TABLE VIII

Some Physical Properties of Esters Prepared by Conventional and in Situ Methods

| | Cloud pt (° C) | | Viscosity (cP)[a] | Density (g/cc)[a] |
|---|---|---|---|---|
| | Conventional | in Situ | Conventional | Conventional |
| Suncross 150 | | | | |
| 15/10 C | 3.0 | 3.0 | 5.9 | 0.88 |
| 21/16 C | -0.8 | -5.5 | 5.8 | 0.88 |
| 24/19 C | -1.0 | -0.8 | 6.8 | 0.88 |
| 27/22 C | -0.8 | -1.3 | 5.6 | 0.87 |
| 30/25 C | -2.5 | -2.0 | 6.2 | 0.87 |
| Hysun 31 | | | | |
| 15/10 C | 1.5 | 2.0 | 5.8 | 0.88 |
| 21/16 C | -1.5 | -3.5 | 5.4 | 0.88 |
| 24/19 C | -2.0 | -2.0 | 6.7 | 0.88 |
| 27/22 C | -2.3 | -2.5 | 6.5 | 0.87 |

[a]Dynamic viscosity and density measurements were taken at 25 C.

- Purification of the esterified crude product by distillation does not significantly change the fatty ester composition of the mixture.
- The presence of moisture in the oilseed reduces the yield of methyl esters obtained from reactions in situ.
- The fatty ester composition of the products derived from reactions in situ is essentially the same as that from conventional transesterification of the pre-extracted oil.
- The cloud points of the esters produced by in situ reactions appear slightly lower than those prepared by conventional methods.

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# Enolate Anions from Lipid Derivatives. Alkylation of Acylisopropylidene Glycerols

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## ABSTRACT

The enolate anions from isopropylidene protected monoacylglycerols have been successfully alkylated with alkyl iodides of various chain length. From these products the corresponding monoacylglycerols and triacylglycerols can be prepared. This is exemplified by the synthesis of 2-butyldodecanoyl-didodecanoyl glycerol, di-2-butyldodecanoyl-dodecanoyl glycerol and tri-2-butyldodecanoyl glycerol.

## INTRODUCTION

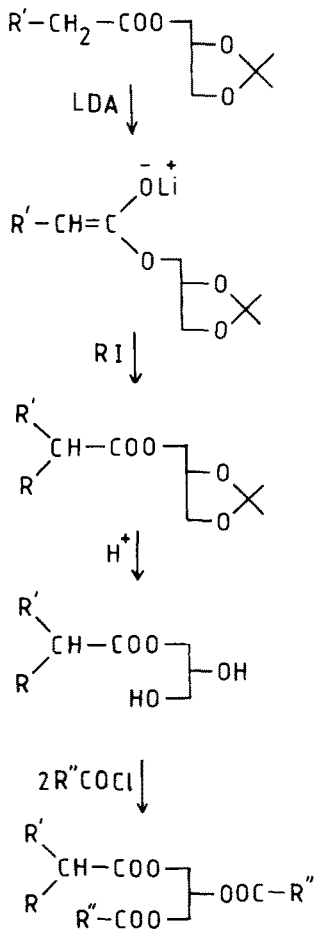
Branched mono- and triacylglycerols are potentially interesting for industrial use, because they have physical properties different from the corresponding straight chain analogues. For example, the 2-alkyl-branched monoacylglycerols have superior surface active properties compared to the straight chain compounds (2).

In a previous paper (1) we described the preparation of 2-alkyl-branched monoacylglycerols from the corresponding 2-alkyl-branched fatty acids. We now present the preparation of such monoacylglycerols directly from the acylisopropylidene glycerols through alkylation of their enolate anions. Cleavage of the isopropylidene group gives the monoacylglycerol, which can be acylated with acid chlorides to give branched triacylglycerols (Scheme 1). We have studied how different chain length of the monoglyceride and of the alkylating agent influence the product yields. We also have compared the efficiency of the direct alkylation method presented here, with the multistep route (1).

