Volume 1
Number 5

# Synthesis of enantiomeric mixed-acid α,β-diglycerides

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[Received for publication April 28, 1960]

## SUMMARY

A procedure has been developed that permits the synthesis of mixed-acid α,β-diglycerides in either one of the four theoretically possible isomeric forms. Each is obtainable as a pure compound devoid of any contamination with positional or spatial isomers. Their fatty acid substituents may consist either of two dissimilar saturated fatty acids or a saturated and an unsaturated fatty acid. The procedure has been applied to the synthesis of D-α-stearoyl-β-oleoylglycerol and D-α-oleoyl-β-stearoylglycerol, the first mixed-acid diglycerides to be obtained in enantiomeric form.

The synthesis of optically active glycerides has been attempted by Abderhalden and Eichwald (1, 2), Bergmann and Sabetay (3), Bergmann *et al.* (4), and Grün and Limpächer (5) by methods that involve the optical resolution of racemic intermediates possessing acidic or basic groups, and the subsequent removal of these groups to obtain the desired glycerides. None of these methods has given optically pure glycerides (6). The preparation of pure enantiomers of asymmetrically substituted glycerides without recourse to the resolution of racemates became possible with the synthesis of D-acetone glycerol (7, 8) and L-acetone glycerol by Baer and Fischer (9). These compounds were obtained from D- and L-mannitol by methods that transfer without loss the asymmetry of carbon atoms 2 and 5 of the mannitols to the respective acetone-glycerols. The D- and L-acetone-glycerols provide the sterochemical links from the glycerides to D- or L-glyceraldehyde, the stereochemical compounds of reference.

The D- and L-acetone glycerols have been used successfully in our laboratory as starting materials for the synthesis of L-α-monoglycerides (7, 10, 11, 12), D-α,β-diglycerides (12 to 17), L-α,β-diglycerides (18), and enantiomeric asymmetrically substituted mixed-acid triglycerides (10, 19), respectively. All such glycerides prepared to date contained solely saturated fatty acid substituents, with the exception of D- and L-α,β-diolein (16). So far, no enantiomeric mixed-acid α,β-diglycerides have been prepared. We now report a general procedure that permits the synthesis of all four theoretically possible isomers of mixed-acid α,β-diglycerides (Table 1). These may contain as substituents either two dissimilar saturated fatty acids or a saturated and an unsaturated fatty acid. The introduction of the dissimilar fatty acids is a four-step process involving (*a*) tritylation of an α-glyceryl benzyl ether (L-, D- or DL), (*b*) acylation of the α-tritylglyceryl-α′-benzyl ether in the β-position, (*c*) removal of the trityl group with a simultaneous shift of the fatty acid from the β to the α position by hydrogen chloride in petroleum ether, and (*d*) introduction of the second fatty acid substituent in the β position. The presence of the benzyl group assures that the asymmetry of the glyceryl moiety is fully maintained throughout this procedure. To obtain a mixed-acid diglyceride with oleic acid as one of the substituents, the double bond of the oleic acid is protected

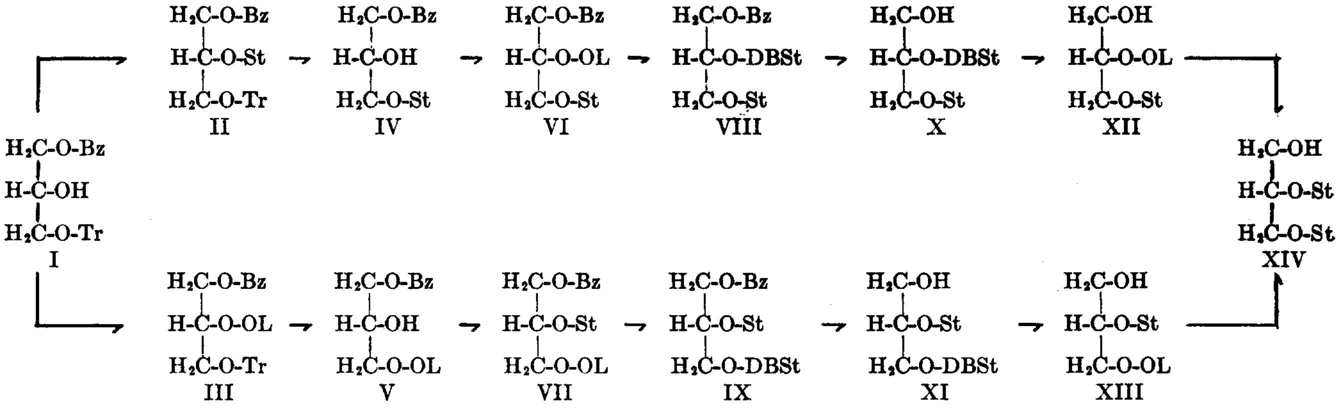
TABLE 1. Possible Structural and Spatial Isomers of Mixed-Acid α,β-Diglycerides

