

Enol Esters XVI: Enol Ethers in Synthesis

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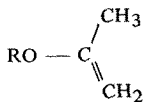
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ABSTRACT

The synthesis of isopropenyl octadecyl ether is reported. This compound is a useful reagent for the synthesis of wax esters by reaction with long chain fatty acids, and of symmetrical or unsymmetrical ethers via reaction with long chain alcohols. The long chain alkyl isopropenyl ether is more sensitive to hydrolysis than the corresponding enol ester and forms successively the ketal 2,2-dioctadecyloxypropane, and octadecanol and acetone. Glycerol reacts with propyne yielding glycerol acetonide, glycerol acetonide isopropenyl ether and diglycerol bisacetonide. New crystalline derivatives of diglycerol are described, useful for the characterization of that substance.

INTRODUCTION

Alkyl isopropenyl ethers have received little attention in the chemical literature. Only the first four homologs in the series have been synthesized. Shostakovskii and Gracheva

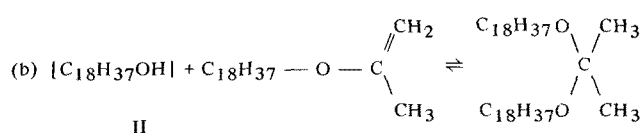
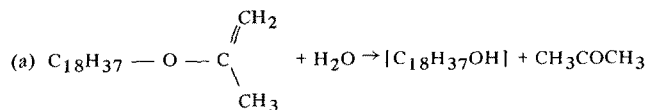


(1) report that these lower homologs react with alcohols to form geminal diethers (viz. acetals). The higher homolog, isopropenyl octadecyl ether under study in the present paper, is inert toward alcohols under the conditions studied by Shostakovskii and Gracheva but reacts at 230-250 C to form monoethers. The purpose of the present investigation was to study the reactions of long chain enol ethers and to compare these reactions with those of vinyl ethers.

RESULTS AND DISCUSSION

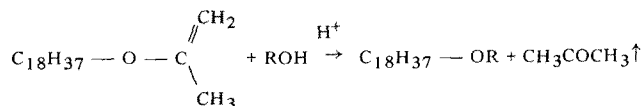
We prepared isopropenyl octadecyl ether I by a modification of the procedure of Shostakovskii and Gracheva (1), involving the addition of propyne to *n*-octadecanol with potassium hydroxide catalyst in a pressure vessel.

Isopropenyl octadecyl ether is distinctly more sensitive to hydrolysis than is isopropenyl stearate. The ether is slowly hydrolyzed by exposure to atmospheric moisture or by chromatographic procedures. The hydrolysis goes in stages; the proximate product is 2,2-dioctadecyloxypropane; the final product, octadecanol. The course of the changes can be monitored by IR analysis (see Experimental Procedures). The hydrolysis to octadecanol may be rationalized by a scheme such as described by equation 1. The actual process must be more complex since, although we can isolate the ketal II after a recrystallization of I from



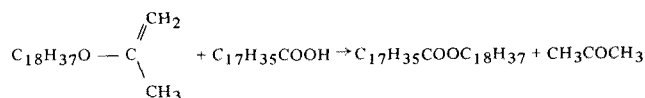
moist solvent, the ketal is not obtainable in a preparatively useful manner by reacting I with octadecanol and acid

catalyst. At high temperature the reaction of isopropenyl octadecyl ether with long chain alcohols with a trace of acid yields higher molecular weight dialkyl ethers. Equation 2 suggests the possibility of using this procedure for the synthesis of mixed ethers.



Occasionally we have succeeded in obtaining mixed ether, single reaction products, e.g., octadecyl tetradecyl ether (see Experimental Procedures), but, more typically, mixtures of the three possible ethers are obtained. Mass spectra clearly reveal the situation attained showing, the parent ion of the mixed ether product only in the exceptional reaction and peaks attributable to the molecular ions of the three components of the mixture in the usual reaction. In further contrast octadecyl vinyl ether reacts spontaneously with alcohols at room temperature in the presence of acid catalyst. The acetal product, ethylidene dioctadecyl ether, has not been previously described in the literature.

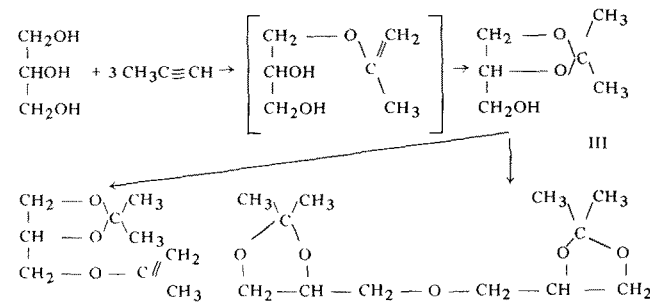
Another novel reaction of isopropenyl long chain alkyl ethers is the formation of esters with long chain fatty acids, equation 3.



