# *Synthesis of αβ-Unsaturated Glycerides.*

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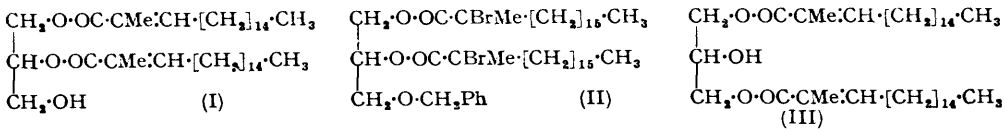
1 : 2-Di-*O*-2′-methyloctadec-2′-enoylglycerol has been synthesised by two different routes. Catalytic hydrogenolysis of 1-*O*-benzyl-2 : 3-di-*O*-2′-methyloctadec-2′-enoylglycerol in the presence of palladium black removes the benzyl group without reducing the αβ-unsaturated acyl groups. An alternative procedure involves reaction of 1-*O*-benzylglycerol with 2-bromo-2-methyloctadecanoyl bromide, followed by catalytic hydrogenolysis and pyridine dehydrobromination of the resulting bromo-substituted diglyceride. 1 : 3-Di-*O*-2′-methyloctadec-2′-enoylglycerol is also prepared.

The present work was undertaken in connection with studies of the lipids of tubercle bacilli. Various lipid fractions from human tubercle bacilli, including the phospholipids, yield on hydrolysis dextrorotatory mixtures of acids of which a main constituent, mycolipenic acid, is now known to be (+)-2 : 4 : 6-trimethyltetracos-2-enoic acid (Bailey, Polgar, and Robinson, *J.*, 1953, 3031; Polgar, *J.*, 1954, 1008). The phospholipid fraction has been shown to consist of glycerinositophosphatides (de Sütö-Nagy and Anderson, *J. Biol. Chem.*, 1947, **171**, 749, 761), and it was, therefore, of interest to study the preparation of αβ-unsaturated glycerides, as possible intermediates towards syntheses of related phosphatides.

The present communication deals with the synthesis of some simple αβ-unsaturated diglycerides, with 2-methyloctadec-2-enoic acid (Bailey, Polgar, Tate, and Wilkinson, *J.*, 1955, 1547) as the acid constituent. The requisite intermediates for the preparation of phospholipids derived from l-glycerophosphoric acid (α-phosphatidic acids) are 1 : 2-diglycerides. For obtaining the latter, hydrogenolysis is usually employed to remove groups blocking the 3-position of glycerol after the acyl groups have been introduced. Accordingly, only saturated 1 : 2-diglycerides have been prepared by these procedures.

Since αβ-unsaturated acids undergo catalytic hydrogenation less readily than those with non-conjugated double bonds, it appeared that esters of 1-*O*-benzylglycerol with αβ-unsaturated acids, on partial catalytic hydrogenation, might lose the benzyl group without reduction of the acyl residues. This proved so. 1-*O*-Benzylglycerol was converted, by reaction with 2-methyloctadec-2-enoyl chloride, into its diacyl derivative. This on hydrogenation in the presence of palladium black afforded 1 : 2-di-*O*-2′-methyloctadec-2′-enoylglycerol (I).



An alternative route involved bromination of 2-methyloctadecanoic acid in the presence of red phosphorus (Hell–Volhard–Zelinsky) and reaction of the resulting α-bromo-acid

bromide with 1-*O*-benzylglycerol to yield the bromo-substituted diacylbenzylglycerol (II). Catalytic hydrogenolysis of the benzyl group, followed by dehydrobromination of the product by pyridine, gave the αβ-unsaturated diglyceride (I).

1 : 3-Di-*O*-2′-methyloctadec-2′-enoylglycerol (III) was prepared by known procedures (cf. Gupta and Malkin, *J.*, 1952, 2405) *via* the monoacyl derivative of *O*-*iso*propylideneglycerol.

## Experimental

Ultraviolet spectra were determined, for MeOH solutions, by Mr. F. Hastings and Dr. F. B. Strauss. M. p.s were determined by means of a hot-stage microscope.

