A SYNTHETIC OPTICALLY ACTIVE TRIALIPHATIC TRIGLYCERIDE AND A METHOD FOR THE DETECTION OF OPTICAL ACTIVITY IN NATURAL ASYMMETRIC TRIGLYCERIDES

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Although many natural triglycerides are asymmetric it is not yet known if such compounds exist naturally as optically active enantiomers or as racemic mixtures. Trialiphatic triglycerides of the common fatty acids do not have measurable optical activity, at least in the visible wavelength range, even when these compounds have been synthesised in optically pure form (Sowden & Fischer, 1941), whereas similarly synthesised triglycerides containing suitable aromatic acids do have measurable rotations. Quite recently, Schlenk (1962) has synthesised some enantiomorphic triglycerides having small but distinct optical rotations in ultraviolet light but the largest rotation obtained in visible light, namely $[\alpha]_D = +1.6^\circ$, was that of the somewhat unnatural triglyceride, 1-trimethylacetyl-2,3-divalerin.

Apparent exceptions to the rule that natural asymmetric triglycerides of symmetric fatty acids do not have measurable optical rotation were recently reported (Maier & Holman, 1964). Triglycerides considered to contain only two normal long-chain acids and either one deca-2,4-dienoic acid or one dodeca-2,4-dienoic acid per triglyceride molecule and having specific rotations of around -20° were isolated from the seed oils of Sapium sebiferum (i.e. stillingia oil) and of Sebastiana lingustrina respectively.

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It was in an effort to elucidate the structure, the absolute optical configuration and the reason for the high optical rotation of these natural optically active triglycerides that the synthetic work here described was carried out.

EXPERIMENTAL

D-1,2-dioctadecanoyl-3-hexa-2,4-dienoyl glycerol (D-αβ-dipalmitin sorbate) was synthesised from D-(+)-isopropylidene glycerol (Baer & Fischer, 1939a) by two alternative routes (Routes A & B) to ensure that the final product was optically pure. These syntheses were carried out by conventional procedures (Baer & Fischer, 1939b; Sowden & Fischer, 1941) and are summarised in Figure 1.

