XLII. SOME ESTERS OF PALMITIC ACID.

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The physiological importance and commercial value of the fats early attracted chemists to the study of their properties and composition. The interest which they then aroused has been fully maintained with the result that the present extensive literature on the compounds of the higher fatty acids deals almost entirely with the esters of glycerol to the exclusion of those of other polyhydric alcohols.

The chemistry of the fats may be said to have had its birth in the work of Chevreul [1823] to whose researches in the first quarter of the nineteenth century we owe the proof that the fats occurring in the animal body are triglycerides of higher fatty acids chiefly of stearic, palmitic and oleic. About forty years later Berthelot [1860] first succeeded in synthesising the mono-, di-, and tri-glycerides of many fatty acids and in identifying the tri-olein, tri-palmitin and tri-stearin so obtained with naturally occurring animal fats.

The method of synthesis adopted by Berthelot consisted in heating together glycerol and the fatty acid in a sealed tube to 200°–250°. This direct method of synthesis with various slight modifications has been largely used by later workers and still enjoys a wider application than the yields which are so obtained appear to warrant. Modifications of this method are chiefly directed towards eliminating the water formed during the reaction and thus enabling the process to be carried out at a lower temperature and also increasing the yield. A modification of this kind was introduced by Scheij [1899] and extended by Belucci and Manzetti [1911]. These workers found that the yields obtained by Berthelot's method could be greatly increased by carrying out the reaction under diminished pressure; thus Belucci and Manzetti synthesised triolein by heating together glycerol and oleic acid to 260° under a pressure of 20 mm., and state that in this way a yield of 95–98 %

was obtained; they afterwards found that the reaction could be carried out equally well under atmospheric pressure if a current of carbon dioxide were passed through the flask. Grün [1905] carried out the synthesis of diglycerides by warming the fatty acid and glycerol in concentrated sulphuric acid; thus α - α -distearin was obtained from glycerol and stearic acid, glycerol-disulphonic acid being formed as an intermediate product. None but primary alcohol groups are esterified in this reaction. Bloor [1910, 1912] applied this method to the condensation of mannitol with stearic and lauric acids; he identified his products as mannitol distearate and mannitol dilaurate respectively.

The halogen derivatives of glycerol have also been used in the preparation of glycerides. Partheil and Von Velsen [1900] prepared trilaurin and tripalmitin by heating the silver salts of these acids and tribromohydrin to 140° to 150° in the presence of xylene. A similar method was used by Guth [1903]; he prepared monostearin by heating together sodium stearate and monochlorohydrin, also α -distearin from α -dichlorohydrin, and β -distearin from β -dibromohydrin; tristearin was obtained from tribromohydrin and excess of sodium stearate. The yields obtained by these last two methods are not given.

Since the esters of the lower fatty acids are so readily prepared by the action of the acid chloride on the alcohol it seemed probable that this method might also be applied to the synthesis of esters of the higher fatty acids, not only with glycerol but also with other polyhydric alcohols. This method has been used recently by Grün and Schreyer [1912] who prepared α -myristo- α -chlorohydrin by the action of myristyl chloride on α -monochlorohydrin, and β -myristo- α - α -dichlorohydrin from myristyl chloride on α - α -dichlorohydrin. This is the only example of the use of this method which the writer has been able to find, though the wide use of the method in other fields makes it seem possible that some cases have been overlooked.

In order to test the efficiency of the above method for the synthesis of fatty bodies, palmityl chloride has been exclusively used and was prepared by the method described by Marie [1896] for melissyl and cerotyl chlorides. Its action was tried on ethylene glycol, glycerol, mannitol and glucose. In the case of glycerol esterification was effected by heating the two substances together to 120°. The action however was slow and this method was abandoned in favour of allowing the substances to react in the presence of pyridine with chloroform as a solvent. The action then took place in the cold and was completed by gently warming on the water bath.

EXPERIMENTAL.

Preparation of palmityl chloride. 45 g. of palmitic acid were mixed with 40 g. of phosphorus pentachloride (calculated amount 38 g.) in a distillation flask and the action started by warming. When the action was complete the excess of phosphorus pentachloride and the phosphorus oxychloride were distilled in vacuo on a boiling water bath; when these substances were removed the temperature was raised; the palmityl chloride distilled over as a colourless oil at 198°–200° under a pressure of 15 mm. Yield obtained 37 g. (77 %).

