, 1915, **48**, 1847) and perhaps by the direct formation of these esters from allyl esters (Part IV, J., 1926, 3146; Hibbert and Carter, *J. Amer. Chem. Soc.*, 1929, **51**, 1606).

They also result from the simple esterification of glycerol, or by the action of metallic salts on monochlorohydrin, but, in all such cases, are liable to be difficultly separable from higher glycerides occurring as by-products.

(iv) β-*Monoglycerides* were formerly believed to be obtainable by method (ii) above, but (see Part V, *loc. cit.*) the true β-isomerides have been produced by this method only when applied in a specially

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* These two papers, and also Parts II and VI (J., 1921, **119**, 2076; 1926, 3240), were published under sectional titles only, and consequently were not numbered.

modified form, glycerol ditrityl ether being used as the initial $\alpha\gamma$-material (Helferich and Sieber, *loc. cit.*).

(v) $\alpha\beta$-*Diethers* of true structure have never been recorded (Part VIII, *loc. cit.*); successful methods for their preparation have been mentioned (Part IX, *loc. cit.*), and a further communication on this subject will be made later.

(vi) $\alpha\gamma$-*Diethers.* All syntheses yet recorded for glycerol diethers, whether "$\alpha\beta$" or "$\alpha\gamma$," produce specimens which are identical after purification (Part VIII, *loc. cit.*) and can be proved to have the $\alpha\gamma$-structure by arguments not yet put forward.

(vii) $\alpha\beta$-*Diglycerides.* Of the various syntheses in the literature, only two would appear to be satisfactory : (*a*) indirect preparations from propylamines by Abderhalden and Eichwald and by Bergmann and co-workers (see Part VII, *loc. cit.*); (*b*) the method of Helferich and Sieber (*loc. cit.*) which employs glycerol α-monotrityl ether.

(viii) $\alpha\gamma$-*Diglycerides.* With the exception of the methods of synthesis mentioned in (vii) above, all known preparations of diglycerides, whether by direct esterification or from chlorohydrins, etc., appear to produce the $\alpha\gamma$-isomerides preferentially, although many statements occur in the literature to the contrary. Probably a chemically pure $\alpha\gamma$-diglyceride is most conveniently prepared by Fischer's method (*Ber.*, 1920, **53**, 1621) from the $\beta\gamma$-di-ester of α-iodohydrin.

(ix) $\alpha\beta\gamma$-*Tri-ethers and -esters*, containing different radicals, but of known constitution, are obtainable by mild methods (Fischer, *loc. cit.*) from the various types of partly substituted glycerols summarised above.

No investigation has yet been made to determine whether the alternative method of Whitby (J., 1926, 1458) for synthesising "symmetrical" glycerides, also used by Thomson (*loc. cit.*), is affected by migratory changes such as have now been proved to occur in the very similar reactions considered in this paper and in Part VII (*loc. cit.*); for the same reasons the structures of the "symmetrical" and "unsymmetrical" triglycerides of Humnicki and Lunkiewicz (*Bull. Soc. chim.*, 1929, **45**, 422) and of Weizmann and Haskelberg (*Compt. rend.*, 1929, **189**, 104) must also be regarded as unproven.

EXPERIMENTAL.

$\alpha\gamma$-*Di-iodohydrin* β-*Laurate*, $C_{11}H_{23}\cdot CO\cdot O\cdot CH(CH_2I)_2$.—(a) A crude material, believed to contain this substance, and obtained as an intermediate in the synthesis of "β"-monolaurin, has been described by Thieme (*loc. cit.*); this complicated preparation has now been repeated, and the expected liquid obtained, but on hydrolysis, as stated below, it yielded α-monolaurin instead of the β-isomeride.

(b) The pure *compound* has now been obtained as a colourless solid, m. p. 34° after recrystallisation from alcohol, by the direct esterification of $\alpha\gamma$-di-iodohydrin by the method described in Part V (*loc. cit.*) for the corresponding ester of $\alpha\gamma$-dichlorohydrin and for the *p*-nitrobenzoate of the latter (Found : C, 36·3 ; H, 5·6 ; I, 51·3. $C_{15}H_{28}O_2I_2$ requires C, 36·4 ; H, 5·7 ; I, 51·4%).