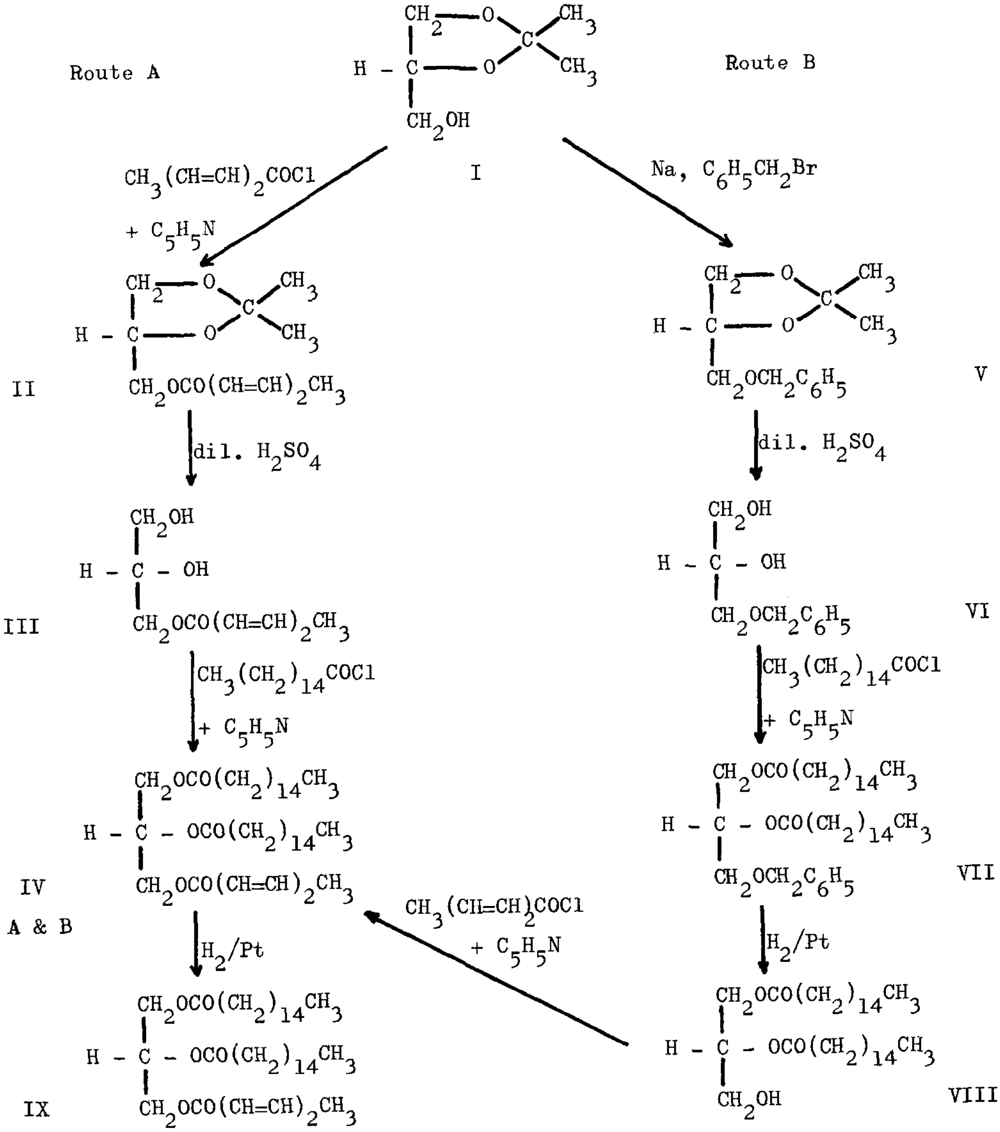
In Route A the D-(+)-isopropylidene glycerol (I) was acylated with sorbic acid chloride to D-isopropylidene glycerol sorbate (II) which, after removal of the isopropylidene group to give L-α-monosorbin (III), was further acylated with palmitoyl chloride to give the desired D-αβ-dipalmitin sorbate (IVA).

In the less direct Route B the benzyl ether (V) of D-isopropylidene glycerol was first prepared and converted via L-α-benzyl glycerol ether (VI) to D-αβ-dipalmitin-α'-benzyl ether (VII). Hydrogenolysis of the benzyl group furnished D-αβ-dipalmitin (VIII) which was acylated with sorboyl chloride to yield again D-αβ-dipalmitin sorbate (IVB).

All steps in these syntheses were checked by thin-layer chromatography and the various intermediates were purified by fractional vacuum distillation, by crystallisation, by countercurrent distribution or by chromatography, whichever procedure was most suitable.

The final products (IVA & IVB) had respectively the following properties: m.pt. 61.5-62.0° and 60.8-61.2°; $\varepsilon_{261\ m\mu}$ 30,750 and 31,240; $[\alpha]^{20^\circ}_{546\ m\mu}$ + 3.71° and + 3.60° in chloroform solution. The fractionally lower rotation of product IVB probably reflects the greater propensity of the diglyceride (VIII) than the monoglyceride (III) to undergo acyl

Figure 1



migration and hence racemisation. Hydrogenation of either product gave D-αβ-dipalmitin hexanoate (IX, m.pt. 39.5-40.0°) which, however, had no measurable rotation.

