

Preparation of 1,3-Diacylglycerols and 1-Alkyl-3-acylglycerols in the Presence of Quaternary Ammonium Salt

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A series of symmetrical and racemic 1,3-diacylglycerols and 1-alkyl-3-acylglycerols were prepared simply, and in high yields, by the reaction of carboxylic acids with glycidyl esters or glycidyl ethers in the presence of quaternary ammonium salt. The effect of reaction conditions on the yield, the ratio of 1,3- and 1,2-diacylglycerols, and the stability of 1,3-diglycerides are also discussed.

Diacylglycerols (diglycerides) represent an important class of food emulsifiers and are used in the preparation of processed foods such as ice cream and peanut butter and for many other uses (1,2). It was reported recently that this class of material also is a potent activator for some enzymes and is attracting the attention of biochemists (3). Diglycerides can be classified into two types, namely, 1,2- and 1,3-isomers. Although several methods for the selective preparation of 1,2- or 1,3-diglycerides (4-8), respectively, have been developed previously, all of the known methods are relatively tedious.

Zlatanov (9) has reported the preparation of mono-glycerides from glycidol and carboxylic acids using phase-transfer catalysts. The preparation of glycidyl carboxylates from epichlorohydrin developed by Aserin (10) also attracted our attention. Recently, we investigated the reactions of epichlorohydrin in the presence of PT catalysts and found several novel and useful reactions (11-13).

The present study was undertaken in an attempt to prepare symmetrical and racemic 1,3-diglycerides and 1-alkyl-3-acylglycerols simply, and in good yield and high purity. This purpose is attained by reacting glycidyl carboxylates or glycidyl ethers with carboxylic acids in the presence of catalytic amounts of lipophilic quaternary ammonium salt and sodium hydroxide.

EXPERIMENTAL PROCEDURES

Glycidyl carboxylates were prepared by the reaction of epichlorohydrin with sodium carboxylate in yields of 80-90% under PT catalytic conditions (10). Glycidyl ethers were prepared from epichlorohydrin and alcohols in the presence of a base, sodium hydroxide. Other materials were purchased from Tokyo Kasei Kogyo Co., Ltd., Japan, and used without further purification.

1,3-Diacylglycerols: Typical procedure. A mixture of 5.12 g (20 mmol) glycidyl laurate, 4.40 g (22 mmol) lauric acid, 0.04 g (1 mmol) sodium hydroxide and 0.34 g (1 mmol) tetrabutylammonium hydrogensulfate in 20 ml of ethanol was refluxed at 80°C for 20 hr. The solid material was removed by filtration through a short column filled with silica gel and washed with dichloromethane. After removal of the solvent by evaporation, the solid reaction mixture was separated by centrifugal partition chromatography (CPC) (14) with acetonitrile-hexane as a distribution system to give a white powder, a mixture of 1,3- and 1,2-dilaurins (80:20, estimated by

¹H-NMR) in 74% yield; m.p. 48-52°C. CPC with this distribution system can separate 1,3- and 1,2-dilaurins as one fraction from other components such as glycidyl laurate, lauric acid and sodium laurate. In another run, the same reaction mixture was also fractionated by recrystallization from methanol to give 4.78 g (yield 52%) 1,3-dilaurin as a white powder; m.p. 55.0-56.0°C (β 54°C, β 56.5°C) (15). The structure and purity of 1,3-dilaurin are ascertained by ¹H-NMR, MS, IR and elemental analyses (within ± 0.4%). No contamination with the 1,2-isomer was ascertained by melting point, ¹H-NMR (Fig. 1A), and thin layer chromatography (silica gel TLC-FID Analyzer, Fig. 2A). In this case, 1,3-dilaurin might be separated from the 1,2-isomer by recrystallization because of its higher melting point. Other diglycerides were obtained analogously.

1-Alkyl-3-acylglycerols. Reaction of glycidyl ethers with carboxylic acids in the presence of quaternary ammonium salt as described for diglycerides produced 1-alkyl-3-acylglycerols that were isolated by CPC. The yields and isomer ratios of symmetrical and racemic 1,3- and 1,2-diglycerides and alkylacylglycerols are summarized in Table 1.