This wax ester synthesis supplements those procedures already in use and has technical advantages in that slow-acting, high-boiling, water-entraining solvents are not required in order to shift equilibria to favor esterification. In a further modification one may use butylammonium carboxylate salts in *n*-butylamine (bp 78 C) to lower the reaction temperature and thereby to give a cleaner product and a slightly increased yield.

By way of generalization one may consider that vinyl ethers and vinyl esters react with long chain alcohols and acids to give addition products, whereas the corresponding isopropenyl ethers and esters give exchange products.

Favorskii and Shostakovskii (2), with ethyne and glycerol, obtained trivinyl glyceryl ether. Under quite comparable conditions with propyne in place of ethyne, we obtained the three reaction products glycerol acetonide III, glycerol acetonide isopropenyl ether IV, and diglycerol bisacetonide V (see equation 4) instead of methylvinylation. Compound III, prepared by other procedures, has been used in the classical synthesis of alpha monoglycerides. We have prepared crystalline tetraesters of diglycerol and they are useful in characterizing diglycerol for which no solid derivatives have been previously reported.



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EXPERIMENTAL PROCEDURES

The purities of the long chain alkyl compounds used as starting materials were greater than 98% as indicated by gas liquid chromatography (GLC) analysis.

Isopropenyl *n*-Octadecyl Ether I

n-Octadecanol (100 g) and 10 g powdered potassium hydroxide were mixed and placed in a pressure vessel. After purging with nitrogen, propyne in excess was admitted at an initial pressure of 365 psi at 95 C. The vessel was then heated to 145 C for 15 hr under a developed gauge pressure of 520 psi. An IR spectrum of an aliquot sample showed complete conversion to isopropenyl octadecyl ether. The analytical sample of the new compound, obtained by extracting with pentane, removing alkali with water-washing, drying the pentane solution with sodium sulfate, reducing the volume and recrystallizing from pentane, melted at 29.5-30 C. It showed IR bands at 800 (strong, sharp), 992 (weak), 1090 (strong), 1283 (very strong and sharp), 1372 cm^{-1} , as well as CH bands at 2860 and 2920 cm^{-1} (CS_2). Analysis calculated for $\text{C}_{21}\text{H}_{42}\text{O}$: C, 81.21; H, 13.63% mol wt 310 g/mole Found: C, 80.57; H, 13.43; mol wt 525 (thermistor).

Diocadecyl Ether

Isopropenyl *n*-octadecyl ether, 4.0 g, (0.013 mole), and *n*-octadecanol, 3.5 g, (0.013 mole), were heated to 230 C for 10 min with 0.5% of the total weight of sulfuric acid or *p*-toluenesulfonic acid catalyst. Chromatography on Florisil gave 3.5 g (52% yield) of analytically pure ether, mp 62-3 C, lit. 62-3 C (3).

n-Octadecyl *n*-Tetradecyl Ether

Isopropenyl *n*-octadecyl ether, 3.1 g (0.010 mole), and *n*-tetradecanol, 2.14 g, were heated for 20 min at 250 C with a trace of concentrated sulfuric acid or *p*-toluenesulfonic acid. A filtration of the product in hexane solution through a short Florisil column removed the acid catalyst and decolorized the product. A single crystallization from hexane gave 2.3 g (50% yield) of *n*-octadecyl *n*-tetradecyl ether, mp 58-58.5 C. Mass spectral analysis showed the parent peak m/e 466, but *no* peaks at mass numbers corresponding to the molecular weights of di-*n*-octadecyl or di-*n*-tetradecyl ether. Slight variations of procedure, in particular when impure starting material containing ketal was used, gave a mixture of product ethers containing $(\text{C}_{18}\text{H}_{37})_2\text{O}$, $(\text{C}_{14}\text{H}_{29})_2\text{O}$ and $\text{C}_{18}\text{H}_{37}\text{OC}_{14}\text{H}_{29}$, extremely difficult to separate in workable quantities but analyzable by GLC or mass spectral techniques. Analysis calculated for $\text{C}_{32}\text{H}_{66}\text{O}$: C, 82.32; H, 14.25. Found: C, 82.34; H, 14.27.

