

XVIII.—*The Partial Esterification of Polyhydric Alcohols. Part VII. The Unreliability of Proofs of the Structure of Disubstituted Glycerols.*

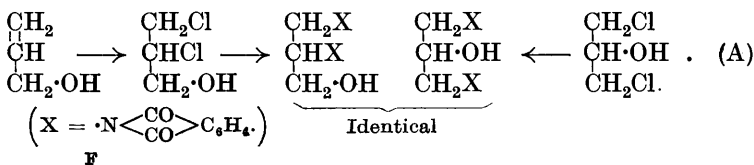
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IT was previously shown (Part V, J., 1926, 3148; *Ann. Reports*, 1927, 90) that the alleged structures of "β"-monoglycerides were untrustworthy.

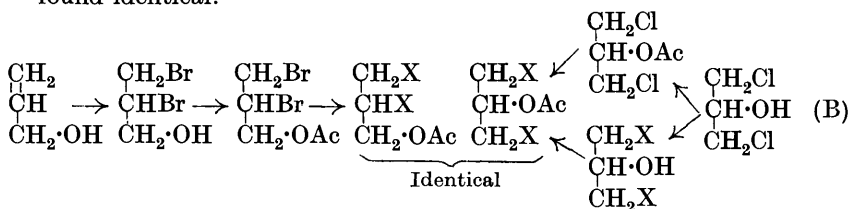
Several "αβ"-disubstituted glycerols have now been prepared, and found identical with their "αγ"-isomerides.

Philippi and Seka (*Annalen*, 1923, 433, 88) obtained the "αβ"-diphthalimido-derivative from αβ-dibromohydrin and converted it into a diamine apparently identical with the necessarily unsymmetrical or αβ-diamine resolved by Abderhalden and Eichwald (*Ber.*, 1916, 49, 2095), and also into other derivatives showing independent evidence of structure.

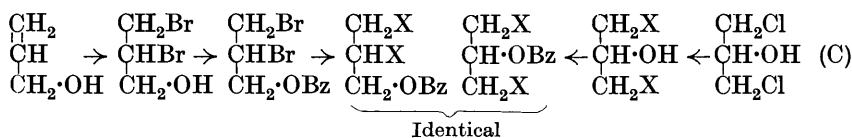
The present authors have repeated this preparation, and have shown by the mixed melting point method that the product is identical with the "αγ"-isomeride as prepared by Gabriel (*Ber.*, 1889, 22, 224. Compare also Gödeckmeyer, *Ber.*, 1888, 21, 2684).



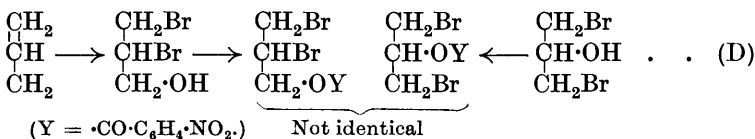
Their *monoacetates* have also been independently prepared and found identical.



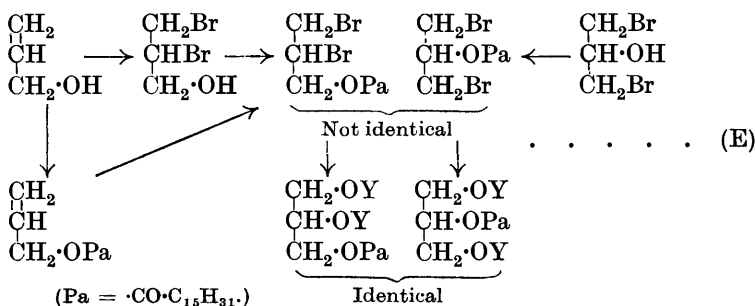
The corresponding *benzoates* have similarly been synthesised, each by methods often regarded as sufficient proofs of structure, and they too are identical.



On the other hand, *different* dibromohydrin *p*-nitrobenzoates have been obtained (Part V, *loc. cit.*).

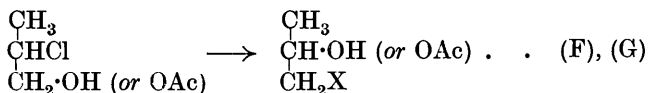


A similar series of syntheses has now also produced *different dibromohydrin palmitates*, but these react to produce identical *di-p-nitrobenzoates*.

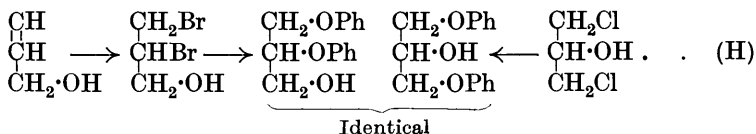


The isolation of the two different dibromohydrin *p*-nitrobenzoates and palmitates, and of two corresponding dichlorohydrin *p*-nitrobenzoates (Conant and Quale, *J. Amer. Chem. Soc.*, 1923, **45**, 2771), serves incidentally to confirm the structures of the dibromohydrins and dichlorohydrins used as the initial materials.