RESULTS AND DISCUSSION

The effect of quaternary ammonium salt on the reaction of glycidyl esters and ethers with carboxylic acids is remarkable. For example, in the reaction of glycidyl

TABLE 1

Yields and the Ratios of 1,3- and 1,2-Isomers of Diglycerides and Alkylacylglycerins

R	R'	Yield ^b (%)	Ratio ^d (1,3:1,2)	m.p. (°C)
Lauroyl	Methyl	73	60:40	Liquid
Caproyl	Pentyl	70	60:40	Liquid
Acetyl	Undecyl	81	80:20	Liquid
Lauroyl	Undecyl	74 (52 ^c)	80:20 100:0	48.0-52.0 55.0-56.0
Abietyl	Undecyl	72	100:0	Thick liquid
Myristoyl	Tridecyl	72 (54 ^c)	80:20 100:0	56.5-61.0 65.5-66.5
Dodecyl	Methyl	72	100:0	Liquid
Dodecyl	Undecyl	88 (73 ^c)	100:0 100:0	44.5-46.0 44.5-46.0
Benzyl	Undecyl	75	100:0	Liquid

^aTetrabutylammonium hydrogensulfate and sodium hydroxide (5 mol% both).

^bIsolated by CPC (centrifugal partition chromatograph-L.L.N. Model-NMF, Sanki Engineering Ltd. Kyoto, Japan).

^cIsolated by recrystallization from methanol.

^dEstimated from ¹H-NMR.

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1,3-DIACYLGLYCEROLS AND 1-ALKYL-3-ACYLGLYCEROLS

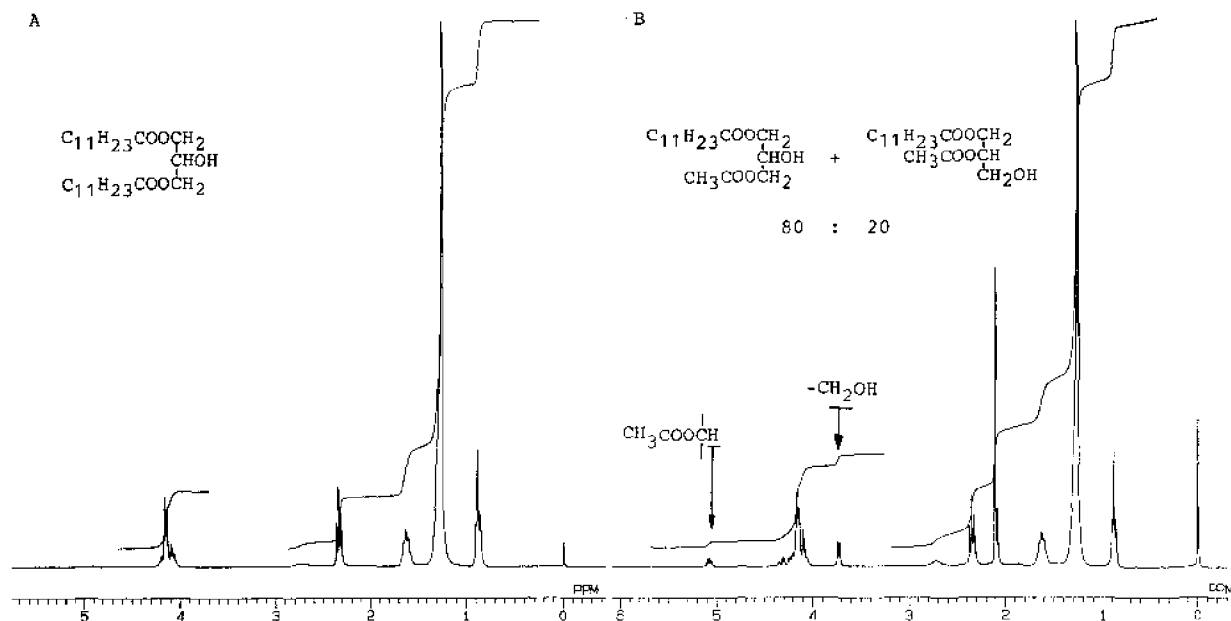


FIG. 1. ¹H-NMR spectra recorded on a JEOL-GSX-270S in CDCl₃ with Me₄Si as internal standard; A, 1,3-dilaurin purified by recrystallization from methanol; B, mixture of 1-lauroyl-3-acetylgllycerol and 1-lauroyl-2-acetylgllycerol (80:20) isolated by CPC (centrifugal partition chromatograph).