Ester Synthesis

Procedure A (acid catalysis) octadecyl octadecanoate (stearyl stearate): Isopropenyl octadecyl ether (5 g in 50 ml heptane), 5 g stearic acid, and a drop of concentrated sulfuric acid were refluxed for 5 hr. After solvent removal the product was isolated in 80% yield by crystallization from acetone. Small early crops containing traces of stearic acid were discarded. The product melted at 61.5-62 C, lit. mp 61.5-62 C (4), $\nu_{\text{max}}^{\text{CS}_2}$ 1737 cm^{-1} .

Procedure B (basic catalysis) n-octadecyl myristate: Myristic acid, 5.45 g (0.025 mole) and 4 ml triethylamine (calculated for equivalency 2.55 g) were melted together to form a homogeneous phase, and 7.82 g (0.025 mole) of isopropenyl *n*-octadecyl ether was added. The mixture was heated from 115-150 C for 40 min during which time the triethylamine as well as gaseous acetone reaction product was lost. The residue was of a pale tan color and was very soluble in hexane and insoluble in ethanol. Recrystallization from a mixture of the two solvents gave an 87% yield

of this new ester, mp 45.5-47 C. Analysis calculated for $\text{C}_{32}\text{H}_{64}\text{O}_2$: C, 79.93; H, 13.42. Found: C, 80.02; H, 13.45.

Ethylidene Diocadecyl Ether

Octadecanol, 27 g, (0.1 mole) and octadecyl vinyl ether, 29.6 g, (0.1 mole) purified by chromatography of a General Aniline and Film Co. commercial product on Florisil, were treated with a drop of sulfuric acid catalyst and let stand 5 min. The catalyst was removed by filtering the product dissolved in pentane through a small column of Florisil. After solvent removal the yield was 50 g (98%), mp 30-1. The product showed no IR hydroxyl bands. Recrystallization five times from pentane gave the analytical sample mp 39-40 C IR (CS_2) 1100, 1136 cm^{-1} , NMR (CCl_4) δ 4.56 (quartet), δ 3.4, δ 1.3. Analysis calculated for $\text{C}_{38}\text{H}_{78}\text{O}_2$: C, 80.49; H, 13.87. Found: C, 80.79; H, 13.92.

Glycerol Acetonide, Glycerol Acetonide Isopropenyl Ether, and Diglycerol *bis*Acetonide.

Anhydrous glycerol (100 g) and powdered potassium hydroxide (10 g) were charged into an autoclave, purged with nitrogen, 280 ml liquid propyne added via pressure burette using nitrogen backup pressure, and the mixture heated to 165 C. A gauge pressure of 400 psi was developed and held for 18 hr. The opened autoclave contained a pale brown syrup which was dissolved in 250 ml water and freed of alkali with methylene chloride. After evaporation of the methylene chloride, distillation in vacuo on a spinning band column gave 30 g glycerol acetonide isopropenyl ether (IV), bp 49 C/4 mm, d_{30}^{30} 0.9859; followed by 30 g glycerol acetonide (III), bp 58 C/4 mm, 84 C/13 mm, lit. 82-3 C/10-11 mm (5); followed by the *bis*acetonide of diglycerol (V), bp 102 C/0.8 mm lit. 97 C/1 mm (6).

Diglycerol Tetraesters

Diglycerol *bis*acetonide was shaken with twice its volume of 2% aqueous hydrochloric acid at room temperature until a single phase was obtained. Evaporation in vacuo left a residue of diglycerol. Mass spectrometry showed the parent ion and peaks at 135, 117, 93, 71 and 56 g/ion in accord with expected fragmentation, NMR in deuterium oxide showed a single degenerate peak at 3.35 ppm with multiple peaklets near 3.5 ppm. Diglycerol. 0.26 g heated to 170 C for 0.5 hr with 2.08 g isopropenyl stearate in the presence of 1 mg. *p*-toluene-sulfonic acid gave crude diglycerol tetrastearate, 80% yield. The analytical sample was eluted from Florisil with ether and was recrystallized from acetone; mp 63 C, $\nu_{\text{max}}^{\text{CS}_2}$ 1745, 1158 cm^{-1} . Analysis calculated for $\text{C}_{78}\text{H}_{150}\text{O}_9$: C, 76.04; H, 12.27; mol wt 1232 g/mole. Found: C, 76.10; H, 12.20; mol wt 1230 g/mole.

The tetrapalmitate, similarly prepared, melted 72-72.5 C. Analysis calculate for $\text{C}_{70}\text{H}_{134}\text{O}_9$: C, 75.08; H, 12.06. Found: C, 75.11; H, 12.09.

The tetralaurate, mp 55.5-56.2, was made similarly but not submitted to analysis.

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