451. *An X-Ray and Thermal Examination of the Glycerides. Part XII.* Chaulmoogric and Hydnocarpic Acids and their Mono-, Di-, and Tri-glycerides.*

By A. Gupta and T. Malkin.

In contrast to the behaviour of straight-chain fatty acids, chaulmoogric and hydnocarpic acids show no evidence of polymorphism. Their glycerides, on the other hand, exhibit the same type of polymorphism as do the glycerides of straight-chain fatty acids, and exist in α-, β′-, and β-forms (cf. Parts I, II, and III, *J.*, 1934, 666; 1936, 1628; 1937, 1409). *X*-Ray and melting-point data for the various forms are recorded.

Chaulmoogric and hydnocarpic acids are the major constituent acids of a number of oils (chaulmoogra, lukrabo, gorli-seed), extracted from the seeds of various *hydnocarpus* species of plants of the Flacourtiaceae family. These oils have long been known in the East for use in cases of leprosy, but it was not until 1904—1905 that Power and Gornell (*J.*, 1904, 838, 851) and Power and Barrowcliff (*J.*, 1905, 884) isolated, characterised, and named chaulmoogric and hydnocarpic acids, respectively, and showed them to be homologues, possessing a normal fatty acid structure, terminated by a *cyclo*pentene ring. Some doubt still existed concerning the position of the double bond, and it remained for Shriner and Adams (*J. Amer. Chem. Soc.*, 1925, **47**, 2727) to establish that chaulmoogric acid was 13-*cyclo*pent-2′-enyltridecanoic acid,† and that hydnocarpic acid was the corresponding undecanoic derivative.

Although these acids have been fully investigated, there is very little known about their glycerides, the only references to which appear to be that of Wagner-Jauregg and Arnold (*Ber.*, 1937, **70**, 1459), who prepared an indefinite mixture of diglycerides of chaulmoogric and hydnocarpic acids, as intermediates in the synthesis of phosphatides, and that of Bömer and Engel (*Z. Unters. Lebensm.*, 1929, **57**, 113) who prepared triglycerides of dihydrochaulmoogric and dihydrohydnocarpic acid, and a diglyceride of the former acid.

We have, therefore, prepared and characterised the 1-mono-, 1 : 3-di-, and tri-glycerides of these acids. The first two groups are of importance in the synthesis of the naturally occurring mixed glycerides, about which it is hoped to report later. The same two groups also offer possibilities as intermediates for the synthesis of antileprosy and/or bactericidal compounds.

A further point of interest is the effect of the terminal ring on the melting points and polymorphism of these compounds. It might reasonably have been expected that the accommodation of terminal rings in the chain structure would have had a weakening effect resulting in lower melting points. The acids, however, in spite of their unsaturation, melt only a few degrees lower than the corresponding saturated straight-chain acids (*e.g.*, chaulmoogric 68·5°, stearic 71·0°), and very considerably higher than any octadecenoic acid [*e.g.*, oleic (*cis*) 16°, elaidic (*trans*) 44·5°; octadec-2-enoic (*trans*), m. p. 59°, has the highest melting point reported for this group]. Our *X*-ray results do not suggest any major difference in structure from the straight-chain fatty acids, *i.e.*, the molecules lie in pairs across the 001 plane, and it would seem that the high melting point is due to the absence of the weakly binding terminal methyl planes, which, in the majority of long-chain compounds, are the main cleavage planes. The glycerides similarly melt much higher than might have been expected.

Any effect the terminal ring may have on the polymorphism of these compounds is noticeable only with the acids, where polymorphism is absent (cf. the A, B, and C forms of straight-chain fatty acids; Piper, Malkin, and Austin, *J.*, 1926, 2310). The glycerides, on the other hand, behave normally and exhibit the same type of polymorphism as the glycerides of straight-chain fatty acids (Parts I, II, and III, *J.*, 1934, 666; 1936, 1628;

* Part XI, 1951, 2663. † Geneva nomenclature (CO_2H = 1).

1937, 1409). Thus, the mono-, di-, and tri-glycerides exist in α-, β′-, and β-forms and, in addition, the triglycerides exist in a vitreous form.