TABLE 2

Effect of Reaction Conditions on the Yields and the Isomer Ratios of Dilaurins

Reaction		Solvent	Yield ^a %	Isomer ratio ^b (1,3:1,2)
Temp. (°C)	Time (hr)			
80	20	Dioxane	71	80:20
80	20	Ethanol	74	80:20
60	20	Ethanol	50	90:10
40	35	Ethanol	16	90:10

^a Isolated by CPC (centrifugal partition chromatograph-L.L.N. Model-NMF, Sanki Engineering Ltd., Kyoto, Japan).

^b Estimated from ¹H-NMR.

acetate with lauric acid, the yields of the diglyceride are 81% in the presence of tetrabutylammonium hydrogen-sulfate and an equal amount of sodium hydroxide, and 11% in the absence of quaternary ammonium salt, respectively. This result can be attributed to the increase of nucleophilicity of the laurate anion through combination with the bulky quaternary cation (16).

Table 1 shows that the main products of the reaction of glycidyl esters and ethers with various carboxylic acids in the presence of quaternary ammonium salt are 1,3-diglycerides and 1-alkyl-3-acylglycerols, respectively. This reaction is viewed as an S_N2 cleavage of the epoxide as proposed by Ulsperger (17). The effects of reaction temperature and solvent on the yields and isomer ratios of 1,3- and 1,2-dilaurins are summarized in Table 2. No obvious effect of solvent on yields or isomer ratios was observed within the present study.

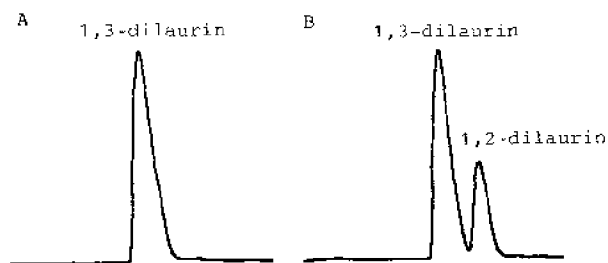


FIG. 2. Thin layer chromatograms by a silica gel TLC-FID Analyzer (Iatroscan TH-10, Iatron Laboratories Inc.) n-hexane, ethyl acetate, and acetic acid (200:20:1) as mobile phase; A, 1,3-Dilaurin recrystallized from methanol; B, Mixture of 1,3- and 1,2-dilaurins (72:28) obtained by treating 1,3-dilaurin (A) with an equivalent weight of lauric acid at 80°C for 5 hr (isolated by using CPC).

The distinctive spectral feature of 1,2-diglycerides in the ¹H-NMR spectra is the existence of the absorptions at δ = 3.73 (d, -CH₂OH) and 5.10 [m, C(O)OCH=] (Fig. 1B), as noted by Johnson (18). 1,3-Diglycerides have no signal in these regions (Fig. 1A). Therefore, the ratio of 1,3- and 1,2-isomers was estimated from ¹H-NMR. 1,3- and 1,2-diglycerides can also be differentiated by a silica gel TLC-FID Analyzer with a mixture of n-hexane, ethyl acetate and acetic acid (200:20:1) as a mobile phase. Figure 2A shows a chromatogram of 1,3-dilaurin purified by recrystallization from methanol. Figure 2B shows that of the mixture of 1,3- and 1,2-diglycerides.

The stability of 1,3-dilaurin was evaluated. No isomerization from the 1,3- to the 1,2-isomer was observed when the material was held at room temperature for several months or at 80°C for 50 hr in ethanol. But under acidic conditions, for example, stirring with an equivalent

weight of lauric acid at 80°C for 50 hr, 1,3-dilaurin partly isomerized to the 1,2-isomer, yielding a 72:28 ratio as determined with a silica gel TLC-FID Analyzer (Fig. 2B) and estimated from ¹H-NMR. 1,3-Dilaurin also isomerized to an 85:15 mixture by stirring with lauric acid in ethanol at 80°C for 20 hr in the presence of catalytic amounts of tetrabutylammonium hydrogensulfate and sodium hydroxide.

The structures of 1-alkyl-3-acylglycerols were ascertained by ¹H-NMR and a silica gel TLC-FID Analyzer. No evidence of the formation of the 1,2-isomer was observed in the product isolated by CPC. It therefore appears that the reaction of glycidyl ethers with carboxylic acids proceeded very selectively, and essentially no isomerization occurred in the reaction. In fact, even stirring with an equivalent weight of lauric acid under rather drastic conditions (80°C, 72 hr), only about 3% of 1-dodecyl-2-lauroylglycerol was formed from the 1,3-isomer (determined with a silica gel TLC-FID Analyzer).

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