| | | | |
|---|---|---|---|
| $H_2C$-OH | $H_2C$-OH | HO-$CH_2$ | HO-$CH_2$ |
| H-C-OOC·R′ | H-C-OOC·R″ | R′·COO-C-H | R″·COO-C-H |
| $H_2C$-OOC·R″ | $H_2C$-OOC·R′ | R″·COO-C-$H_2$ | R′·COO-$CH_2$ |
| D | D | L | L |

with bromine and regenerated with activated zinc after the protective benzyl group has been removed by catalytic hydrogenolysis. The configuration of the α,β-diglyceride is determined by that of the starting material, the L-α-glyceryl benzyl ether yielding D-α,β-diglycerides and the D-α-glyceryl benzyl ether yielding L-α,β-diglycerides. The procedure permits the preparation of either one of the two theoretically possible positional isomers of each enantiomer by reversing the order of introduction of the fatty acid substituents.

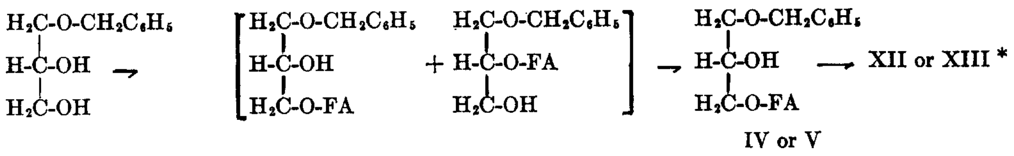
In the experimental part we describe the application of the procedure to the synthesis of D-α-stearoyl-β-oleoylglycerol (XII) and D-α-oleoyl-β-stearoylglycerol (XIII). The mixed-acid diglycerides were obtained as shown by Reaction Scheme 1. Both D-α-stearoyl-β-oleoylglycerol and D-α-oleoyl-β-stearoylglycerol on catalytic reduction gave in excellent yields D-α,β-distearin with the specific rotation ([α]D —2.7°) of authentic D-α,β-distearin (13). This confirms, simultaneously, the D configuration of the diglycerides XII and XIII, and their optical purity. The antipodes of the diglycerides XII and XIII, and their racemic compounds are obtainable by the same sequence of reactions using as starting materials D-α- or DL-α-glyceryl benzyl ether, respectively.

Reaction Scheme 1



Tr = trityl; Bz = benzyl; St = stearoyl; OL = oleoyl; DBSt = 9,10-dibromostearoyl.

Reaction Scheme 2



FA=saturated or unsaturated fatty acid.

* Via the intermediates VI, VIII and X, or VII, IX, and XI of Reaction Scheme 1.

The hydrogen chloride-catalyzed shift of the fatty acid substituents from the β to the α position is not quantitative. The reaction yields mixtures of the desired α-monoacylglyceryl-α'-benzyl ethers (IV or V) and by-products that we have reasons to believe may be cyclic monoesters of glyceryl-α-benzyl ethers. The components of these reaction mixtures can be readily separated by column chromatography on silicic acid. The pure D-α-monoacylglyceryl-α'-benzyl ethers (IV and V) were obtained in yields from 50% to 52% of theory.

To ascertain whether or not compounds IV and V are free of β-acyl isomers, D-α-stearoylglyceryl-α'-benzyl ether (IV) was freed of its benzyl group by catalytic hydrogenolysis. The crude D-α-monostearin ([α]D +4.0° in pyridine) was obtained in a yield of 98% of theory, and on titration with periodic acid assayed for the pure (100%) α-isomer. Two crystallizations from ether gave D-α-monostearin that melted from 76° to 77° and possessed the specific rotation + 4.1° (in pyridine). This confirms the structural purity of D-α-stearoylglycerol-α′-benzyl ether (IV) and, by implication, that of D-α-oleoylglyceryl-α′-benzyl ether (V).