The preparation and alkylation of ester enolate anions has been well studied (3-14), and has been reviewed by Petragnani and Yonashiro (15). One problem with this type of reactions is the tendency of enolate anions to undergo self-condensation to form the corresponding β-ketoesters (3,7). This side reaction can, however, be suppressed by the use of a low reaction temperature (-70 C) during anion preparation. Rathke and coworkers (3) have shown that even though the amount of self-condensation product is large when the anions are generated at 0 C, anions prepared at -70 C are stable even at room temperature. They also have shown that the alkylation of lithio-t-butylacetate is successful, while a mixture of condensation and alkylation products is obtained with lithio ethyl acetate. Furthermore, they found that lithio ethyl hexanoate could be alkylated in good yields. Thus, it seems that a long alkyl chain in the acid part and a bulky alcohol part favor alkylation compared to side reactions. If the α-position is sterically hindered, for instance through alkyl groups in the β-position, it is even possible to prepare and alkylate the enolate anion at 0 C without condensation (6). The product yields also are dependent on the temperature and the solvent used in the alkylation step. Addition of the enolates to the alkylating agent in a mixture of tetrahydrofuran and dimethylsulfoxide at room temperature gives the best yields, according to Rathke (3), while Cregge and his coworkers (4) suggest that direct addition of the alkyl halide in THF/HMPA to the enolate at -70 C is better. On the other hand, MacPhee and Dubois (6) have found that alkylation is slow at -70 C, and that the reaction mixtures should reach room temperature before work-up. They also have reported that changing the alkylating agent from methyl to ethyl to isopropyl iodide has little effect on the yield, in the alkylation of an ester with a secondary α-carbon.

## EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 298 spectrometer. $^1$H NMR



SCHEME 1

R and R' as in Table I; R'' = $C_{11}H_{23}$ –

spectra were recorded on a Jeol MH-100 NMR spectrometer. Mass spectra were obtained using a Finnigan 4021 mass spectrometer operating at 70 eV. Gas chromatographic analyses were performed on a Varian 3700 or a Varian 1400 gas chromatograph equipped with a flame ionization detector. The columns used were a 2.5 m column of 3% OV17 on Varaport 30, 100-120 mesh, a 0.5 m column of 5% OV101 on Gaschrom Q, 100-120 mesh, and a 0.5 m glass column of 1.5% OV1 on Gaschrom Q. Elemental micro analyses were performed at Ilse Beetz Mikroanalytisches Laboratorium, Kronach, West Germany.

All alkyation reactions were carried out in an atmosphere of dry nitrogen. THF was dried by refluxing over sodium followed by distillation under nitrogen. Diisopropylamine and dimethylsulfoxide were distilled from calcium hydride and were stored over molecular sieves. Alkyl iodides were purchased from Fluka and Aldrich and were used without purification.

Butanoyl-, dodecanoyl- and octadecanoylisopropylidene glycerols were prepared through standard procedures (1,18) from the acid chlorides and isopropylidene glycerol.

### General Procedures for the Alkylation of Isopropylidene Glycerols

*Alkylation of butanoyl and dodecanoylisopropylidene glycerols.* To 12.1 g (0.12 mol) of dry diisopropylamine in 100 ml of dry THF at 0 C, 73 ml (0.11 mol) of 1.51 M butyllithium in hexane was added. The mixture was stirred at 0 C for 15 min and then cooled to -70 C. A solution of the acylisopropylidene glycerol (0.1 mol) in 100 ml of dry THF was added slowly, so that the temperature did not exceed -60 C. When all of the ester had been added, the clear solution was stirred at -70 C for 15 min. The cold enolate solution was then quickly transferred into a solution of the alkyl iodide (0.15 mol) in 120 ml of a 1:1 mixture of dry THF-DMSO kept at about 20 C. The yellow solution was stirred at room temperature for 15 min and then poured into ammonium hydroxide and ether. The ether phase was separated and the water solution extracted with three portions of ether. The combined ether layers were washed with ammonium hydroxide, cold diluted hydrochloric acid and finally with saturated sodium chloride. The solution was dried with $MgSO_4$ and evaporated. The crude product was purified through distillation or column chromatography on neutral alumina, eluting with hexane-ether mixture.