Experimental

X-Ray and Thermal Examination.—This was carried out as described in Parts I and II. Melting-point and *X*-ray data are given in Table 1.

Table 1. *M. p.s and X-ray data for chaulmoogric and hydnocarpic acids and their glycerides.*

	M. p.				Long spacings (Å)		Short spacings (Å)	
	Vitreous	α	β′	β	β′	β	β′	β
Chaulmoogric acid ...				68·5°	—	32·4	—	3·44w, 3·62w, 3·78vs 4·42s, 4·61m, 4·74s
Hydnocarpic acid ...				59·5	—	29·4	—	3·44w, 3·62w, 3·78vs 4·12s, 4·61m, 4·74s
1-Monochaulmoogrin		53·5°	57·5°	58·5 –59	43·5	38·1	3·8w, 3·98s, 4·58vs	3·9s, 4·1s
1-Monohydnocarpin		39·5	47	49	40·0	35·4	3·8w, 4·0s, 4·6vs	3·9s, 4·1s
1 : 3-Dichaulmoogrin		52	57	59	—	36·7	—	3·1w, 3·9m, 4·2m, 4·6s
1 : 3-Dihydnocarpin		42	47	49	–	32·7		3·4w, 3·7m, 4·0m, 4·6s
Trichaulmoogrin ...	27°	35	41·5	44·5	39·2	39·2	4·0m, 4·3m, 4·6s	4·1s, 4·6s
Trihydnocarpin	15	24	31	34	36·1	36·0	4·05m, 4·32m, 4·6s	4·1s, 4·58s

vs = very strong, s = strong, m = moderate, w = weak.

Chaulmoogric and hydnocarpic acids. The molten acids supercool over 5—6° before solidifying, but only one m. p. could be observed for each. Also, after they had been crystallised from a variety of solvents and " pressed " or " melted " layers and rods, there was no indication of any change in the *X*-ray photographs. The long spacings, 32·4 and 29·4 Å respectively, correspond to a tilt of the molecules across the 001 planes of 35° 30′ (being calculated from only two members of the series, this is probably not more accurate than ±30′).

1-*Monoglycerides.* The first form to separate from the melt is the α-form which changes slowly, at room temperature, into the β′-form. When the experiment starts with the molten glyceride, these are the only forms observed. The high-melting β-form is obtained by slow crystallisation from solvents, and it is not easy to obtain it entirely free from β′-form. In contrast to the monoglycerides of straight-chain fatty acids (Part II), whose long spacings for β′- and β-forms are identical, the long spacings of the two forms are quite distinct, and correspond to tilts of 31° for the β-form and 44° for the β′-form. It was not possible to record long spacings of the α-forms, which, before changing to the β′-form, pass quickly into an intermediate phase noted in Part II. The short spacing of this form is the same as that given in Part II, Plate, Fig. 6, *i.e.*, a strong line at 4·2 Å, associated with a few weaker lines close on either side.

1 : 3-*Diglycerides.* These differ from most other diglycerides in crystallising in large flakes, very similar in appearance to straight-chain fatty acids. Under the microscope, between crossed nicols, they exhibit a striking spherulite formation. Three distinct forms can be detected by the capillary melting-point methods, *viz.*, α, β′, and β, but the changes α ⟶ β′ ⟶ β are so rapid that only the α- and the β-forms are observed on the cooling and heating curves. When the molten glyceride is cooled in a capillary, there is solidification at the α-m. p. and, if the temperature is raised when only a small portion has solidified, remelting occurs at the same temperature. It is not easy, however, to avoid transition to the β′- and even to the β-form, and some repetition is usually necessary to observe the m. p.s of the α- and the β′-forms. *X*-Ray data could be determined only for the stable β-form, and the allocation of the α-structure to the lowest-melting form is based on analogy (cf. Part III, p. 1412). From the long spacings, the tilt of the chains is found to be ≏ 50°.