The procedure for the synthesis of mixed-acid α,β-diglycerides outlined by Reaction Scheme 1 can probably be shortened somewhat by omitting the tritylation step. Glyceryl-α-benzyl ethers may be acylated in such a manner that mainly the monoglyceride benzyl ethers and little of the diglyceride benzyl ethers are obtained. The separation of the mono- and diglyceride benzyl ethers, and treatment of the mixture of α- and β-monoglyceride benzyl ethers with gaseous hydrogen chloride in petroleum ether, followed by chromatographic separation of the reaction products on a silicic acid column should yield pure α-monoglyceride-α′-benzyl ethers (Reaction Scheme 2).

By applying the stepwise introduction of fatty acid substituents, with or without the help of trityl intermediates as outlined by Reaction Schemes 1 and 2, to α-iodo-L-propylene glycol (20), α-iodo derivatives of mixed-acid α,β-diglycerides can be obtained. These may make suitable starting materials for the synthesis of mixed-acid α-phosphatides and related compounds, if it can be shown that the replacement of the iodine by phosphate ester groups proceeds without any migration, a point which has not yet been established satisfactorily. Since mixed-acid α-iododiglycerides can be obtained with any desired mono- or polyunsaturated fatty acid substituent, the synthesis of mixed-acid α-phosphatides and related compounds containing any unsaturated fatty acid (as well as oleic acid) thus is possible.

The synthesis of enantiomeric mixed-acid α-phosphatides from mixed-acid α,β-diglycerides and derivatives is in progress in this laboratory.

## EXPERIMENTAL

*Materials.* L-α-Glyceryl benzyl ether was prepared from D-acetone glycerol (21) by the method of Sowden and Fischer (13) using the modifications introduced by Howe and Malkin (22) for the preparation of the corresponding racemic compound. The trityl chloride was prepared by either one of the two methods of Gomberg (23, 24) as described by Bachmann (25). For further purification the trityl chloride was distilled *in vacuo*, b.p. 155° at 0.1 to 0.08 mm Hg, m.p. 113°-114°. Anhydrous pyridine was prepared from the best commercial grade of pyridine available, by refluxing it over barium oxide and distilling it with the exclusion of moisture. The benzene was free of thiophene and was dried over sodium wire. Chloroform for use in polarimetric and infrared work was freed of ethanol by distilling from phosphorus pentoxide. The silicic acid was Mallinckrodt, 100 mesh (powder), Analytical Reagent, with a 12% weight loss on ignition. It was used as provided by the manufacturer, which is important if it is to be used for detritylation purposes. The palladium catalyst was prepared by the reduction of palladium chloride with formic acid as described by Tausz and Putnoky (26), except that the palladium, after having been washed thoroughly with water, was suspended several times in fresh portions of glacial acetic acid to remove water, and then was stored under glacial acetic acid until used. By avoiding drying of the palladium, a much more active catalyst is obtained.

D-α-*Tritylglyceryl*-α′-*Benzyl Ether* (I). To an ice-cold solution of 83.6 g (0.3 mole) of pure trityl chloride in 200 ml of anhydrous benzene was added slowly with stirring, and under anhydrous conditions, a solution of 54.7 g (0.3 mole) of L-α-glyceryl benzyl ether and 32.0 g (0.4 mole) of anhydrous pyridine in 80 ml of benzene, and the reaction mixture was kept at room temperature (20° to 25°) for 24 hours. At the end of this period 1 liter of ether was added and the mixture was filtered with suction. The filtrate was washed successively with three 600 ml portions of ice-cold 2 N sulfuric acid, one 600 ml portion of distilled water, two 600 ml portions of a saturated sodium bicarbonate solution, and finally with two 600 ml portions of distilled water. The solution was dried with 200 g of anhydrous sodium sulfate, and the solvents were removed by distillation under reduced pressure from a bath at 30° to 35°. The remaining material was kept in a vacuum of 0.02 mm Hg until its weight was constant. The D-α-tritylglyceryl-α′-benzyl ether, a viscous syrup, weighed 124.0 g (97.4% of theory), and, as shown by fractional precipitation from ether with petroleum ether, was a homogeneous substance. It is highly soluble at room temperature in benzene, chloroform, or ether; sparingly soluble in petroleum ether; and insoluble in water. $n_D^{21}$ 1.5985. $[\alpha]_D^{23}$ $-4.5°$ in 10% (w/v) anhydrous benzene; $[\alpha]_D^{23}$ $-2.0°$ in 10% (w/v) ethanol-free chloroform. $M_D$ $-19.1°$ in benzene, $M_D$ $-8.5°$ in chloroform.