*Alkylation of octadecanoylisopropylidene glycerol.* As above, but the enolate was prepared at -30 C to -20 C.

All of the alkylated isopropylidene glycerols were identified by IR (1735 $cm^{-1}$, C=O, ester, 1370, 1380 $cm^{-1}$ isopropyl group), MS (m/e = $M^+$-15, $M^+$-$RCOOCH_2$) and $^1H$ NMR ($CDCl_3$) [$\delta$ = 0.88 ppm (t, $-CH_3$), $\delta$ = 1.10-1.96 ppm (m, $-CH_2-$), $\delta$ = 2.1-2.7 ppm (m, >CHCO), $\delta$ = 1.36 ppm (s, $-CH_3$), $\delta$ = 1.43 ppm (s, $-CH_3$), $\delta$ = 3.62-3.88 ppm (m, >CH-O), $\delta$ = 3.94-4.46 ppm (m, $-CH_2-O$) and also $\delta$ = 1.14 ppm (d, $-CH_3$) in the methyl branched analogues].

Satisfactory elemental analyses were obtained for all 2-alkyl branched acylisopropylidene glycerols. The GLC purity of the compounds was determined against an internal standard (tridecane or eicosane) and found to be at least 95%. On TLC they gave one single spot.

Yields and physical data for the compounds synthesized are summarized in Table I.

### Synthesis of Triacylglycerols

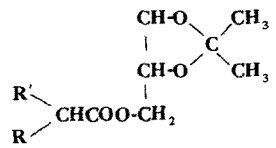
2-Butyldodecanoyl monoglyceride was prepared as previously described (1). 2-Butyldodecanoyl-didodecanoyl glycerol, mp 31.0-32.0 C, di-2-butyldodecanoyl-dodecanoyl glycerol and tri-2-butyldodecanoyl glycerol (2) were prepared according to standard procedures (18) in 30-80% isolated yield. The new triacylglycerols were characterized on the basis of satisfactory elemental and spectroscopic analyses. $^1H$ NMR ($CDCl_3$): $\delta$ = 0.88 ppm (t, $-CH_3$), $\delta$ = 1.1-1.9 ppm (m, $-CH_2-$), $\delta$ = 2.16-2.50 ppm (m, $-CH_2-CO$, >CH-CO), $\delta$ = 4.0-4.5 ppm (m, $-CH_2-O-$), $\delta$ = 5.0-5.5 ppm (m, >CH-O-).

## RESULTS AND DISCUSSION

In the present study we chose butanoyl-, dodecanoyl- and octadecanoyl-isopropylidene glycerols as representatives for short-, medium- and long-chain glycerol esters, and as alkylating agent we used methyl, butyl, decyl and hexadecyl iodide. In order to find suitable conditions for anion formation and alkylation, we studied the influence of some variables (19) on the product yield, when butanoylisopropylidene glycerol was alkylated with methyl iodide in THF. In a fractional factorial design (16,17), we found that among these variables, the one that seemed to have the most important influence on the yield was the temperature of the alkylating agent. The best result was obtained when we used lithium diisopropyl amide (LDA) as base, prepared the enolate at -70 C for 15 min and quickly transferred the cold enolate to a solution of the methyl iodide in THF at room temperature. The GLC yield determined with internal standard was then 88%. Pure 2-methylbutanoylisopropylidene glycerol was isolated through distillation in 65% yield. When the same reaction conditions as above were used in the alkylation with butyl iodide, the GLC yield of 2-ethylhexanoylisopropylidene glycerol dropped to 45%. However,