Several similar cases of structural confusion in compounds of the glycerol type occur in the literature, and various explanations have been put forward to account for them. For instance, Gabriel and Ohle (*Ber.*, 1917, **50**, 804) found that β -chloro-*n*-propyl alcohol was converted into phthalimidoisopropyl alcohol (F) by potassium phthalimide, and that the acetate (G) behaved similarly.

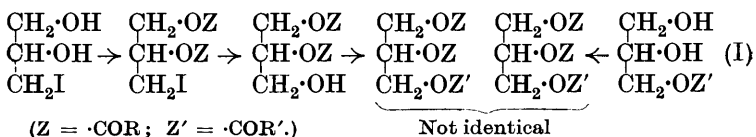


They suggest that these results may be due to the formation of propylene oxide through loss of hydrogen chloride, either during the reaction in case (F), or previously, with the production of an impure initial material, in case (G). Their explanation can easily be extended to apply to the partial substitutions of glycerol by regarding epichlorohydrin as the corresponding ethylene oxide (compare Gödeckmeyer, *loc. cit.*), an hypothesis put forward by Boyd (J., 1901, **79**, 1221) to account for his obtaining identical diphenyl ethers from $\alpha\beta$ -dibromohydrin and $\alpha\gamma$ -dichlorohydrin.



On the other hand, the hypothesis cannot explain, for example, the formation of the identical *p*-nitrobenzoates in (E).

Moreover, Fischer (*Ber.*, 1920, **53**, 1621) has studied reactions where this explanation seems untenable. " $\alpha\beta$ "-Diacylidohydrins were found to be convenient initial materials for the preparation of " $\alpha\gamma$ "-compounds. Triglycerides were then synthesised from these.

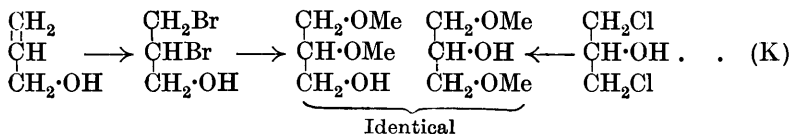
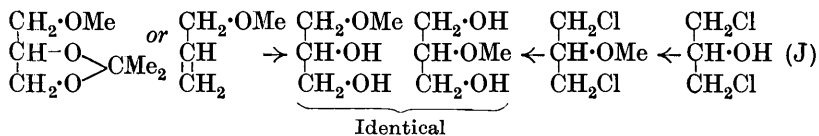


He thought that conversion probably occurred during the removal of the iodine, and involved the formation of a complex intermediate of the ortho-ester type—a suggestion not dissimilar from that of Grün (*Ber.*, 1921, **54**, 290), who held that both the wandering of acyl groups in glycerides generally and also the curious phenomenon of double melting points shown by certain glycerides, including tristearin, are due to the two forms of the carboxyl group identified by Hantzsch (*Ber.*, 1917, **50**, 1422). It is noteworthy in this

connexion that the two solvents which cause alternation of melting point of glyceryl tribenzoate (J., 1925, **127**, 2759) are actually those by which Hantzsch obtained different absorption spectra.

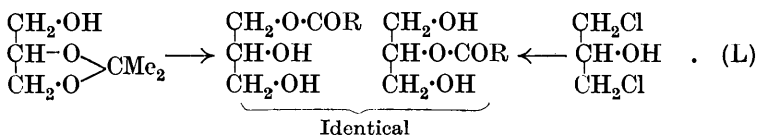
Nevertheless, no such explanation can account for (A) and (F) above, or for (J), (K), and (M) below.

Gilchrist and Purves (J., 1925, **127**, 2735) prepared the "α"-monomethyl ether and the "αβ"-dimethyl ether of glycerol, and proved identity in each case with the supposed isomeride by methods other than that of "mixed melting point."

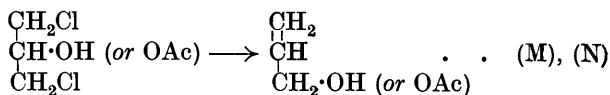


Their suggestion that the conversions might be due to unsatisfactory αγ-dichlorohydrin is negated by the experiment of Conant and Quale (*loc. cit.*).

Two exactly similar cases to (J), but each involving esters instead of ethers, were recorded previously (Part V, *loc. cit.*), and it may be added that no water was introduced during the reactions.