*Analysis.* For $C_{29}H_{28}O_3$ (424.6), Calculated, C 82.05, H 6.65; Found, C 82.06, H 6.83.

The D-α-tritylglyceryl-α′-benzyl ether when chromatographed on a column of fresh silicic acid hydrolyzes, yielding triphenyl carbinol (m.p. 161°-162°) and L-α-glyceryl benzyl ether ($[\alpha])_D^{25}$ $+ 5.58°$ in substance, $n_D^{23}$ 1.5293). The latter is recovered from the column with a mixture of ether and methanol 1/1 (v/v).

*D-α-Trityl-β-stearoylglyceryl-α′-Benzyl Ether* (II). To a solution of 63.7 g (0.15 mole) of freshly prepared D-α-tritylglyceryl-α′-benzyl ether (I) and 16.0 g (0.2 mole) of anhydrous pyridine in 200 ml of benzene was added a solution of 45.5 g (0.15 mole) of freshly distilled stearoyl chloride (27) in 150 ml of benzene, and the mixture was kept under anhydrous conditions at 40° for 20 hours. The reaction mixture then was diluted with 1.2 liters of ether, and the solution was washed successively with three 600 ml portions of ice-cold 2 N sulfuric acid, one 600 ml portion of distilled water, two 600 ml portions of a saturated sodium bicarbonate solution, and finally with two 600 ml portions of water. The solution was dried with 200 g of anhydrous sodium sulfate, and the solvents were removed by distillation under reduced pressure.* The remaining oil, weighing 98.0 g, was dissolved in 600 ml of low boiling petroleum ether, and the solution was kept overnight at +6°. The solution was cleared by filtration, and the filtrate was concentrated under reduced pressure. The residue was redissolved in 500 ml of anhydrous acetone, and the solution was kept for 2 hours at —80°. The precipitate was collected by a brief centrifugation in a refrigerated centrifuge at as low a temperature as possible, and was freed from solvent by distillation in a vacuum that was gradually lowered to 0.05 mm Hg, while the temperature of the bath was raised slowly to 40°. The remaining D-α-trityl-β-stearoylglyceryl-α′-benzyl ether, a viscous oil ($n_D^{23}$ 1.5375) weighing 84.0 g (81.4% of theory) solidified gradually. This material is pure enough ($[\alpha]_D^{26}$ —8.7 in 10% w/v chloroform) for the preparation of the D-α-stearoylglyceryl-α′-benzyl ether.

To obtain analytically pure material D-α-trityl-β-stearoylglyceryl-α′-benzyl ether was chromatographed on silicic acid, although it involves a considerable loss of material. A solution of 10 g of the benzyl ether (II) in 100 ml of benzene (U.S.P., redistilled) was passed through a 130 g Mallinckrodt fresh silicic acid column, 2.5 cm wide and 60 cm long, and the column was washed with benzene until the eluate was free of solute. The first 250 ml of the eluate contained pure D-α-trityl-β-stearoylglyceryl-α′-benzyl ether. The remaining benzene eluate contained mostly triphenylcarbinol (2.1 g). The rest of the material was recovered by passing through the column a mixture of benzene and ether 3/1(v/v), and was identified as β-stearoyl L-α-glycerylbenzyl ether[1] (2.5 g m.p. 34°-35°).

The first 250 ml of the benzene eluate was concentrated under reduced pressure, and the residue was freed of solvents in a vacuum of 0.05 mm Hg at a bath temperature of 35° to 40°. The D-α-trityl-β-stearoylglyceryl-α′-benzyl ether, a viscous oil ($n_D^{21}$ 1.5400), weighing 4.5 g (45% recovery), solidified gradually. M.p. 30°-31°, $[\alpha]_D^{25}$ —9.5° in 10%(w/v) chloroform. $M_D$ —65.5° in chloroform.

*Analysis.* For $C_{47}H_{62}O_4$ (691), Calculated, C 81.69, H 9.04; Found, C 81.70, H 9.00.

