

416. *Experiments on the Direct Esterification of Higher Fatty Acids with Glycerol and with Ethylene Glycol.*

By T. P. HILDITCH and J. G. RIGG.

It is well known (cf. Berthelot, *Ann. Chim.*, 1854, **41**, 238) that the higher fatty acids can be converted into their glycerol or glycol esters by heating them with either alcohol under reduced pressure at a somewhat high temperature (180° upwards), and also that the reaction temperature can be lowered to 140—160° if the esterification is catalysed by the presence of small proportions of an aromatic sulphonic acid, for example, naphthalene- β -sulphonic acid. In this way it is possible to prepare, by heating an excess of the acid with either alcohol, triglycerides or diacylated glycols (Bhattacharya and Hilditch, *Proc. Roy. Soc.*, 1930, *A*, **129**, 468; *J.*, 1931, 901).

In studying this reaction further with the object of ascertaining how far it might be possible to produce mono- or di-glycerides (especially the former) as the main product, we have observed that even in presence of a large excess of glycerol (10 mols. per mol. of fatty acid) the product is a mixture in which diglycerides predominate; and, although triglycerides are probably only present in small proportions, not much more than 40% of the mixed esters consists of monoglycerides. This seems to be the result of the comparative immiscibility of glycerol and the higher fatty acids or their glycerol esters: the monoglycerides first formed pass mainly into the fatty acid phase, and production of di- or even to some extent of tri-glycerides is favoured even in presence of a large excess of glycerol.

We have found that the yield of monoglycerides can be very much increased by employing a medium in which both glycerol and the higher fatty acids are freely soluble. The choice of such solvents is somewhat restricted, especially as it is desirable to use one which does not boil below about 180° and is at the same time readily removable from the products of the reaction. Phenol or cresols fulfil all the required conditions, and in the experiments now described phenol was used as solvent, in a quantity equal to the weight of fatty acid taken. Under these conditions much higher yields of monoglyceride are obtainable, according to the temperature, time of reaction, and the ratio of glycerol to fatty acid in the reaction mixture; in the most favourable circumstances the product may contain about 90% of monoglyceride.

The esterification of lauric, palmitic, stearic, and oleic acids has been studied in this way and similar results have been obtained both with glycerol and with ethylene glycol, and in presence or absence of a sulphonic acid catalyst. Presence of the latter leads to considerable increase in the total yield of esters, but is usually accompanied by some diminution in the proportion of monoglyceride in the product. Following a suggestion of Professor Smiles, we have replaced naphthalene- β -sulphonic acid as catalyst by Reychler's

camphor- β -sulphonic acid; the latter is definitely more efficient as an esterification catalyst in this reaction, and has the further advantage that it leads to much less darkening in colour of the products than does the use of naphthalene- β -sulphonic acid.

In presence of a solvent (phenol), the amount of esterification, and also the proportion of monoglyceride in the resulting esters, is dependent on four factors, namely, the proportion of glycerol to fatty acid present in the reaction mixture, the quantity of camphor- β -sulphonic acid used as a catalyst, the temperature of the reaction, and the length of time during which the reaction has been allowed to proceed. In general it may be said that the greater the proportion of glycerol to fatty acid, the higher is the percentage of monoglyceride obtained. Addition of camphor- β -sulphonic acid increases the yield of mixed glycerides but somewhat lowers the percentage of monoglyceride. When the temperature of the reaction is increased, the yield of product rises and the percentage of monoglyceride falls slightly; when the time of reaction is prolonged, an increase in yield and a fall in the percentage of monoglyceride occur. The percentage of monoglycerides in the products of esterification of stearic or oleic acid is less susceptible to variations in the conditions of reaction than in the case of the corresponding esters from acids of lower molecular weight.

In similar experiments with ethylene glycol, the results obtained were of the same general nature as those for the glycerides; but both the total yield of esters and the proportion of mono-acylated glycol therein were larger than in experiments with glycerol under the same conditions.

In the glyceride series, it is possible to prepare pure monolaurin or monopalmitin by crystallisation from ether at 0°, but the solubilities of the mono- and di-stearins are not sufficiently different to enable complete separation to be effected by this means. This procedure is unsuitable for the glycol esters, because in this series the di-acylated glycols are definitely less soluble in ether than the mono-acylated derivatives.

Almost exclusive formation of α -monoglycerides takes place in this reaction, as evidenced by their behaviour on oxidation with lead tetra-acetate (method of Criegee, *Ber.*, 1931, **64**, 260), and by the melting points of the purified monolaurin and monopalmitin.

EXPERIMENTAL.