Preparation of glycol dipalmitate. 1 g. of dry glycol and 5 g. of pyridine were added to 12.8 g. of palmityl chloride (4 g. in excess of that required for complete esterification); about 50 cc. of dry chloroform were then added to dissolve the solid compound of pyridine and palmityl chloride formed; the contents of the flask turned a deep orange colour. The flask was closed and allowed to stand for 24 hours, it was then gently warmed on the water bath and well shaken; the chloroform was evaporated off and dilute sulphuric acid added to liberate the pyridine from its combination with palmityl chloride; the insoluble ester and palmitic acid (from excess of reagent) were filtered off and washed free from sulphuric acid and pyridine on a hot water filter; they were then dissolved in hot absolute alcohol and the free palmitic acid neutralised with alcoholic potash; the solution was evaporated to dryness and the residue transferred to a Soxhlet apparatus and extracted with ether. The ester crystallised from the ethereal solution on cooling in clusters of fine needles.

Yield before recrystallisation 7.5 g. (94 %). The substance so obtained was brownish yellow in colour and was soluble in hot and cold alcohol and also in chloroform, ether, ethyl acetate and the usual solvents for fats. It was recrystallised from a mixture of chloroform and alcohol since it was found that by this method the crystals obtained were white whereas when other solvents were used the colouring matter was thrown down with the crystals. The crystals so obtained were deposited in rosettes of fine needles; after four recrystallisations the substance had a constant m.p. of 65° (corrected). It was dried to constant weight in vacuo over sulphuric acid; it still, however, contained traces of moisture, which were only finally removed by heating in a toluene bath to 106°. The substance was identified by the results of elementary analysis and by the percentage of palmitic acid estimated by Hehner's method. As these values calculated for glycol monopalmitate,

glycol dipalmitate and for palmitic acid approach somewhat nearly to each other, these figures are appended for purposes of comparison.

	% Hydrogen	% Carbon	% Palmitic acid
Calculated for glycol monopalmitate	12.00	72.00	85.3
„ „ glycol dipalmitate	12.27	75.84	95.2
„ „ palmitic acid	12.5	75.01	100

Analysis :

- (1) 0.2195 g.; 0.2406 g. H₂O; 0.6108 g. CO₂.
 (2) 0.2598 g.; 0.2913 g. H₂O; 0.7227 g. CO₂.
 (3) 1.8598 g.; 1.7750 g. palmitic acid.

	% Hydrogen	% Carbon	% Palmitic acid
Analysis (1)	12.44	75.9	—
„ (2)	12.45	75.84	—
„ (3)	—	—	95.5

The compound may therefore be identified as glycol dipalmitate corresponding to the formula

Glycerol tripalmitate (tripalmitin). 1.2 g. of glycerol and 9 g. of pyridine were added to 15.8 g. of palmityl chloride (4.7 g. in excess of that required for complete esterification); 30 cc. of chloroform were added. The procedure followed was the same as that described for the glycol compound. In this case the ester obtained from the ether extract was brown in colour and much difficulty was experienced in obtaining white crystals. After two recrystallisations from chloroform and alcohol followed by four from ether the substance, though melting sharply at 62°, was still biscuit coloured. It was then dissolved in wet ether and boiled for six hours with charcoal. The substance which crystallised from the ether after filtration was quite white and was deposited in fine needles; m.p. 62° (corrected). It was sparingly soluble in hot alcohol and soluble in ether, chloroform and all the usual solvents for fats. Traces of charcoal clung to the substance with great obstinacy and could not be removed by the filtration of the ethereal solution. They were finally removed by filtering the substance itself in the steam oven through a very small filter. The substance was dried at 110°, and identified by the results of elementary analysis; the corresponding values calculated for di- and tripalmitin and for palmitic acid are appended for comparison.

		% Hydrogen	% Carbon
Calculated for dipalmitin		11.90	74.06
" " tripalmitin		11.91	75.95
" " palmitic acid		12.5	75.01
<i>Analysis:</i>			
(1)	0.2055 g.; 0.2222 g. H ₂ O; 0.5728 g. CO ₂ .		
(2)	0.1945 g.; 0.2155 g. H ₂ O; 0.5405 g. CO ₂ .		
		% Hydrogen	% Carbon
Analysis (1)		12.01	76.00
" (2)		12.30	75.78

The substance was therefore identified as tripalmitin.