α- *and* " β "-*Monolaurin*, $C_{11}H_{23}\cdot CO\cdot O\cdot CH_2\cdot CH(OH)\cdot CH_2\cdot OH$.—(a) The supposed " β "-monolaurin of Thieme was obtained from the crude $\alpha\gamma$-di-iodohydrin β-laurate as described by him. It unquestionably had the α- and not the β-structure, however, since it melted at 61—62°, alone or mixed with an authentic specimen of α-monolaurin prepared by Fischer's method (*Ber.*, 1920, **53**, 1600).

(b) The pure $\alpha\gamma$-di-iodohydrin β-laurate described above was also hydrolysed in an identical manner to α-monolaurin, m. p., alone or mixed, 61—62°.

α-*Monolaurin* $\beta\gamma$-*Diphenylurethane*,
$C_{11}H_{23}\cdot CO\cdot O\cdot CH_2\cdot CH(O\cdot CO\cdot NHPh)\cdot CH_2\cdot O\cdot CO\cdot NHPh$.
—(a) α-Monolaurin was warmed with excess of phenylcarbimide and kept for several days. The *diphenylurethane*, recrystallised from ligroin, melted at 90° (Found : C, 68·0 ; H, 7·9 ; N, 5·7. $C_{29}H_{40}O_6N_2$ requires C, 67·9 ; H, 7·8 ; N, 5·5%).

(b) A sample prepared in an identical manner from the " β "-monolaurin of Grün and Skopnik (*Ber.*, 1909, **42**, 3750 ; see Part V, *loc. cit.*) melted, alone or mixed with (a), at 90°. The two samples therefore behave in the same way with phenylcarbimide, thus disposing of one of the arguments of Grün in support of the supposed " β " structure of his preparation.

" $\alpha\beta$ "- *and* " $\alpha\gamma$ "-*Dilaurins*, $(C_{11}H_{23}\cdot CO\cdot O)_2C_3H_5\cdot OH$.—(a) A specimen of " $\alpha\beta$ "-dilaurin, prepared from α-monochlorohydrin by Thieme's method (*loc. cit.*), melted at 56°.

(b) A specimen of " $\alpha\gamma$ "-dilaurin, prepared from $\alpha\gamma$-dichlorohydrin by Grün's method (*Ber.*, 1912, **45**, 3691), melted, alone or mixed with (a), at 56—57°, their identity thus being proved.

α- *and* " β "-*Monomyristin*, $C_{13}H_{27}\cdot CO\cdot O\cdot C_3H_5(OH)_2$.—(a) The supposed " β "-monomyristin of Grün, Schreyer, and Weyrauch (*Ber.*, 1912, **45**, 3420) was prepared as described by them ; it melted at 68°.

(b) An authentic specimen of α-*monomyristin* was prepared from myristyl chloride and *iso*propylideneglycerol by means of the general method for preparing α-mono-esters described by Fischer, Bergmann, Bärwind, and Pfähler (*Ber.*, 1920, **53**, 1589, 1606, 1621). 10 G. of myristyl chloride were cautiously added with shaking to a mixture of 5·2 g. of *iso*propylideneglycerol and 5·8 g. of quinoline ; after 2 days, the whole was treated with ether and the extract was washed with *N*/2-sulphuric acid, potassium bicarbonate solution, then with water, and dried with anhydrous sodium sulphate. The product was shaken with hydrochloric acid (*d* 1·19); after crystallising several times from ether, it melted at 68°, alone or mixed with (a) (Found: C, 67·8; H, 11·1. $C_{17}H_{34}O_4$ requires C, 67·6; H, 11·2%).

The supposed "β"-monomyristin is therefore α-monomyristin.

"αβ"- *and* "αγ"-*Dimyristin*, $(C_{13}H_{27}\cdot CO\cdot O)_2C_3H_5\cdot OH$.—(a) The supposed "αβ"-dimyristin prepared by the method of Grün and Theimer (*Ber.*, 1907, **40**, 1792) melted at 64—65°.

(b) A specimen of "αγ"-dimyristin, prepared as described by the same authors (*loc. cit.*), also melted at 64—65°, alone or mixed with (a). Their two processes therefore gave rise to the same compound.