The fatty acids were prepared (by fractionation of their methyl esters) from the following sources: Lauric acid, by repeated fractionation of the methyl esters from coconut oil mixed fatty acids; palmitic acid and oleic acid, by lead salt separation of the mixed fatty acids of palm oil, followed by suitable refractionation of the methyl esters of the "solid" and "liquid" acids thus obtained (the oleic acid finally produced contained about 10% of linoleic acid, the removal of which was considered unnecessary for the purpose of the present experiments); stearic acid, by hydrogenation of some of the methyl oleate isolated in the preparation of oleic acid, and subsequent hydrolysis and crystallisation from alcohol.

In all experiments the fatty acid (20 g.) was mixed with an equal weight of phenol and the appropriate weight of glycerol or ethylene glycol in a round-bottomed flask fitted with a cork carrying an inlet tube dipping well below the surface of the liquid and an exit tube connected to a reflux air-condenser. The flask was heated in an oil-bath maintained at the desired temperature and during the reaction a gentle current of dry carbon dioxide was passed through the flask to effect agitation and to assist in removal of water vapour. At the end of the experiment, when phenol had been used as solvent, it was removed as far as possible by distillation in steam; the non-volatile residue was taken up in ether, unchanged fatty acid removed by aqueous potassium carbonate, the ethereal solution washed free from soap with water, and the mixture of glycerides or glycol esters freed from solvent, weighed, and analysed.

Determination of the saponification equivalents of the products was mainly relied upon as an indication of their composition. This value is of course insufficient by itself to define the composition in terms of mono-, di-, and tri-glycerides, but it serves to give the limits between which the proportions of monoglyceride present must lie. Thus, for example, in the case of the palmitins (saponification equivalent of monopalmitin 330, dipalmitin 286, tripalmitin 268.7) a product with a mean equivalent of 304.8 might consist of 45% of mono- and 55% of di-palmitin, or of 59% of mono- and 41% of tri-palmitin, or any other mixture between these limits; in this case, therefore, the limiting proportions of monopalmitin will be 45—59%.

Our results are given in this form throughout, the lower figure indicating that for a mixture of mono- and di-glycerides. From the results of oxidations with lead tetra-acetate, it is clear that the lower figure approximates nearest to the truth, so that the production of triglyceride in these experiments was relatively small.

In the case of glycol esters, determination of the equivalent alone is of course sufficient to define the composition of the product.

In many cases we also determined the saponification equivalents of the glycerol esters after the latter had been acetylated. The resulting data acted as a useful control on those obtained from the direct saponification equivalents, but, of course, equally failed to define the precise composition of the possible ternary mixture of mono-, di-, and tri-glycerides.

On the other hand we found that a modification of the method of Criegee (*loc. cit.*) could be used to determine the approximate proportion of α -monoglycerides present in the saturated esters. Criegee recommends the use of lead tetra-acetate in glacial acetic acid solution at 20° for 20 hours, but we find that in the case of α -monoglycerides oxidation at a higher temperature for a shorter time is necessary in order to obtain approximately quantitative results. This is illustrated by the following experiments carried out on a specimen of synthetic α -monostearin (containing 95% α -monostearin, m. p. 79—79.5°) which had been prepared by the method of Fischer, Bergmann, and Bärwind (*Ber.*, 1920, 53, 1589):

Oxidation of 95% α -Monostearin with Lead Tetra-acetate.

Temp.	Time, hours.	α -Monostearin (Found, %).
20°	20	67.8, 67.8
50	3	89.3
"	6	96.8, 95.0, 94.2
"	12	102.9, 102.3

It thus appears that contact of the reagent for 6 hours at 50° gave results closely approximating to the known content of α -monostearin, and these conditions were employed in the analysis of our esterified products by this method.

A specimen of synthetic β -monostearin (m. p. 75°) prepared by the method of Bergmann and Carter (*Z. physiol. Chem.*, 1930, 191, 214) was also submitted to the lead tetra-acetate reagent at 50° for 6 hours (Found: 1.5, 2.0%, calculated as α -monostearin); these results showed that the reagent only interacts to a very minor extent with β -monoglycerides.

The experimental results obtained under various conditions with glycerol and glycol are summarised in the following tables. The amount of glycerol present in each experiment is