Triglycerides. When one starts with the molten glycerides, both capillary m. p.s and cooling and heating curves show the existence of vitreous, α-, and β′-forms. The β-form can be obtained only by slow crystallisation from non-polar solvents, or by holding the β′-form near its m. p. for some hours. Crystallisation from ethanol or acetone usually gives the β′-form. Cooling curves (cooling jacket from 0° to room temperature) fall to the vitreous m. p. and then

rise to the α-m. p. and, if the heating curve is taken when the curve again begins to fall, there is a single arrest at the β′-m. p. Thus, the change α ⟶ β′ is moderately rapid. Within experimental error, the long spacings of the β′- and the β-forms are identical, but the two forms are distinguished by their short spacings. Both triglycerides exhibit typical spherulite formation.

Isolation of Chaulmoogric and Hydnocarpic Acids from Hydnocarpus Oil.—The preparation of these acids from various oils has been described by a number of workers (Power *et al.*, *loc. cit.*; Shriner and Adams, *loc. cit.*; Sacks and Adams, *J. Amer. Chem. Soc.*, 1926, **48**, 2395; Dean and Wrenshall, *ibid.*, 1920, **42**, 2626; Hashimoto, *ibid.*, 1925, **47**, 2325; Buu-Hoï and Janicaud, *Compt. rend.*, 1941, **212**, 577), who either fractionally crystallised the acids obtained by saponification of the oil, or fractionally distilled their ethyl esters. With the vastly improved modern columns, the latter method is much to be preferred, and we obtained excellent results using the type of column developed by Floyd Todd (*Ind. Eng. Chem. Anal.*, 1945, **17**, 175) which, in a single distillation, gave fractions of esters, from which it was possible to obtain acids of the highest purity, after a few crystallisations from ethanol and/or light petroleum.

The fatty acids obtained from hydnocarpus oil by the usual alkaline saponification were crystallised once from 80% ethanol to remove the bulk of low-melting and liquid fatty acids, and then converted into their ethyl esters (ethanol–sulphuric acid). The set point of the mixture was −10°. 140 G. of ester were fractionated as indicated in Table 2. The low set points of fraction 3 and 4 are almost certainly due to the presence of the ester of gorlic acid, which is known to exist in this oil and differs from chaulmoogric acid only in possessing an additional (6 : 7-) double bond. This acid is readily separated from chaulmoogric acid by crystallisation. Fraction 2 was known to consist mainly of palmitic acid, and was not treated further.

TABLE 2.

Fraction	Set point	B. p./1 mm.	Wt. (g.)	%	M. p. crude acid	Wt. pure acid *	M. p. pure acid †	$[\alpha]_D^{16}$ in $CHCl_3$ †
1	−15·5°	164—165°	78	55·7	53°	2·95	59·5°	+68·5°
2	−10·5	172—174	11	7·9	—	—	—	—
3	− 5·5	177—178	32	22·8	66·5	3·5	68·5	} +62
4	− 2·5	178—179	13	9·3	67·5	4·1	68·5	
residue	—	—	≏6	4·3	—	—	—	—

* From 5 g. of ester. Set points, ethyl chaulmoograte, 1·2°; ethyl hydnocarpate −16·8°.
† Shriner and Adams (*loc. cit.*) give: chaulmoogric acid, m. p. 68—68·5°, $[\alpha]_D$ +62·4°; hydnocarpic acid, m. p. 59—60°, $[\alpha]_D$ +68·3°.

Chaulmoogroyl Chloride.—Thionyl chloride (3 3c.c.; freshly distilled over quinoline and linseed oil) was added dropwise to molten chaulmoogric acid (6·5 g.), and the mixture was heated for 2 hours at 80°. After removal of excess of thionyl chloride under reduced pressure, the product was distilled *in vacuo*, to give 6·2 g. of colourless liquid, b. p. 175—180°/5 mm. It is important to add the thionyl chloride very slowly, otherwise the yield is greatly reduced.