*D-α-Trityl-β-Oleoylglyceryl-α′-Benzyl Ether* (III). The acylation of the D-α-tritylglyceryl-α′-benzyl ether (63.7 g, 0.15 mole) with freshly prepared oleoyl chloride (27) (45.2 g, 0.15 mole) and anhydrous pyridine (16.0 g, 0.2 mole), and the isolation of the acylation product were carried out as described for the D-α-trityl-β-stearoylglyceryl-α′-benzyl ether (II) according to the description preceding the asterisk. The material thus obtained (97.0 g) was dissolved in 600 ml of low boiling petroleum ether, and the solution was kept overnight at —25°. After removal of a small turbidity by centrifugation in a refrigerated centrifuge, the clear supernatant was concentrated under reduced pressure. The residue was redissolved in 500 ml of anhydrous acetone, and the solution was kept for 1 hour at —80°. The precipitate then was removed by a brief centrifugation at as low a temperature as possible in a refrigerated centrifuge, and the supernatant solution was concentrated by distillation under reduced pressure from a bath at 35° to 40°. The rest of the solvent was removed in a vacuum of 0.02 mm Hg. The D-α-trityl-β-oleoylglyceryl-α′-benzyl ether (III) weighing 79.5 g (76.9% of theory) was pure enough to be used directly for the preparation of D-α-oleoylglyceryl-α′-benzyl ether (V).

To obtain analytically pure benzyl ether (III), a small amount of the above material was purified by chromatography on a silicic acid column as described for the corresponding stearoyl compound (II). The D-α-trityl-β-oleoylglyceryl-α′-benzyl ether was recovered in an approximate yield of 50%; $n_D^{21}$ 1.5405; $[\alpha]_D^{25}$ —9.5 in 10% (w/v) dry and ethanol-free chloroform. $M_D$ —65.5° in chloroform.

*Analysis.* For $C_{47}H_{60}O_4$ (689), Calculated, C 81.93, H 8.78, Iodine no. 36.8; Found, C 81.69, H 8.72, Iodine no. 37.5 and 36.5.

*D-α-Stearoylglyceryl-α′-Benzyl Ether* (IV). Into a dry 1 liter three-necked flask with ground joints, equipped with an oil-sealed, mechanically driven stirrer and a calcium chloride tube, was placed a solu-

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[1] The detritylation of D-α-trityl-β-stearoylglyceryl-α′-benzyl ether by fresh silicic acid takes place without fatty acid migration. The experimental application of the detritylation procedure with silicic acid to the preparation of mixed-acid α,β-diglycerides will be reported later.

tion of 65.0 g of D-α-trityl-β-stearoylglyceryl-α′-benzyl ether (II) in 600 ml of anhydrous petroleum ether (b.p. 35°-60°). The flask was immersed in an ice bath and was connected with a hydrogen chloride gas generator. Through the cold solution was passed, with stirring, a rapid stream of dry hydrogen chloride gas for 30 minutes. At the end of this period the cold bath was removed, and the reaction mixture was kept at room temperature for 1 hour. The precipitate (trityl chloride) was removed by filtration with suction, the filtrate was transferred to a 2 liter separatory funnel with the aid of three 100 ml portions of petroleum ether, and the combined solutions were washed successively with 600 ml of cold water, three 600 ml portions of an ice-cold 5% solution of potassium carbonate, and finally with three 600 ml portions of water. The solution was dried with 200 g of anhydrous sodium sulfate, filtered, and the filtrate was concentrated under reduced pressure. The residue consisting of D-α-stearoylglyceryl-α′-benzyl ether, triphenylcarbinol, and a by-product, presumably a cyclic ester of L-α-glyceryl benzyl ether, was extracted thoroughly with three 300 ml portions of petroleum ether. The combined extracts were kept at 20° for 15 hours. The extract was filtered, the filtrate was concentrated under reduced pressure, and the residue was freed of solvent by keeping it in a vacuum of 0.01 mm Hg until its weight was constant. The remaining material, weighing 42.0 g, was dissolved in 400 ml of benzene, and the solution was passed through a column of 700 g of silicic acid, approximately 60 cm long and 6 cm wide, and the column was washed with benzene until the effluent was free of solute (cyclic ester followed by triphenylcarbinol). Approximately 1.5 liters of benzene were required. Through the column then were passed 2 liters of a mixture of benzene and ether 3/1(v/v). The first 500 ml of the effluent was free of solute. The rest, containing the D-α-stearoylglyceryl-α′-benzyl ether, was evaporated under reduced pressure, and the residue was kept in a vacuum of 0.01 mm Hg at a bath temperature of 35° to 40° until its weight was constant. The D-α-stearoylglyceryl-α′-benzyl ether (IV) weighed from 21 to 22 g (50% to 52% of theory based on D-α-trityl-β-stearoylglyceryl-α′-benzyl ether) with a m.p. of 42°-43°. Crystallization from low boiling petroleum ether gave a product that melted from 43° to 44°, $[\alpha]_D^{25}$ +2.0° in 10% (w/v) chloroform. $M_D$ +9.0° in chloroform.

