

THE SYNTHESIS OF D-1:2-BISDECANOYLGLYCEROL AND D-1:2-BISDODECANOYLGLYCEROL*

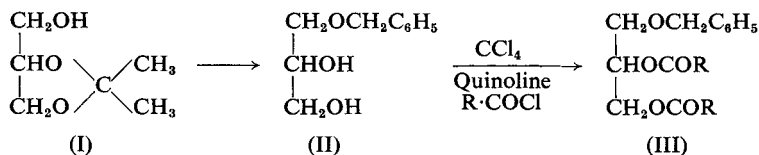
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IN the course of investigations reported elsewhere¹ it became necessary to prepare 1:2-diacylglycerols of D configuration and containing normal fatty acid chains with approximately 10 carbon atoms. The synthesis of 1:2-bisdecanoyl and 1:2-bisdodecanoylglycerol reported below follows the elegant procedure of Sowden and Fischer², each step of which has been shown to proceed with full retention of configuration.

Thus D-1:2-*isopropylidene*glycerol (I) was obtained from D-1:2:5:6-di-*isopropylidene*mannitol by oxidative cleavage with lead tetra-acetate followed by catalytic hydrogenation of the intermediate glyceraldehyde. Benzoylation of (I) followed by mild acid hydrolysis furnished D-glyceryl 3-benzyl ether (II).



Acylation with the appropriate acid chloride in carbon tetrachloride/quinoline gave the requisite diacylglyceryl benzyl ethers (III) (R = C₉H₁₉ and C₁₁H₂₃) as undistillable liquids. Although purification of (III; R = C₉H₁₉) was achieved by crystallisation from ether at -70°, chromatography on silica gel proved simpler and applicable to either case (Fig. 1), a graded elution technique with continuously increasing concentrations of acetone in light petroleum (b.p. 60 to 80°) being used. This method was also used to effect separation of D-1:2-bisdecanoylglycerol from its benzyl ether (see Figure 2 for a typical separation).

Catalytic hydrogenolysis of the D-1:2-diacylglyceryl 3-benzyl ethers furnished the required D-diglycerides as solids of low melting point. Their optical rotations were too small to permit of accurate determination, and only the values for the 3-benzyl ethers are recorded.

EXPERIMENTAL

Melting and boiling points are uncorrected. Microanalyses were performed by Mr. G. S. Crouch of this school.

D-Glyceryl 3-benzyl ether. D-1:2-*iso*Propylidene-glyceryl 3-benzyl ether

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was prepared from D-1 : 2-*isopropylidineglycerol* (35 g.) by the method of Howe and Malkin³. The product was distilled once *in vacuo* and without further purification was hydrolysed with dilute acetic acid to give D-glyceryl 3-benzyl ether. After redistillation, 21.2 g. (56 per cent) of the required product was obtained, b.p. 138 to 139°/0.2 mm., $n_D^{16} = 1.5342$, $[\alpha]_D^{20} = +5.7^\circ$.

D-1 : 2-*Bisdecanoylglyceryl 3-benzyl ether*. To a solution of D-glyceryl 3-benzyl ether (8.4 g.) in dry carbon tetrachloride (25 ml.) was added dry

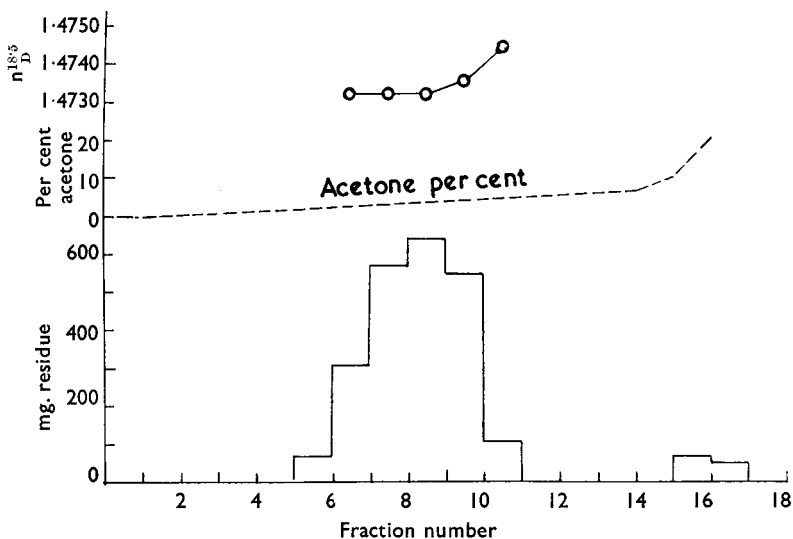


FIG. 1. Chromatographic purification of D-1 : 2-bisdecanoylglyceryl 3-benzyl ether.

quinoline (17.0 ml.). The flask containing the solution was immersed in a cooling bath and a solution of decanoyl chloride (17.4 g.) in the same solvent (25 ml.) added dropwise over a period of five minutes with gentle agitation. The reaction mixture was allowed to stand, with occasional shaking, for 20 hours, then extracted with ether (200 ml.). The filtered ethereal extract, washed successively with N hydrochloric acid, water, 1 per cent sodium hydrogen carbonate and water, was dried over anhydrous sodium sulphate. Evaporation of the solvent furnished 21.4 g. (96 per cent) of crude product, $n_D^{20} = 1.4733$.