Hydnocarpoyl Chloride.—This was prepared similarly (b. p. 168—170°/5 mm.) in 89% yield.

iso*Propylideneglycerol Chaulmoograte.*—To *iso*propylideneglycerol (0·66 g., 0·005 mole) and dry pyridine (2 c.c.) in sodium-dried benzene (20 c.c.) was added, with shaking, chaulmoogroyl chloride (1·5 g., 0·005 mole). A copious precipitate of pyridine hydrochloride separated, and the mixture was left overnight. After being washed with dilute sulphuric acid and water, the benzene solution was dried (Na_2SO_4) and the solvent removed under reduced pressure. Two crystallisations of the *ester* from ethanol gave colourless needles (1·6 g., 83%), m. p. 30° (Found: C, 72·8; H, 10·4. $C_{24}H_{42}O_4$ requires C, 73·0; H, 10·65%).

l-*Monochaulmoogrin.*—The above ester (1·3 g.) in ether (10 c.c.) was cooled in an ice-bath, and ice-cold concentrated hydrochloric acid (10 c.c.) was added slowly with vigorous shaking. From the mixture, which at first appeared to be quite homogeneous, there soon began to separate a white precipitate. The mixture was kept for ½ hour in the ice-bath with frequent shaking, after which ice-cold water (50 c.c.) was gradually added to complete the precipitation. The precipitate was collected, washed free from mineral acid with water, and dried *in vacuo* over calcium chloride. After two quick and one slow crystallisations from ether, there remained colourless l-*monochaulmoogrin*, m. p. 58·5—59° (1 g., 90%), $[\alpha]_D^{16}$ +50° (in chloroform) (Found: C, 70·8; H, 10·6. $C_{21}H_{38}O_4$ requires, C, 71·1; H, 10·7%).

l-*Monohydnocarpin.*—This *glyceride*, prepared similarly (yield, 78%), had m. p. 49°, $[\alpha]_D$ +54°

(in chloroform) (Found: C, 70·1; H, 10·4. $C_{19}H_{34}O_4$ requires, C, 70·0; H, 10·4%). The intermediate *iso*propylideneglycerol hydnocarpate was obtained an an oil in 94% yield, and was converted directly into monohydnocarpin.

1 : 3-*Dichaulmoogrin.*—To 1-monochaulmoogrin (1·5 g.) in dry benzene (30 c.c.) was added dry pyridine (3 c.c.) and then gradually slightly more than one mol. of chaulmoogroyl chloride (1·4 g.). Next morning the mixture was refluxed for 2 hours, washed with dilute sulphuric acid and water, dried (Na_2SO_4), and evaporated. Two crystallisations from ethanol and two from hexane yielded the *diester* as flakes (1·5 g., 57%), m. p. 59°, $[\alpha]_D^{16}$ +58° (in chloroform) (Found: C, 76·0; H, 10·8. $C_{39}H_{68}O_5$ requires C, 76·0; H, 11·0%).

1 : 3-*Dihydnocarpin.*—1 : 3-Dihydnocarpin, prepared similarly (50%), had m. p. 49°, $[\alpha]_D^{16}$ +61·9° (Found: C, 74·7; H, 10·6. $C_{35}H_{62}O_5$ requires C, 74·9; H, 10·7%).

Trichaulmoogrin.—To 1-monochaulmoogrin (0·9 g.) in dry benzene (30 c.c.) was added dry pyridine (4 c.c.) and then gradually chaulmoogroyl chloride (2·15 g.). Next morning the mixture was refluxed for 4 hours. Working up as above gave the *triester*. Two crystallisations from ethanol and two very slow crystallisations from benzene–ethanol (1 : 2) gave asbestos-like needles (1·9 g.), m. p. 44·5°, $[\alpha]_D^{16}$ +56·4° (Found: C, 77·8; H, 10·9. $C_{57}H_{98}O_6$ requires C, 77·9; H, 11·1%).

Trihydnocarpin.—Trihydnocarpin was prepared similarly in a 90% yield, with m. p. 34°, $[\alpha]_D^{16}$ +61·1 (Found: C, 76·8; H, 10·7. $C_{51}H_{84}O_6$ requires C, 77·0; H, 10·8%).

Direct esterification of glycerol with these acids in the presence of catalysts (toluene or camphorsulphonic acid) gave unsatisfactory products and yields.

We thank the Royal Society for a grant, and gratefully acknowledge gifts of hydnocarpus oil from Burroughs Wellcome and Company.

THE UNIVERSITY BRISTOL. [*Received, March 14th,* 1952.]