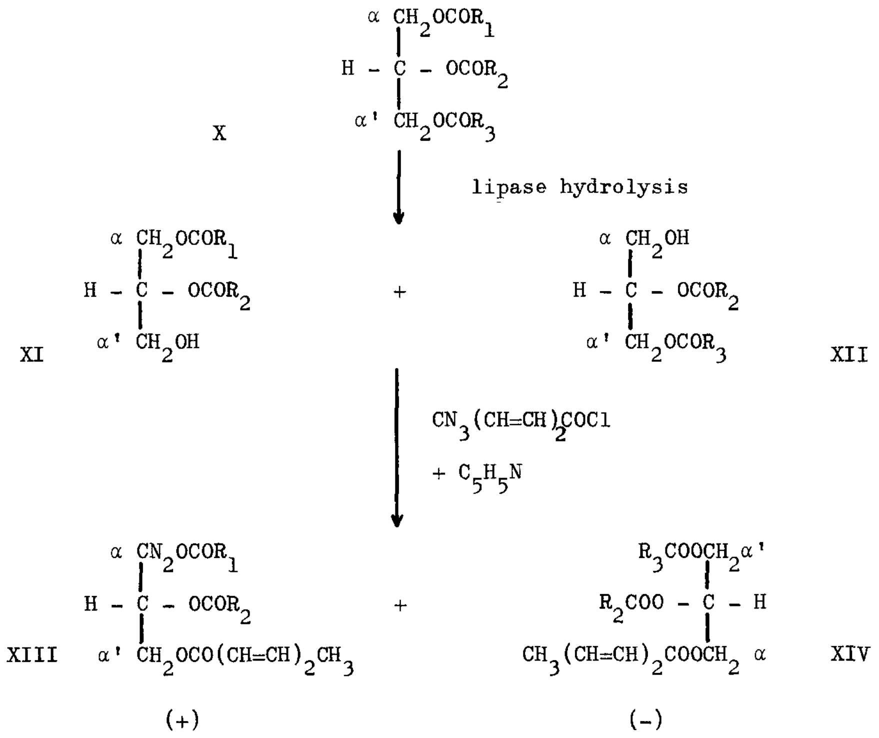
DISCUSSION

The D-αβ-dipalmitin sorbate thus synthesised should have served as an excellent compound for comparison with the supposed deca-2,4-dienoic and dodeca-2,4-dienoic acid containing triglycerides from stillingia and <u>Sebastiana</u> seed oils respectively. The finding that it had less than one fifth of the optical rotary power of these materials indicated that the structures previously attributed to them were in all probability false. This has proved to be the case and Holman and his collaborators (Holman, 1964) have shown that the optically active triglyceride of stillingia oil has one hydroxyallenic acid and two common acids per glycerol and that deca-2,4-dienoic acid is a fourth acid combined not with glycerol but with the hydroxy group of the allenic acid. The glyceride from <u>Sebastiana</u> oil is also a tetra-acid triglyceride but of a somewhat different structure, and the high optical activity of these materials is clearly due to these constituent acids rather than any asymmetry of the glycerides themselves.

The present work, however, has also shown that a trialiphatic triglyceride can be prepared which has, in the context of this class of compounds, a substantial optical rotation. The possibility of deriving such a compound from a normal diglyceride means that a method is now available, as an alternative to Schlenk's physico-chemical approach (Schlenk, 1962), to determine if individual natural asymmetric triglycerides are in fact optically active. If they are, it will be possible at the same time to differentiate between the fatty acids esterified on the α- and α'-positions of glycerol in such compounds. This is one of the last major problems in glyceride analysis and it can be resolved as summarised in Figure 2.

Individual asymmetric triglycerides (X) must be isolated pure, an operation now considerably simplified by combination of argentation-chromatography with more traditional methods, and to facilitate separation of the ultimate products the acids esterified on positions α and α' should differ in degree of unsaturation rather than in chain-length. Pancreatic lipase hydrolysis, which is established to be specific for the α- and α'-positions of a triglyceride, will provide the diglycerides XI

Figure 2



and XII. The possibility of acyl migration and consequent racemisation militates against separation and measurement of optical rotation of these compounds but they may immediately be reacylated by reaction with sorbic acid chloride (or with some other suitable acid chloride or anhydride) to yield the stable reconstituted triglycerides XIII and XIV. These are virtually enaniomers differing only in the degree of unsaturation of the original acid radicals R_1- and R_3- and by virtue of this difference they can be separated from each other by argentation-chromatography. If the original triglyceride (X) were indeed optically active then the derived triglycerides(XIII & XVI) will have opposite rotations of approximately equal magnitude to that of the synthetic dipalmitin sorbate described in this paper.

A more detailed account of the work herein described and of the application of the procedure for detecting optical activity to pure asymmetric triglycerides from natural sources will be published elsewhere.

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