Owing to the difficulty experienced in purification sufficient substance was not available for a determination of palmitic acid.

Yield before recrystallisation 5.5 g. (50 %).

Yield of pure substance 2 g.

Mannitol hexapalmitate. 1.5 g. of mannitol and 8 g. of pyridine were added to 19.2 g. of palmityl chloride (4.8 g. in excess of that required for complete esterification). The procedure followed was identical with that described for glycol. The total yield of ester obtained after extraction in the Soxhlet apparatus and before further purification was 11.2 g. (78 %). The substance obtained was almost insoluble in cold alcohol, and very sparingly soluble in hot alcohol; it was easily soluble in ether, light petroleum, chloroform and ethyl acetate. It crystallised readily from a mixture of chloroform and alcohol or from ethyl acetate in rosettes of fine needles; m.p. 64.5 (corrected). It was dried at 106°.

The substance was identified by the results of elementary analysis and by the percentage of palmitic acid estimated by Hehner's method; these values calculated for mannitol hexapalmitate, mannitol pentapalmitate and for palmitic acid are also appended.

		% Hydrogen	% Carbon	% Palmitic acid
Calculated for mannitol hexapalmitate		12.05	76.03	95.4
" " mannitol pentapalmitate		11.90	75.26	93.37
" " palmitic acid		12.5	75.01	100
<i>Analysis:</i>				
(1)	0.2245 g.; 0.2430 g. H ₂ O; 0.6270 g. CO ₂ .			
(2)	0.2135 g.; 0.2335 g. H ₂ O; 0.5940 g. CO ₂ .			
(3)	1.7067 g.; 1.6220 g. of palmitic acid.			
		% Hydrogen	% Carbon	% Palmitic acid
Analysis (1)		12.03	76.19	—
" (2)		12.14	75.90	—
" (3)		—	—	95.06

The substance was therefore identified as mannitol hexapalmitate corresponding to the formula

Glucose pentapalmitate. 1 g. of glucose and 9 g. of pyridine were added to 8.3 g. of palmityl chloride (2.4 g. in excess of that required for complete esterification). The procedure followed was the same as that previously described; as in the case of the glycerol compound decolorisation with charcoal and subsequent filtration of the melted ester were necessary. The total yield obtained after extraction in the Soxhlet apparatus was about 5 g. (83 %). The total yield of purified material was 2.8 g.

The substance obtained was very slightly soluble in cold alcohol and only sparingly soluble in hot alcohol; it dissolved readily in all the solvents commonly used for fats. It was recrystallised from ethyl acetate and melted at 62° (corrected). The substance was readily hydrolysed by alcoholic potash as was shown by the rapid darkening of the solution due to the action of the alkali on glucose, coupled with the fact that the substance was soon completely dissolved. The action of the glucose on the alkali prevented a saponification value from being taken. An attempt was made to estimate the palmitic acid by Hehner's method; a known weight of the substance was saponified with alcoholic potash, the alcohol evaporated off and the soap dissolved in water. The solution was very dark owing to the presence of the resins already mentioned, and it was found on acidifying and attempting to filter off the palmitic acid that the presence of these substances caused the palmitic acid to pass through the filter paper. An attempt to effect the complete acid hydrolysis and afterwards to estimate the glucose was next made; 0.397 g. of the ester was placed in a flask with 50 cc. of absolute alcohol in which, even on boiling, it only partially dissolved, the greater part sinking as oily drops; 25 cc. of 20 % hydrochloric acid were added and the flask boiled under a reflux condenser for 84 hours. At the end of this time the hydrolysis was still incomplete as was shown by the presence of small drops of insoluble ester in the boiling alcohol. When the contents of the flask were filtered to remove the unchanged ester and the filtrate neutralised the presence of glucose was shown by the reduction of Fehling's solution. Owing to the impossibility of removing the unchanged ester quantitatively the glucose could not be estimated. It was therefore necessary to rely solely on the combustion results for the identification of the substance.

0.2233 g.; 0.2410 g. H₂O; 0.6163 g. CO₂.

	% Hydrogen	% Carbon
Analysis	11.99	75.26
Calculated for glucose pentapalmitate	11.82	75.32
" " " tetrapalmitate	11.66	74.20

The substance was therefore identified as glucose pentapalmitate corresponding to the formula

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