Purification was effected by chromatography on silica gel⁴ (Hopkin and Williams Ltd.). The adsorbent (20 g.) in light petroleum (b.p. 60 to 80°) was packed in a tube of internal diameter 2.0 cm. The above 1 : 2-diglyceride 3-benzyl ether (2.4 g.) in light petroleum (b.p. 60 to 80°) (30 ml.) was placed on the column and elution carried out with graded concentrations of acetone (0 to 2.5 per cent) in light petroleum (b.p. 60 to 80°). Fractions of 30 ml. eluate were collected and the progress of the elution was followed by determining the refractive index of the residue obtained on evaporating the solvent from each fraction (Fig. 1). For analysis the central, isorefractive fractions were again chromatographed.

D-1 : 2-BISDECANOYLGLYCEROL

Found: C, 73.1; H, 10.08. $C_{30}H_{50}O_5$ requires C, 73.4; H, 10.27 per cent; $n_D^{20^\circ}$ 1.4744; $[\alpha]_D^{22^\circ} +11.3^\circ$; $d_4^{22^\circ}$ 0.966; m.p. 6 to 7° .

A further portion of the crude product was purified by crystallisation from ether at -70° . Three crystallisations gave a product of m.p. 5 to 6° ; $n_D^{20^\circ}$ 1.4740; $[\alpha]_D^{20^\circ} +10.3^\circ$.

D-1:2-Bisdecanoylglyceryl 3-benzyl ether was similarly prepared in 78 per cent crude yield, and purified chromatographically. Found: C, 74.9; H, 10.54. $C_{34}H_{58}O_5$ requires C, 74.7; H, 10.69 per cent; $n_D^{15^\circ}$ 1.4672; $n_D^{20^\circ}$ 1.4747; $n_D^{24^\circ}$ 1.4731; $[\alpha]_D^{24^\circ} +9.8^\circ$; $d_4^{22^\circ}$ 0.957.

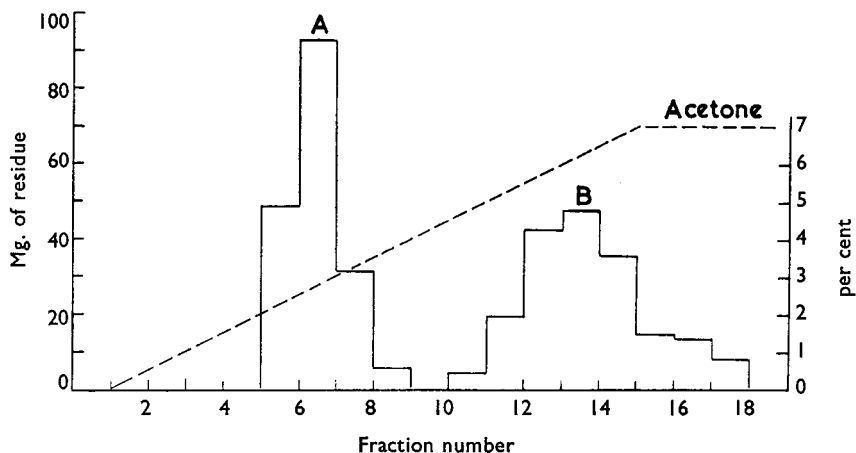


FIG. 2. Chromatographic separation of D-1:2-bis-decanoylglycerol from its 3-benzyl ether.

A. Diglyceride benzyl ether. B. Diglyceride.

The substance exhibited dimorphism, a phenomenon of common occurrence among the glycerides^{4,5}. The modification stable at room temperature melted at $20.5 - 21.5^\circ$.

D-1:2-Bisdecanoylglycerol. D-1:2-Bisdecanoylglyceryl 3-benzyl ether (4.9 g.), in *n*-hexane (40 ml.) was shaken at atmospheric pressure with palladium black (Johnson Matthey and Co.)* (0.5 g.) in an atmosphere of hydrogen. When the theoretical volume of gas had been absorbed (*c.* $4\frac{1}{2}$ hours) the solution was filtered, the catalyst washed with a little solvent, and the combined filtrate and washings concentrated to dryness *in vacuo*. The residue (3.6 g., 89 per cent, m.p. 28 to 29°) consisted of almost pure D-1:2-bisdecanoylglycerol. For analysis it was twice chromatographed on silica gel as already described (acetone concentrations of 0 to 10 per cent in light petroleum b.p. 60 to 80° being used). Found: C, 69.0; H, 10.86. $C_{23}H_{44}O_5$ requires C, 69.0; H, 11.07 per cent, m.p. 28.5 to 29° .

* Of a number of palladium black preparations tried in this laboratory this catalyst was the only one which proved to be sufficiently active and reproducible in catalytic debenzylolation.

D-1:2-Bisdodecanoylglycerol was similarly prepared in 95 per cent yield; m.p. 44.5 to 45°, not raised by further chromatography. Found: C, 71.2; H, 11.39. $C_{27}H_{52}O_5$ requires C, 71.0; H, 11.46 per cent.

Chromatographic separation of D-1:2-bisdecanoylglycerol from its 3-benzyl ether (Fig. 2)

A sample of 0.2 g. of each of the above substances in *n*-hexane (30 ml.) was applied to a column of silica gel (8 g. column diameter 2.2 cm.) made up in the same solvent. Elution was carried out with light petroleum (b.p. 60 to 80°) in which the acetone concentration continuously rose from 0 to 7 per cent as shown: 30 ml. fractions of eluate were collected. The elution curve (Fig. 2) showed satisfactory separation of the two substances.

SUMMARY

The synthesis of two new D-1:2-diacylglycerols is reported, and a chromatographic method for the purification of their 3-benzyl ethers is described.

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