Allyl alcohol, which enters directly or indirectly into most of the synthetic proofs of "αβ"-disubstitution (compare the above reactions; J., 1921, **119**, 1035; 1926, 3146; Part V, *loc. cit.*; and also particularly Irvine, Soutar, and Macdonald, J., 1915, **107**, 337; Fischer, Bergmann, and Bärwind, *Ber.*, 1920, **53**, 1589; Fischer and Pfähler, *ibid.*, p. 1606), can itself be produced from αγ-dichlorohydrin by means of sodium (Lourenco, *Ann. Chim.*, 1863, **67**, 323) (M), and its acetate may be produced in a similar way (Bigot, *ibid.*, 1891, **22**, 433) (N).



$\alpha\beta$ -Dibromohydrin reacts similarly with sodium (Aschan, *Ber.*, 1890, **23**, 1831).

No explanation, common to all these very similar conversions, having been advanced, it is considered that the only absolute proof of unsymmetrical structure in disubstituted glycerols is resolution into optically active forms (Abderhalden and Eichwald, *Ber.*, 1914, **47**, 1856, 2880; 1915, **48**, 1847; *loc. cit.*; Bergmann and co-workers, *Ber.*, 1921, **54**, 936; *Z. physiol. Chem.*, 1924, **137**, 27, 47); and that even this proof cannot normally be regarded as extending with any certainty to derivatives.

When direct rotatory evidence is not available, and until the matter is better understood, it would seem reasonable, therefore, (a) when a disubstituted glycerol exists as two isomerides, to assume, in the absence of proof to the contrary, that these have the structures of their respective parent substances, or derivatives; and (b) in all other cases, to appreciate that conversion may have occurred. Such conversions are usually supposed to lead preferentially to $\alpha\gamma$ -disubstituted glycerols, but, in any case, the structures recorded, for example, by Gilchrist and Purves (*loc. cit.*) for glycerol dimethyl ether and for glycerol glucoside must clearly be regarded as unproven. The significance of these difficulties in relation to work on the higher polyhydric alcohols generally will be appreciated.

EXPERIMENTAL.

Diphthalimidohydroxypropane (A).—Specimens prepared by the methods of Philippi and Seka (*loc. cit.*) and of Gabriel (*loc. cit.*) for synthesising the " $\alpha\beta$ "- and the " $\alpha\gamma$ "-diphthalimide, respectively, melted, alone or mixed, at 204°. The supposed isomerides are therefore identical.

Diphthalimidoacetoxypropane (B).—(a) A mixture of $\alpha\beta$ -dibromohydrin (1 mol.) and acetyl chloride (1.5 mols.) was refluxed for $\frac{1}{2}$ hour; the excess of the latter was then removed under reduced pressure. The " $\alpha\beta$ "-dibromomonoacetin distilled at 227—228° (compare Aschan, *Ber.*, 1890, **23**, 1826).

3.6 G. of this product were intimately mixed with 5 g. of potassium phthalimide and heated, first at 140°, and later at 160—170° for $\frac{1}{2}$ hour. The cooled product was extracted with glacial acetic acid; the acetate obtained, after being washed with alcohol and ether, melted at 194° (Found: C, 64.6; H, 4.5; *M*, ebullioscopic in acetone, 428. $C_{21}H_{16}O_6N_2$ requires C, 64.3; H, 4.1%; *M*, 392). The structure of this substance is discussed in the theoretical section (compare Philippi and Seka, *loc. cit.*, who prepared probably the same compound from allyl acetate).

(b) 3 G. of " $\alpha\gamma$ "-dichloromonoacetin, b. p. 202—208°, prepared

from $\alpha\gamma$ -dichlorohydrin by Henry's method (*Ber.*, 1871, 4, 701), was intimately mixed with 6.5 g. of potassium phthalimide and heated at 150—170° for $\frac{1}{2}$ hour. The product, treated in the manner described above, gave an acetate which, alone or mixed with that obtained as in (a), melted at 194°.

(c) A mixture of 0.5 g. of " $\alpha\gamma$ "-diphthalimidohydroxypropane (Gabriel, *loc. cit.*) and 3 c.c. of acetyl chloride was refluxed for 10 minutes and then poured into ice-water. The acetate, isolated and purified as described above, melted at 194°, alone or mixed with that obtained as in (a) or as in (b).

Diphthalimidobenzoyloxypropane (C).—(a) 6.4 G. of dibromohydrin monobenzoate, prepared in a similar manner as the above dibromohydrin monoacetate, from $\alpha\beta$ -dibromohydrin (compare Philippi and Seka, *loc. cit.*), and 7.4 g. of potassium phthalimide were intimately mixed and heated at 170° for $\frac{1}{2}$ hour, liquefaction occurring. The mass was extracted with glacial acetic acid, and the *benzoate* crystallised from the extract in colourless prisms, m. p. 194—195° (Found : C, 68.9; H, 4.1. $C_{26}H_{18}O_6N_2$ requires C, 68.7; H, 3.9%).