I. Esterification of Glycerol with Fatty Acids.

Mols. glycerol per mol. acid.	Camphor- β -sulphonic acid, %.	Time, hours.	Temp.	Esterified product.			Monoglyceride content, %.	
				Yield, g.*	M. p. °	Sapon. equiv.	Limits (from s.e.).	By lead tetra-acetate.
(a) <i>Glycerol and palmitic acid (20 g.) without solvent.</i>								
3	—	4	180°	17.3	54.5°	304.8	45—59	46.2
1	—	4	160	12.1	55	299.4	34—50	32.1
2	—	4	160	14.4	55	302.0	39—55	39.5
3	—	4	160	15.5	55.5	303.1	42—56	39.8
3	0.2	4	160	21.3	54.5	305.6	47—60	48.2
10	—	4	160	12.8	55	304.8	45—59	43.6
(b) <i>Glycerol and lauric acid (20 g.) in presence of phenol (20 g.).</i>								
10	—	1	180°	6.1	55.5°	274.3	100	98.0
8	—	1	180	6.1	54.5	270.6	93—94	92.9
3	—	4	180	11.5	53.5	265.9	82—87	81.3
3	0.1	1	180	16.4	53.5	265.3	81—86	82.1
3	0.5	4	180	20.7	53.5	266.5	84—88	85.0
3	—	4	160	9.6	54.5	270.2	92—94	91.8
1	—	4	160	8.6	53.5	266.3	83—88	83.1
3	0.1	1	160	9.4	54	268.5	88—91	89.2
3	0.1	2	160	15.5	53.5	266.5	84—88	84.4
3	0.1	4	160	20.6	53	264.0	78—84	80.1
2	0.1	4	160	19.0	52.5	261.9	73—80	74.2
1	0.1	4	160	16.0	52	257.6	64—73	67.0
3	0.1	4	140	18.8	53.5	265.7	82—87	80.8
3	0.1	4	120	16.1	54	267.0	85—89	83.2

Mols. glycerol per mol. acid.	Camphor- β -sulphonic acid, %.	Time, hours.	Temp.	Esterified product.			Monoglyceride content, %.	
				Yield, g.	M. p.	Sapon. equiv.	Limits (from s.e.).	By lead tetra- acetate.
(c) <i>Glycerol and palmitic acid (20 g.) in presence of phenol (20 g.).</i>								
10	—	1	180°	10·0	65°	322·1	83—87	86·7
3	—	1	180	11·1	65	321·8	82—87	83·4
3	—	2	180	12·2	65	320·5	80—85	82·1
3	—	4	180	13·0	66	320·3	79—84	84·5
3	—	6	180	14·0	66	318·8	76—82	79·8
3	0·1	2	180	21·0	62·5	315·4	68—76	68·7
3	0·1	4	180	21·0	62·5	315·1	68—76	67·0
3	0·1	6	180	21·0	62·5	315·4	68—76	67·8
10	0·1	4	160	17·9	66·5	324·9	89—92	93·2
3	—	4	160	11·8	67	320·3	79—84	82·2
3	0·1	1	160	11·4	67	325·6	91—93	91·3
3	0·1	2	160	13·4	66	320·7	80—85	86·8
3	0·1	4	160	18·2	66·5	320·5	79—85	81·9
3	0·2	4	160	18·5	64	316·4	70—78	71·2
3	0·5	4	160	20·0	66	315·5	69—76	72·7
3	0·1	4	140	17·0	66	319·7	78—83	83·9
3	0·1	4	120	13·3	66	322·9	85—89	88·2
(d) <i>Glycerol and stearic acid (20 g.) in presence of phenol (20 g.).</i>								
10	—	1	180°	4·0	65·5°	346·9	76—82	80·4
3	—	1	180	4·4	68	346·9	76—82	82·2
3	—	4	180	11·9	72	349·4	82—86	80·5
3	0·1	1	180	16·0	69	348·4	79—84	78·2
3	—	4	160	8·2	68·5	348·4	79—84	74·6
3	0·1	1	160	13·6	69	347·7	78—83	82·2
3	0·1	2	160	20·0	68	347·9	78—84	82·1
3	0·1	4	160	20·0	69	346·7	75—81	79·1
3	0·1	4	140	13·1	68·5	342·5	67—75	74·2
3	0·1	4	120	10·9	68	346·7	76—82	79·5
(e) <i>Glycerol and oleic acid (20 g.) in presence of phenol (20 g.).</i>								
10	—	1	180°	3·0	23°	352·4	92—94	—
3	—	1	180	3·5	23	350·5	88—91	—
3	—	4	180	6·8	23	349·9	87—90	—
3	0·1	1	180	12·7	23	350·3	88—91	—
3	0·5	4	180	21·0	21	346·1	79—84	—
3	—	4	160	6·2	22	348·7	84—88	—
1	—	4	160	6·1	21	338·4	62—71	—
3	0·1	1	160	7·4	23	353·7	95—96	—
3	0·1	2	160	12·6	22	349·6	86—90	—
3	0·1	4	160	18·9	22	349·1	85—89	—
2	0·1	4	160	16·8	22	345·1	76—82	—
1	0·1	4	160	13·6	21	333·7	52—64	—
3	0·1	4	140	10·7	23	349·9	87—90	—
3	0·1	4	120	4·4	23	351·1	89—92	—

indicated as the number of mols. of glycerol per mol. of fatty acid, and the concentration of camphor- β -sulphonic acid catalyst is expressed as a percentage of the weight of fatty acid taken.