*Analysis.* For $C_{28}H_{48}O_4$ (448.7), Calculated, C 74.95, H 10.78; Found, C 75.03, H 10.80.

D-*α-Oleoylglyceryl-α′-Benzyl Ether* (V). The detritylation of D-α-trityl-β-oleoylglyceryl-α′-benzyl ether (III), and the separation of the reaction products were carried out as described for the corresponding stearoyl compound (II). The pure D-α-oleoylglyceryl-α′-benzyl ether, a viscous oil, was obtained in yields from 50% to 52% of theory based on D-α-trityl-β-oleoylglyceryl-α′-benzyl ether. $n_D^{22}$ 1.4935. $[\alpha]_D^{23}$ +2.0° in 10% (w/v) chloroform. $M_D$ +9.0° in chloroform.

*Analysis.* For $C_{28}H_{46}O_4$ (446.6), Calculated, C 75.29, H 10.38, Iodine no. 56.8; Found, C 75.23, H 10.29, Iodine no. 57.0.

D-*α-Stearoyl-β-Oleoylglyceryl-α′-Benzyl Ether* (VI). To a solution of 22.4 g (0.05 mole) of D-α-stearoylglyceryl-α′-benzyl ether (IV) and 8.0 g (0.1 mole) of anhydrous pyridine in 160 ml of dry benzene was added in one portion 15.0 g (0.05 mole) of freshly prepared oleoyl chloride (27), and the mixture was kept under anhydrous conditions at 40° for 20 hours. At the end of this period it was brought to room temperature, diluted with 600 ml of ether, and the solution washed in succession with three 500 ml portions of ice-cold 2 N sulfuric acid, 500 ml of distilled water, two 500 ml portions of a saturated sodium bicarbonate solution, and finally with two 500 ml portions of water. The solution was dried with 150 g of anhydrous sodium sulfate, the solvents were removed by distillation under reduced pressure, and the residue was kept in a vacuum of 0.1 mm Hg at a bath temperature of 35° to 40° until its weight was constant. The D-α-stearoyl-β-oleoylglyceryl-α′-benzyl ether (VI), a colorless oil, weighed 33.8 g (95% of theory), $n_D^{20}$ 1.4775, $d_4^{20}$ 0.9234, $[\alpha]_D^{23}$ +6.0° in 10% (w/v) chloroform; $[\alpha]_D^{24}$ +7.25° in substance. $M_D^{24}$ +42.7° in chloroform, $M_D^{24}$ +51.7° in substance.

*Analysis.* For $C_{46}H_{80}O_5$ (713.1). Calculated, C 77.47, H 11.30, Iodine no. 35.6; Found, C 77.56, H 11.05, Iodine no. 36.0.

If the optical activity of the material should be unsatisfactory, it can be improved by passing its benzene solution through a column of silicic acid (20 g of silicic acid per 1 g of substance), and recovering the material by washing the column with benzene. The impurities are present in the first part of the eluate.

D-*α-Oleoyl-β-Stearoylglyceryl-α′-Benzyl Ether* (VII). The acylation of D-α-oleoylglyceryl-α′-benzyl ether (22.4 g, 0.05 mole) with stearoyl chloride (15.0 g, 0.05 mole) and pyridine (8.0 g. 0.1 mole), and the purification of the D-α-oleoyl-β-stearoylglyceryl-α′-benzyl ether (VII) if necessary, were carried out as described for the structural isomer (VI). The D-α-oleoyl-β-stearoylglyceryl-α′-benzyl ether, a colorless oil, was obtained in a yield of 92.0% (32.7 g). $n_{\mathrm{D}}^{21}$ 1.4780, $d_4^{20}$ 0.9234, $[\alpha]_{\mathrm{D}}^{26}$ +6.0° in 10% (w/v) chloroform; $[\alpha]_{\mathrm{D}}^{25}$ +7.3° in substance. $M_{\mathrm{D}}$ +42.8° in chloroform, $M_{\mathrm{D}}$ +52.0° in substance.