1 : 2-*Di*-O-2′-*methyloctadec*-2′-*enoylglycerol*.—(i) 2-Methyloctadec-2-enoyl chloride (5·2 g.), prepared from 2-methyloctadec-2-enoic acid (Bailey, Polgar, Tate, and Wilkinson, *loc. cit.*) by means of oxalyl chloride, in carbon tetrachloride (10 c.c.) was added to a mixture of 1-*O*-benzylglycerol (1·5 g.) (Howe and Malkin, *J.*, 1951, 2663), pyridine (1·3 g.), and carbon tetrachloride (20 c.c.). The mixture was kept overnight at the room temperature, then at 40° for 12 hr. The product was taken up in ether, and the ethereal solution washed, successively, with 1% hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and dried ($Na_2SO_4$). Removal of the solvent gave the diacyl derivative (4·7 g.) which was hydrogenated in *n*-hexane (20 c.c.) and glacial acetic acid (a few drops) in the presence of palladium black (0·6 g.; Willstätter and Waldschmidt-Leitz, *Ber.*, 1921, **54**, 113) at room temperature and pressure. The theoretical amount of hydrogen (1 $H_2$) was absorbed after 12 hr. Filtration of the solution, and removal of the solvent under reduced pressure gave the 1 : 2-*diglyceride* (3·5 g.), m. p. 42° after crystallisation from ethanol at 0° (Found : C, 75·8; H, 11·6. $C_{41}H_{76}O_5$ requires C, 75·9; H, 11·8%). Ultraviolet absorption : max. at 2180 Å (log ε 4·37).

(ii) 2-Methyloctadecanoic acid (12 g.) was heated with bromine (23 g.) in the presence of red phosphorus (1·2 g.) for 6 hr. (cf. Bailey, Polgar, Tate, and Wilkinson, *loc. cit.*). Distillation of the product gave the bromo-acid bromide as a pale yellow oil (13 g.), b. p. 225—235°/6 mm. This was added to 1-*O*-benzylglycerol (2·7 g.) and pyridine (2·3 g.) in carbon tetrachloride (30 c.c.) and the mixture kept at the room temperature overnight, then at 40° for 12 hr. The product, isolated in the usual manner, was hydrogenated as above until the theoretical amount of hydrogen was taken up (7 days). After removal of the catalyst and solvent the product (a 3·8-g. portion) was refluxed with pyridine (12 g.) for 16 hr., then worked up in the manner previously described for similar dehydrobrominations (Bailey, Polgar, Tate, and Wilkinson, *loc. cit.*). 1 : 2-Di-*O*-2′-methyloctadec-2′-enoylglycerol (1 g.) was obtained as a pale yellow solid (Found : C, 75·8; H, 11·5%), absorption max. at 2180 Å (log ε 4·35).

The diglyceride gave on hydrolysis with ethanolic potassium hydroxide 2-methyloctadec-2-enoic acid (Found : C, 76·7; H, 12·2. Calc. for $C_{19}H_{36}O_2$ : C, 77·0; H, 12·2%), absorption max. at 2140 Å (log ε 4·12).

1 : 3-*Di*-O-2′-*methyloctadec*-2′-*enoylglycerol*.—Gupta and Malkin's procedure (*loc. cit.*) was employed. Reaction between 2-methyloctadec-2-enoyl chloride (5 g.) and *iso*propylideneglycerol (2·1 g.) in benzene (30 c.c.) in the presence of pyridine (1·3 g.) gave the acyl derivative as a pale yellow oil (3·4 g.). To a solution of this in ether (10 c.c.), cooled in ice, was added ice-cold concentrated hydrochloric acid (10 c.c.) with vigorous shaking, and the mixture kept at 0° for 0·5 hr. Ice-water (50 c.c.) was then gradually added and the product (2·8 g.) isolated by means of ether. It was then subjected to the action of 2-methyloctadec-2-enoyl chloride (2·4 g.) in benzene (50 c.c.) in the presence of pyridine (0·6 g.). The resulting crude diglyceride (4·7 g.) was chromatographed in benzene on a silica column prepared in the same solvent. Elution with ether–benzene (1 : 25) gave the *diglyceride*, m. p. 47—49° after crystallisation from ethanol at 0° (Found : C, 76·0; H, 11·7. $C_{41}H_{76}O_5$ requires C, 75·9; H, 11·8%), absorption max. at 2160 Å (log ε 4·44).

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