(b) An attempt to prepare the compound from " $\alpha\gamma$ "-dichlorohydrin monobenzoate was not successful. 0.5 G. of the " $\alpha\gamma$ "-diphthalimide described above was therefore dissolved in 2 c.c. of benzoyl chloride and warmed on a water-bath for $\frac{1}{2}$ hour, the excess of benzoyl chloride then being destroyed by means of warm water and dilute sodium carbonate solution. The residual solid, after crystallising from chloroform-alcohol, had m. p. 195°, alone or mixed with the benzoate obtained as in (a). (A mixture with the corresponding acetoxy-compound, which has nearly the same melting point, melted indefinitely at about 175°.)

Allyl Palmitate, $C_{15}H_{31}\cdot CO\cdot O\cdot CH_2\cdot CH\cdot CH_2$.—13.5 G. of palmitic acid and 27 c.c. of thionyl chloride were warmed at 60° for an hour, the excess of the latter was distilled under reduced pressure, 4 c.c. of allyl alcohol were added, and the mixture was refluxed on a water-bath for 90 minutes. After removal of the unchanged allyl alcohol under diminished pressure, the residue was extracted in ether, shaken with water, dilute sodium bicarbonate solution, and again with water, dried over sodium sulphate, and boiled with charcoal. The light brown oil finally obtained solidified in ice; m. p. 20—25°. The quantity was not sufficient for final purification or combustion, but the ester brominated to produce $\alpha\beta$ -*dibromohydrin palmitate* which, alone or mixed with a specimen obtained as described immediately below, melted at 34°.

$\alpha\beta$ -*Dibromohydrin Palmitate*, $CH_2Br\cdot CHBr\cdot CH_2\cdot O\cdot CO\cdot C_{15}H_{31}$.—The details of the preceding preparation and purification were followed almost exactly, 12.9 g. of $\alpha\beta$ -dibromohydrin being used

in place of 4 c.c. of allyl alcohol. The product crystallised from alcohol in colourless needles, m. p. 34° (Found: C, 49.9; H, 7.9; Br, 35.0. $C_{19}H_{36}O_2Br_2$ requires C, 50.0; H, 7.9; Br, 35.1%).

The reason for assigning the $\alpha\beta$ -formula to this isomeride is discussed at the end of the theoretical section.

$\alpha\gamma$ -Dibromohydrin palmitate, $C_{15}H_{31}\cdot CO\cdot O\cdot CH(CH_2Br)_2$, m. p. 35.5° , was obtained in the same way as the $\alpha\beta$ -compound, 7.3 g. of palmitic acid, 15.2 c.c. of thionyl chloride, and 6.5 g. of $\alpha\gamma$ -dibromohydrin being used (Found: Br, 34.7%). Mixed with the $\alpha\beta$ -isomeride, it melted at about 28° . Attempts to act upon either isomeride with potassium phthalimide were not successful.

Monopalmitin Di-p-nitrobenzoate (E).—(a) 1.1 G. of silver *p*-nitrobenzoate and 5.8 g. of $\alpha\beta$ -dibromohydrin palmitate were intimately mixed with the aid of dry ether and heated to 150° ; partial liquefaction then occurred. The mixture was maintained at 130 – 140° for 3 hours with frequent stirring, cooled, and extracted with chloroform. The extract was boiled with charcoal and caused to crystallise by the addition of alcohol. Recrystallisation from chloroform–alcohol yielded colourless needles, m. p. 102° (Found: C, 62.7; H, 6.9; *M*, cryoscopic in benzene, 625. $C_{33}H_{44}O_{10}N_2$ requires C, 63.1; H, 7.0%; *M*, 628).

(b) An exactly similar preparation carried out with $\alpha\gamma$ - instead of $\alpha\beta$ -dibromohydrin palmitate gave the same product, m. p. 102° , and mixed m. p. 102° .

$\alpha\gamma$ -Dichlorohydrin Triphenylmethyl Ether,
 $CH_2Cl\cdot CH(O\cdot CPh_3)\cdot CH_2Cl$.

—A solution of 10 g. of triphenylmethyl chloride and 4 c.c. of $\alpha\gamma$ -dichlorohydrin in 25 c.c. of pyridine was kept at 100° for 2 hours, allowed to stand for 12 hours, and then poured into 100 c.c. of water. The product, which solidified during $\frac{1}{2}$ hour, was ground with water and extracted with ether. The ether isolated from the extract, after crystallising several times from alcohol, melted at 108 – 109° , was stable to aqueous potash, and did not react with potassium phthalimide (Found: Cl, 19.5. $C_{22}H_{20}OCl_2$ requires Cl, 19.1%). That it possesses the β -triphenylmethyl structure is probable from the work of Helferich and Sieber (*Z. physiol. Chem.*, 1927, **170**, 31).

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