*Analysis.* For $C_{46}H_{80}O_5$ (713.1). Calculated, C 77.47, H 11.30, Iodine no. 35.6; Found, C 77.70, H 11.21, Iodine no. 34.8.

D-*α-Stearoyl-β-9,10-Dibromostearoylglyceryl-α′-Benzyl Ether* (VIII). In a 500 ml three-necked flask equipped with an oil-sealed stirrer, calcium chloride tube and dropping funnel, was placed a solution of 23.5 g (0.33 mole) of D-α-stearoyl-β-oleoylglyceryl-α′-benzyl ether (VI) in 300 ml of petroleum ether (b.p. 35°-60°). The flask was immersed in a bath of salt and crushed ice at —16°, and a solution of 5.6 g (0.035 mole) of bromine in 50 ml of petroleum ether was added with stirring over a period of 30 minutes, maintaining the bath temperature at —16°. The reaction mixture then was washed immediately with two 300 ml portions of a 0.5 N solution of sodium thiosulfate, two 300 ml portions of a saturated solution of sodium bicarbonate, followed by two 300 ml portions of water. The petroleum ether solution was dried with 150 g of anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure. The residual oil was kept in a vacuum of 0.02 mm Hg until its weight was constant. The D-α-stearoyl-β-9,10-dibromostearoylglyceryl-α′-benzyl ether (VIII), a viscous oil at room temperature, weighed 27.0 g (93.7% of theory). $n_{\mathrm{D}}^{22}$ 1.4950, $[\alpha]_{\mathrm{D}}^{24}$ +5.0° in 10% (w/v) chloroform. $M_{\mathrm{D}}$ +43.6° in chloroform.

*Analysis.* For $C_{46}H_{80}O_5Br_2$ (872.9). Calculated, Br 18.31; Found, Br 18.35.

D-*α-9,10-Dibromostearoyl-β-Stearoylglyceryl-α′-Benzyl Ether* (IX). Compound IX was prepared from D-α-oleoyl-β-stearoylglyceryl-α′-benzyl ether (VII) as described above for the structural isomer (VIII). It was obtained in a yield of 95% of theory, $n_{\mathrm{D}}^{22}$ 1.4950; $[\alpha]_{\mathrm{D}}^{24}$ +5.1° in 10% (w/v) chloroform. $M_{\mathrm{D}}$ +44.5° in chloroform.

*Analysis.* For $C_{46}H_{80}O_5Br_2$ (872.9). Calculated, Br 18.31; Found, Br 18.28, 18.93.

D-*α-Stearoyl-β-9,10-Dibromostearoylglycerol* (X). A solution of 25.0 g (0.028 mole) of D-α-stearoyl-β-9,10-dibromostearoylglyceryl-α′-benzyl ether (VIII) in 250 ml of glacial acetic acid, together with 4.0 g of palladium black, was shaken vigorously in an atmosphere of pure hydrogen at room temperature and a pressure of approximately 45 cm of water until the absorption of hydrogen ceased. The hydrogenolysis was complete at the end of 1 hour with the uptake of 1.0 mole of hydrogen. The hydrogen was replaced with nitrogen, the reaction mixture was centrifuged, the catalyst was washed with small amounts of ether, and the combined solutions were freed of solvents by distillation under reduced pressure from a bath at 35° to 40°. The residue was dissolved in 500 ml of ether, and the ether solution was washed successively with two 500 ml portions of a saturated sodium bicarbonate solution and three 500 ml portions of water. The ether solution was dried with 100 g of anhydrous sodium sulfate, and was concentrated under reduced pressure. The residue was kept for several hours in a vacuum of 0.02 mm Hg at a bath temperature of 35° to 40°. The D-α-stearoyl-β-9,10-dibromostearoylglycerol (X) weighed 21.0 g (93.7% of theory). If this material in a 10% (w/v) solution of chloroform has a specific rotation of less than 2.0°, it can be purified by passing its benzene solution through a column of silicic acid, washing the column with benzene until the effluent was free of solute, recovering the D-α-stearoyl-β-9,10-dibromostearoylglycerol (X) by eluting the column with a mixture of benzene and ether 3/1(v/v), and removing the solvent by distillation under reduced pressure. $[\alpha]^{25}$ —2.0° in 10%(w/v) chloroform. $M_{\mathrm{D}}$ —15.6° in chloroform; $n_{\mathrm{D}}^{21}$ 1.4834.

