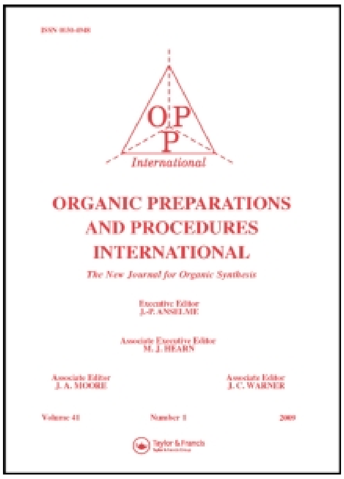

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DIRECT SYNTHESIS OF TRIOCTANOIN FROM GLYCEROL AND OCTANOIC ACID

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DIRECT SYNTHESIS OF TRIOCTANOIN FROM GLYCEROL AND OCTANOIC ACID[1]

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Three decades ago, trioctanoin (tricaprylin) was introduced as an inert vehicle to dissolve or suspend carcinogenic agents.[2] This non-toxic synthetic triglyceride has had wide acceptance. The demand for this vehicle will grow markedly as screening programs expand. The large-scale preparation of this triglyceride by two similar procedures[3,4] is based on the conversion of octanoic acid to its acid chloride which is purified and then treated with glycerol. Yields from these procedures are about 80% based upon glycerol. We now report a more convenient synthesis of trioctanoin by direct esterification of octanoic acid with glycerol using *p*-toluenesulfonic acid as a catalyst. This method requires much less time and gives yields equal to or exceeding those of the other procedures and can be a model for the preparation of other triglycerides.

EXPERIMENTAL

Trioctanoin. To a mixture of glycerol and octanoic acid in a molar ratio of 1:4 were added benzene corresponding to about 1/4 of the combined volume of the two reactants, and p-toluenesulfonic acid monohydrate, in a quantity of 0.01 mole (2g) per mole of glycerol. The mixture was refluxed and the distillate condensed into a Dean-Stark trap until the amount of water collected remained constant. Benzene, p-toluenesulfonic acid and unreacted octanoic acid were recovered between 90° and 104° by distillation at 1 torr. The distillation was continued and the trioctanoin fraction came off rapidly at 240-250° (1 torr).

For further purification, the pale yellow liquid was mixed with activated charcoal (about 0.5g/100ml) and agitated continuously for 24 hrs. The mixture was centrifuged and filtered 3 or 4 times through high grade filter paper. Vacuum distillation of the filtrate gave trioctanoin as the main fraction, boiling at 240-241°/1 torr. In order to avoid cracking, this fraction was allowed to distill rapidly. The trioctanoin obtained by this procedure was a colorless liquid. The yield, based on glycerol, was 80% or better, m.p. 8.5-9.0°.

Saponification number showed purity of 99+%. Tlc of fraction prior to final purification (using Silica gel G plate and solvent of hexane:ethyl acetate:acetic acid; 85:15:1 and color developed with iodine, or 2,4-dichlorofluorecene, or Rhodamine B)[5,6] gave R_f 0.54 for triglyceride and a very faint spot at 0.20 for 1,2-diglyceride. The final redistilled trioctanoin had one spot R_f 0.54.

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