(b) The products obtained from glycerol and lauric acid in presence of phenol yielded pure α -monolaurin when crystallised from ether. For instance, a mixture (40 g.) which contained about 80% of monolaurin yielded, after one crystallisation from ether (250 c.c.), 22 g. of ester, m. p. 61°, sapon. equiv. 272·6 (97—98% monolaurin); a second crystallisation gave the pure α -monolaurin, m. p. 62° (cf. Fischer, Bergmann, and Bärwind, *loc. cit.*).

(c) A product (40 g.) containing about 75% of monopalmitin was crystallised once from ether (300 c.c.) at 0°, α -monopalmitin (20 g., m. p. 75°, sapon. equiv. 330) being obtained.

(d) Crystallisation of the crude monostearins from ether was less successful than in the preceding instances. A product (33 g.) containing about 75% of monostearin yielded, on a first crystallisation from ether (400 c.c.), a mixture (24 g., m. p. 78°) which contained about 85% of monostearin; a further crystallisation only increased the monostearin content to 90% (15 g., m. p. 80°).

II. Esterification of Ethylene Glycol with Fatty Acids.

Ethylene glycol with lauric, palmitic, stearic, or oleic acid (20 g.) in presence of phenol (20 g.)

Acid.	Mols. ethylene glycol per mol. acid.	Camphor- β -sulphonic acid, %.	Time, hours.	Temp.	Esterified product.			
					Yield, g.	M. p.	Sapon. equiv.	Mono-ester, %.
Lauric	10	0.1	4	180°	20.0	27.5°	244.5	100
"	3	0.1	4	180	20.1	27.5	243.4	98
"	3	0.5	4	180	20.1	27.5	244.4	100
Palmitic ...	10	0.1	4	180	22.1	47.5	300.1	100
" ...	3	0.1	4	180	22.1	46.5	296.3	89
" ...	1	0.1	4	180	18.7	47	290.3	71
" ...	3	—	4	180	15.5	47	296.4	89
" ...	3	0.5	4	180	22.1	47	297.0	91
" ...	3	0.1	1	180	20.2	47	296.1	89
" ...	3	0.1	4	120	18.8	47	294.5	84
Stearic	10	0.1	4	180	22.1	56	327.9	100
"	3	0.1	4	180	22.1	55	325.7	93
"	3	0.5	4	180	22.1	56	327.4	98
Oleic	10	0.1	4	180	21.2	1	326.8	100
"	3	0.1	4	180	21.0	1	325.0	97
"	3	0.5	4	180	21.2	1	326.8	100

Without solvent (phenol), ethylene glycol (3 mols.) and palmitic acid (1 mol.), heated at 180° for 4 hours in presence of 0.1% of camphor- β -sulphonic acid, gave a product (21.5 g., m. p. 48°, sapon. equiv. 289.8) containing 69% of glycol monopalmitate.

The glycol mono-esters of lauric, palmitic, and stearic acids are more soluble in ether than the corresponding di-esters. By removal of successive crops of crystals from an ethereal solution, with concurrent concentration of the latter, it was possible to remove all the glycol di-esters (together, of course, with much mono-ester), so that the final mother-liquors contained only the latter; subsequent crystallisation of the residues from the mother-liquors caused no change in melting point, and the equivalents of the purified mono-esters agreed with the theoretical values. The melting points of the glycol mono-esters, together with those given by Bhattacharya and Hilditch (J., 1931, 901) for the corresponding di-esters, are as follows :

	Ethylene glycol	
	mono-ester.	di-ester.
Laurate	27.5°	49°
Palmitate	47.5	69
Stearate	56	73

Whereas monoglycerides have higher melting points and are in general less soluble than the corresponding diglycerides, the reverse holds for the glycol esters of the higher fatty acids. For any of the above three fatty acids, the melting points fall in the following order : α -Monoglyceride > $\alpha\alpha'$ -diglyceride > glycol di-ester > triglyceride > fatty acid > glycol mono-ester; the last-named have much lower melting points than the other members of each series.

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THE UNIVERSITY, LIVERPOOL.

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417. *Optical Activity in Relation to Tautomeric Change. Part V. Kinetic Status of Ionic Intermediates in Prototropy.*

By SHING KONG HSÜ, CHRISTOPHER K. INGOLD, and CHRISTOPHER L. WILSON.

THIS paper deals with the intimate mechanism of prototropic change, the method of attack being a development of that initiated in Part II (Ingold and Wilson, J., 1934, 92). The enquiry is directed to determine whether or not catalysed prototropic change involves short-lived intermediates, and if so, whether they are of the nature of transition complexes or entities with some degree of kinetic stability and independence. These questions are