"αβ"- *and* "αγ"-*Dipalmitin*, $(C_{15}H_{31}\cdot CO\cdot O)_2C_3H_5\cdot OH$.—(a) "αβ"-Dipalmitin prepared from αβ-dibromohydrin by the method of Guth (*Z. Biol.*, 1903, **44**, 78) melted at 69°.

(b) "αγ"-Dipalmitin prepared from αγ-dichlorohydrin by a method also recommended by him (*loc. cit.*) melted at 69°, alone or mixed with (a). When pure, therefore, these specimens of Guth's "αβ"- and "αγ"-dipalmitins are identical.

αγ-Dichlorohydrin β-Stearate, $C_{17}H_{35}\cdot CO\cdot O\cdot CH(CH_2Cl)_2$.—In an attempt to apply Grün's method for the synthesis of "β"-monoglycerides to the preparation of "β"-monostearin, in a similar manner to that used in the previous investigations of the supposed "β"-monolaurin, "β"-monomyristin, and "β"-monopalmitin, αγ-dichlorohydrin was esterified by stearyl chloride in quinoline; the resulting αγ-dichlorohydrin β-stearate, after crystallising from alcohol, melted at 39° (Found: C, 63·6; H, 10·0; Cl, 17·8. Calc. for $C_{21}H_{40}O_2Cl_2$: C, 63·8; H, 10·1; Cl, 18·0%).

Whitby (J., 1926, 1458) obtained a compound of this melting point by treating epichlorohydrin with stearyl chloride, a result that must be regarded as an example of an acyl group spontaneously entering the β-position in the glycerol molecule. Humnicki also (*Bull. Soc. chim.*, 1929, **45**, 279) prepared probably the same compound by direct esterification of dichlorohydrin with free stearic acid.

Attempts to hydrolyse this product to the α- or "β"-monoglyceride, either by the method described in Part V (*loc. cit.*), or after preliminary treatment with potassium iodide such as was used in Thieme's process mentioned above, have been unsuccessful. It was recorded in Part V that, although the corresponding laurate and palmitate of αγ-dichlorohydrin were successfully hydrolysed, the *p*-nitrobenzoate, the 3 : 5-dinitrobenzoate, and also the corresponding *p*-nitrobenzoate of αγ-dibromohydrin could not be hydrolysed in that way. Grün was of opinion (*Ber.*, 1910, **43**, 1288) that it is the esters of simple acids, such as acetic and benzoic acids, which give only poor yields but it would appear that other radicals can produce the same effect. The stability of the halogen atoms is perhaps significant in connexion with the formation of αβ-oxidic rings (Part VII, *loc. cit.*) which account for some of the migratory changes that frequently occur. In this connexion there may also be mentioned the very stable β-methyl and β-trityl ethers of dichlorohydrin (Parts IX and VII), the distearate of monochlorohydrin (Grün and Theimer, *Ber.*, 1907, **40**, 1792), and the chloride of *iso*propylideneglycerol (Fischer and Pfähler, *Ber.*, 1920, **53**, 1606).

This ester also resisted an attempt to displace its chlorine atoms by means of potassium phthalimide in the manner described in Part VII.

" αβ- " and " αγ "-Distearins, $(C_{17}H_{35}\cdot CO\cdot O)_2C_3H_5\cdot OH$.—(a) " αβ "-Distearin has been prepared from αβ-dibromohydrin by the method of Guth (*loc. cit.*) and Renshaw (*J. Amer. Chem. Soc.*, 1914, **36**, 537), and obtained with the m. p. 78—79°.

(b) Another specimen of " αβ "-distearin has been prepared from α-chlorohydrin βγ-distearate by repeating the synthesis of Grün and Theimer (*loc. cit.*); it melted at 78—79°, alone or mixed with (a).

(c) " αγ "-Distearin was prepared from αγ-dichlorohydrin by the method of Guth (*loc. cit.*; compare Bömer and Limpricht, *Z. Unters. Nahr. Genussmittel*, 1913, **25**, 354). This again melted at 78—79°, alone or mixed with either (a) or (b).

Throughout the work described in this paper, many recrystallisations from alternating solvents were frequently necessary in preparing specimens of supposed isomerides for mixed melting point determinations.

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