

GLYCERIDE SYNTHESES

II. PREPARATION OF SYMMETRICAL SATURATED MONOACID DIGLYCERIDES FROM 2-O-BENZYLGLYCEROL¹

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ABSTRACT

A direct preparation of symmetrical saturated monoacid diglycerides is described. The synthesis involves the preparation of 2-O-benzylglycerol, acetylation, interesterification with either methyl stearate or methyl palmitate, and hydrogenolysis to yield the desired 1,3-diglyceride. The melting points of the symmetrical diglycerides are slightly higher than those obtained previously by other methods of synthesis which involve a 1,2 to 1,3 shift of acyl groups.

A previous publication from this laboratory (1) dealt with methods for the synthesis of symmetrical diglycerides by interesterification between the methyl esters of long chain fatty acids and 1,2-O-diacetyl glycerides, wherein the third hydroxyl of the glycerol was blocked. The present paper is a continuation of this research and concerns a procedure for the direct preparation of 1,3-O-disaturated glycerides which avoids the 1,2 to 1,3 shift and the use of fatty acid chlorides.

The starting material, 1,3-O-benzylideneglycerol, was readily prepared in large quantities by the procedure outlined by Verkade and van Roon (3), and was converted to 1,3-O-benzylidene-2-O-benzylglycerol by reaction with benzyl chloride in the presence of potassium hydroxide. The benzylidene group was removed by acid hydrolysis and the resultant 2-O-benzylglycerol was acetylated in 91% yield. This product was interesterified with methyl stearate or methyl palmitate to the respective 1,3-O-diacyl-2-O-benzylglycerol in 85% yield. Hydrogenolysis at normal pressure and 50° C. over palladous oxide gave the respective 1,3-O-diglycerides in nearly quantitative yield and high purity. The melting points of the symmetrical diglycerides are slightly higher than those found for other preparations of these products in which a 1,2 to 1,3 shift occurred. The method is very useful for the preparation of large quantities of saturated diglycerides owing to ease of purification of intermediates and final products.

EXPERIMENTAL

All melting points were taken on a heating stage microscope.

1,3-O-Benzylideneglycerol

1,3-O-Benzylideneglycerol was prepared by the procedure outlined by Verkade and van Roon (3). Reagent grade benzaldehyde and glycerol were used without further purification or drying. Fifteen times the amounts of starting materials employed by Verkade and van Roon were heated in a vigorous stream of carbon dioxide at 170° C. for four hours. The solid product was 'Manuscript received April 18, 1955.

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dissolved in chloroform instead of benzene. The same yield (60%) as reported by Verkade and van Roon was obtained. The 1,3-O-benzylideneglycerol was recrystallized from benzene – petroleum ether (Skellysolve "B") to a melting point of 79-82° C., reported m.p. 82.5-83.5° C. (3).

1, 3-O-Benzyl idene -2-O-benzyl glycerol

The crude 1,3-O-benzylideneglycerol (250 gm.) was dissolved in 2 liters of benzyl chloride (reagent grade, distilled in vacuo and stored over potassium hydroxide pellets) by stirring with a high speed stirrer (Ultra-Turrax, Canadian Laboratory Supplies). Finely powdered potassium hydroxide (470 gm.) was added portionwise to the solution with continuous stirring and the temperature of the reaction mixture was maintained between 80° and 90° C. by cooling. After the addition was completed the stirring was continued at the same temperature for one hour with no precautions to exclude moisture. The reaction mixture was cooled to room temperature, washed three times with twice the volume of water, and dried over anhydrous potassium carbonate. The excess benzyl chloride was removed by distillation under 5 mm. pressure. The residue solidified on cooling and was dissolved in 440 ml. of hot benzene. One liter of hot petroleum ether (Skellysolve "B") was added to the solution and a precipitate appeared on cooling. The mixture was allowed to stand overnight in a refrigerator and was filtered, yield 294 gm. (78% of the theoretical amount), m.p. 76-78° C. Recrystallization from 220 ml. of benzene and 600 ml. of Skellysolve "B" gave 278 gm. of product, m.p. 77-78° C., reported m.p. 75.5-76.5° C. (4).

The product was also prepared by using an ordinary laboratory stirrer but the reaction time was extended to four to five hours at 100° C. and moisture was excluded from the reaction mixture. A similar yield was obtained but the crude product had a melting range of 70° to 75° C.