TABLE I

Isolated Yields and Physical Data for 2-Alkyl-branched Isopropylidene Glycerols



| Isopropylidene glycerol | R | R' | GLC yield (%) | Isolated yield (%) | Mp °C Bp °C/mmHg | $n_D$ |
|---|---|---|---|---|---|---|
| 2-Methyl-butanoyl- | $CH_3$- | $C_2H_5$- | 88 | 65 | 93.5-96/4 | $1.4280^{23.5}$ |
| 2-Ethyl-hexanoyl- | $C_4H_9$- | $C_2H_5$- | 70 | 63 | 95.0-100.0/1 | $1.4348^{21}$ |
| 2-Ethyl-dodecanoyl- | $C_{10}H_{21}$ | $C_2H_5$- | 67 | 60 | 126-134/$5\cdot10^{-2}$ | $1.4450^{23.5}$ |
| 2-Ethyl-octadecanoyl- | $C_{16}H_{33}$- | $C_2H_5$- | 66 | 60 | oil | $1.4487^{23.5}$ |
| 2-Methyl-dodecanoyl- | $CH_3$- | $C_{10}H_{21}$- | 89 | 73 | 128-130/$5\cdot10^{-2}$ | $1.4425^{23.5}$ |
| 2-Butyl-dodecanoyl- | $C_4H_9$- | $C_{10}H_{21}$- | 72 | 65 | oil | $1.4450^{23.5}$ |
| 2-Decyl-dodecanoyl | $C_{10}H_{21}$- | $C_{10}H_{21}$- | 64 | 53 | oil | $1.4498^{23.5}$ |
| 2-Methyl-octadecanoyl | $CH_3$- | $C_{16}H_{33}$- | 76 | 50 | oil | $1.4489^{23.5}$ |
| 2-Butyl-octadecanoyl- | $C_4H_9$- | $C_{16}H_{33}$- | 63 | 53 | 25 | — |
| 2-Decyl-octadecanoyl- | $C_{10}H_{21}$- | $C_{16}H_{33}$- | 63 | 45 | 35.0-36.0 | — |
| 2-Hexadecyl-octadecanoyl- | $C_{16}H_{33}$- | $C_{16}H_{33}$- | 51 | 41 | 54.5-56.5 | — |

GLC yield of alkylated product determined with tridecane or eicosane as internal standard.

the yield was raised to 70% by the use of THF/DMSO as solvent in the alkylation step. Further elongation of the chain in the alkyl iodide gave somewhat lower yields, as shown in Table I. On changing the ester from butanoylisopropylidene glycerol to dodecanoylisopropylidene glycerol, we observed no different behavior: the GLC yield for methylation was 89%, with a slight decrease of the yield as the chain length of the iodide is increasing. For the long chain octadecanoylisopropylidene glycerol the GLC yields as a whole are lower, but the same tendency still remains within the series of alkyl halides. This lower yield could be a consequence of the much lower solubility of the starting glycerol in THF at -70 C. To be able to dissolve this compound, we had to raise the temperature to -30 to -20 C and prepare the enolate anion at this temperature. In this case it thus seems that this variable is of some importance for the product yield. Although the yields are lower, it is possible to prepare the very long chain 2-hexadecyloctadecanoylisopropylidene glycerol in 41% isolated yield. All of the compounds in Table I were isolated through distillation or column chromatography in yields ranging from 41 to 73%. Acidic cleavage of the ketal group gives the 2-alkyl branched monoglycerides. The total yield of monoacylglycerols prepared via this reaction path is about 35%, based on the straight chain free fatty acids. This may be compared to the overall yield of about 20% that we obtained in the sequence used in our previous work (1). The possibility of using the same starting material in many different alkylations constitutes another advantage of the direct alkylation of acylisopropylidene glycerols. Triacylglycerols can be prepared from the branched monoacylglycerols through acylation with acid chlorides. As examples, we have prepared the mono-2-butyldodecanoyl-di-dodecanoyl glycerol, the di-2-butyldodecanoyl-dodecanoyl glycerol and the tri-2-butyldodecanoyl glycerol. As can be expected, the branched triacylglycerols have lower melting points than the saturated straight chain analogues with the same carbon number. One example is tri-2-butyldodecanoyl glycerol ($C_{48}$), which is an oil at -50 C, while trihexadecanoyl glycerol ($C_{48}$, tripalmitin) melts at 66 C. This lowered melting point might be of importance in the search for liquid lubricating oils with high stability towards oxidation.

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19. Variables: base (lithium diisopropylamide or lithium cyclohexylisopropylamide), reaction temperature and time at the formation of enolate, mode of addition (direct or inverse) of methyl iodide, temperature of the enolate and alkylating agent, addition rate on alkylation.

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