*Analysis.* For $C_{39}H_{74}O_5Br_2$ (782.8). Calculated, Br 20.4; Found, Br 23.3.

D-*α-9,10-Dibromostearoyl-β-Stearoylglycerol* (XI). This compound was prepared by catalytic hydrogenolysis of D-α-9,10-dibromostearoyl-β-stearoylglyceryl-α′-benzyl ether (IX), as described above for the structural isomer (X). Yield, 90% of theory, $n_{21}^{\mathrm{D}}$ 1.4834, $[\alpha]_{\mathrm{D}}^{25}$ —2.0° in 10%(w/v) chloroform.

*Analysis.* For $C_{39}H_{74}O_5Br_2$ (782.8). Calculated, Br 20.4; Found, Br 21.4.

D-*α-Stearoyl-β-Oleoylglycerol* (XII). To a vigorously stirred solution of 19.5 g (0.025 mole) of D-α-stearoyl-β-9,10-dibromostearoylglycerol (X) in 400 ml of ether in a wide-necked flask, was added, over a period of 5 minutes, freshly prepared "activated zinc" that had been obtained from 100 g of zinc dust, as described by Baer and Buchnea (16). After the zinc had been added, the stirring was continued until the vigorous reaction subsided (approximately 20 minutes). The reaction mixture was filtered with suction, using a filter coated with Kieselguhr. The filtrate was washed with distilled water until the wash-water was free from bromine ions, and was dried with anhydrous sodium sulfate. The solvent was removed by distillation under reduced pressure from a bath at 35° to 40°. The residue, weighing 16.6 g, was dissolved in 200 ml of benzene, the solution was passed through a silicic acid column 60 cm long and 6 cm wide containing approximately 400 g of silicic acid, and the column was washed with benzene until the effluent was free from solute. The diglyceride was recovered by passing through the column a mixture of benzene and ether 3/1 (v/v), concentrating the eluate under reduced pressure, and keeping the residue in a vacuum of 0.02 mm Hg at a bath temperature of 35° to 40° until its weight was constant. The D-α-stearoyl-β-oleoylglycerol (XII), a waxy solid at room temperature, weighed 14.0 g (89.8% of theory), $[\alpha]_D^{25}$ —2.8° in 10% (w/v) chloroform. $M_D$ —17.4° in chloroform. The mixed diglyceride was stored under anhydrous conditions at —10°.

*Analysis*. For $C_{39}H_{74}O_5$ (623). Calculated, C 75.18, H 11.97, Iodine no. 40.7; Found, C 75.08, H 12.01, Iodine no. 40.5.

D-α-*Oleoyl*-β-*Stearoylglycerol* (XIII). This compound, a white paste at room temperature, was prepared from D-α-9,10-dibromostearoyl-β-stearoylglycerol (XI) as described above for D-stearoyl-β-oleoylglycerol. Yield, 85.5% of theory, $[\alpha]_D^{25}$ —2.8° in 10% (w/v) chloroform. $M_D$ —17.4° in chloroform.

*Analysis*. For $C_{39}H_{74}O_5$ (623). Calculated, C 75.18, H 11.97, Iodine no. 40.8; Found, C 75.21, H 11.95, Iodine no. 40.5.

D-α,β-*Distearin* (XIV). The reduction of 1.0 g of either D-α-stearoyl-β-oleoylglycerol (XII) or D-α-oleoyl-β-stearoylglycerol (XIII) in 20 ml of glacial acetic acid with pure hydrogen at a positive pressure of 50 cm of water in the presence of 0.2 g of palladium black, and two recrystallizations of the reduction products (0.97 g) from ether gave in excellent yields D-α,β-distearin, m.p.'s 74°-75°, $[\alpha]_D^{24}$ —2.7° in 10% (w/v) chloroform. Authentic D-α,β-distearin (13) m.p. 74.5°-75.0°, $[\alpha]_D$ —2.7°.

At room temperature, compounds II to XIII are soluble in acetone, chloroform, ether, or benzene. Compounds II to IX are soluble also in petroleum ether (b.p. 35°-60°). Compounds X to XIII are sparingly soluble in petroleum ether, acetic acid, methanol, or ethanol, whereas compounds II to IX are insoluble in methanol or ethanol. All compounds are insoluble in water.

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