2-O-Benzylglycerol

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The procedure of West and Ludwig (4) was modified slightly. Pure 1,3-Obenzylidene-2-O-benzylglycerol (250 gm.) was added to a solution of 80 ml. of concentrated sulphuric acid in 600 ml. of water and 400 ml. of ethanol. The mixture was refluxed for six hours, cooled to room temperature, steam distilled, and the residue extracted with ethyl ether. The ethereal solution was dried and the ether evaporated *in vacuo*, yield 178 gm. (96% of the theoretical amount). A product, m.p. 37–39° C. (reported m.p. 38.5–40° C. (4)), was obtained by recrystallization from benzene.

1,3-Di-O-acetyl-2-O-benzylglycerol

A mixture of 180 gm. 2-O-benzylglycerol, m.p. 37–39° C., 900 ml. acetic anhydride, and 60 gm. anhydrous sodium acetate was maintained at 100° C. for three hours with occasional shaking. The major portion of the excess acetic anhydride was removed by distillation under reduced pressure. The sodium acetate which precipitated caused bumping and was removed by cooling the mixture and filtering. The remainder of the acetic anhydride was removed by distillation under reduced pressure, and the residual oil was distilled *in vacuo*.

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Yield of colorless liquid was 239 gm. (91% of the theoretical amount), b.p. 142° at 0.7 mm. Removal of excess acetic anhydride was also accomplished by heating with methanol and addition of ether. Sodium acetate, methyl acetate, and acetic acid were washed from the ethereal solution with water, 5-10% aqueous sodium carbonate, and water, successively.

A second distillation yielded a pure product, m.p. 14° C., $n_{\rm D}^{25}$ 1.4884. Calc. for C₁₄H₁₈O₅: C, 63.14%; H, 6.81%. Found: C, 63.36%; H, 6.91%. Acetylation with pyridine and acetic anhydride in the usual manner gave an equally satisfactory yield of the diacetate. 1,3-Di-O-acetyl-2-O-benzylglycerol is miscible with ethanol, ethyl ether, and benzene, slightly soluble in petroleum ether (Skellysolve "F"), and insoluble in water.

1,3-Di-O-stearoyl-2-O-benzylglycerol

A mixture of 20 gm. 1,3-di-O-acetyl-2-O-benzylglycerol (0.075 mole), 44.8 gm. methyl stearate (0.15 mole), and 1.2 ml. of 1.0 N sodium methoxide in methanol was heated at 100° C. on a rotary evaporator at 20 mm. Hg pressure for one hour. The reaction mixture was taken up in 400 ml. ethyl ether. The ethereal solution was washed twice with 500 ml. water, dried over anhydrous sodium sulphate, and the ether was evaporated under reduced pressure. The crude product was crystallized from 500 ml. acetone, yield 46 gm. (85% of the theoretical amount), m.p. 48.5° C. Further recrystallizations from acetone gave the analytically pure compound, m.p. 49.5° C. Calc. for C₄₆H₈₂O₅: C, 77.26%; H, 11.56%. Found: C, 77.36%; H, 11.54%.

The 1,3-di-O-stearoyl-2-O-benzylglycerol is soluble in acetone, petroleum ether (Skellysolve "F"), chloroform, benzene, and ethyl acetate, slightly soluble in methanol and ethanol, and insoluble in water.

1,3-Di-O-palmitoyl-2-O-benzylglycerol

This compound was prepared as described above for the stearoyl derivative in 85% yield. The crystallized product had m.p. 40° C. Calc. for $C_{42}H_{74}O_5$: C, 76.54%; H, 11.32%. Found: C, 76.52%; H, 11.39%.

1,3-Di-O-stearoylglycerol

A solution of pure 1,3-di-O-stearoyl-2-O-benzylglycerol (10 gm.) in 100 ml. of ethyl acetate (reagent grade) was hydrogenated for three hours at normal pressure and 50° C. with 200 mgm. palladous oxide. The catalyst was removed by filtration and the 1,3-di-O-stearoylglycerol was precipitated by cooling the solution in a dry ice – acetone bath, yield 8.6 gm. (98% of the theoretical amount), m.p. 80° C. (reported m.p. 79.5° C. (2)).

1,3-Di-O-palmitoylglycerol

This product was obtained in the same manner in 97% yield, m.p. 73.5° C., reported m.p. 72.5° C. (2).

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