Specific Diacid Triglycerides by a Simple Two-Step Procedure

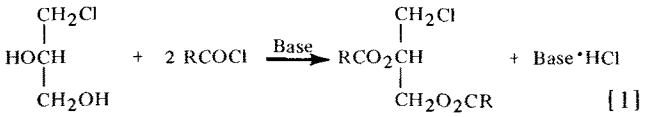
ABSTRACT

A simple two-step synthesis of specific diacid triglycerides is described. This process avoids the use of blocking groups and the problem of acyl group migration. In principle any naturally occurring diacid triglyceride can be synthesized by this procedure.

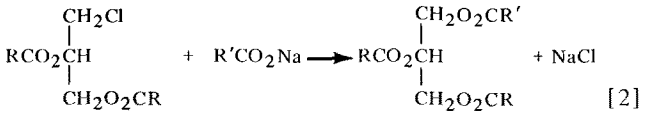
Specific triglycerides, those having acid groups individually placed in known positions on the glyceryl backbone, are usually prepared by multistep procedures (1-3). These procedures are characterized by the use of blocking groups. The blocking groups are necessary to direct the esterification exclusively on one hydroxyl group of glycerol at a time. Removal of blocking groups must be conducted under mild conditions to avoid acyl group migrations in mono- and diglyceride intermediates. Such migrations of acyl groups to adjacent free hydroxyl groups occur readily under the influence of acid, base or heat (3).

We have developed a simple two-step synthesis of specific diacid triglycerides. This process avoids the use of blocking groups and the problem of acyl group migration. At no point in the synthesis are acyl and free hydroxyl groups adjacent to each other.

Unsymmetrical diacid triglycerides were prepared starting with 3-chloropropane-1,2-diol as shown:

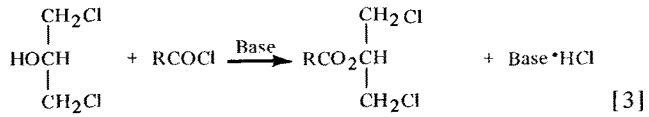


[1]

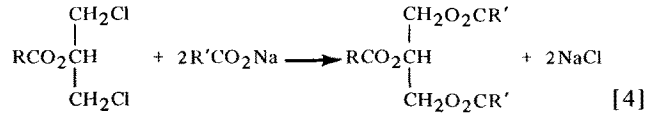


[2]

Similarly symmetrical diacid triglycerides were prepared from 1,3-dichloro-2-propanol as shown:



[3]



[4]

Results are summarized in Table I.

The first step (equation 1 or 3) was conveniently carried out in ethanol-free chloroform-pyridine (2). The second step (equation 2 or 4) utilized a dipolar aprotic solvent (4,5). Dimethylformamide (DMF), hexamethylphosphoramide (HMPA) and dimethyl sulfoxide (DMSO) were used. DMF and HMPA were found to be superior to DMSO for reactions involving long chain sodium carboxylates because of formation of soap-like emulsions in DMSO. At this point the yields have not been optimized.

In a typical procedure, 3-chloropropane-1,2-diol was esterified with palmitoyl chloride and pyridine in chloroform (2). Intermediate chloroesters were purified by column chromatography and/or recrystallization until their VPC trace showed only one peak. Infrared and NMR spectra were consistent with the assigned structure for 3-chloropropane-1,2-diol dipalmitate, mp 51-52.5 C (lit. mp 48-50 C) (6). This chlorodiester, 5.92 g (8.37 mmoles), dry sodium stearate (7), 3.06 g (10.0 mmoles) and 50 ml HMPA (dried over Type 4A Molecular Sieves) were charged to a dry flask. The mixture was stirred and heated at 122-130 C for 1.5 hr. The mixture was cooled and diluted with water and hexane. The resulting emulsion was heated to the boiling point of hexane to separate the layers. The aqueous layer was washed with hot hexane and the combined organic extracts dried briefly over sodium sulfate. The solution was concentrated and cooled to give crystals of 3-stearo-1,2-dipalmitin, 4.10 g (58.5%), mp 61.5-63.5 C (lit. mp 62.7 C) (9). Further concentrating the filtrate gave 0.44 g of a second crop, mp 59-62 C.

The examples in the table show that short chain or long chain, saturated or unsaturated acyl groups can be accommodated. Thus it should be possible to synthesize any naturally occurring diacid triglyceride. Readily available starting materials are used. The overall process requires two simple steps. For these reasons this process should be more adaptable for large quantities of specific diacid triglycerides than methods involving blocking groups.

Studies are in progress on a related three-step synthesis of specific triacid triglycerides.

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REFERENCES

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TABLE I

Diacid Triglycerides

Triglyceride[a]	Solvent	Time, hr	Temperature, C	Isolated yield, %	mp or bp, C	
					This study	Literature
3-propiono-1,2-diacetin	DMSO	117	75	48	95-102/0.6 mm	150/12 mm (8)
3-stearo-1,2-dipalmitin	HMPA	1.5	130	58	61.5-63.5	62.7 (9)
2-aceto-1,3-dipropionin	DMSO	112	86	57	100-104/0.4 mm	---
2-oleo-1,3-distearin	DMF	2	153	57	40.5-42.5	41.6 (9)
2-stearo-1,3-dipalmitin	HMPA	4.25	130	54	64-67	68.6 (9)

[a]All products gave IR and NMR spectra consistent with assigned structures.

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