REVIEW

The Alkyl Glycidyl Ether as Synthetic Building Blocks

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Alkyl glycidyl ether is one of the most useful key materials for industrial applications because the addition reaction of various kinds of nucleophilic reagents to the reactive epoxy bond of the glycidyl ethers has led to glyceryl ether derivatives. Glyceryl ether exhibits many interesting physical and pharmacological properties. The alkyl glycidyl ether can presently be produced at an industrial scale under the phase-transfer catalytic Williamson ether synthesis. We have reviewed some addition reactions of the alkyl glycidyl ether and possibilities for use as the building blocks for the syntheses of surfactants, pharmaceuticals, etc. that contain glyceryl ether skeletons. Typical examples of alkyl glyceryl ether derivatives include: amino ether as cosmetic material, and isodiglycerin mono- and dialkyl ethers and triglycerin monoalkyl ether as a cosmetic or a pharmacologically useful material, respectively. Another interesting reaction is the rearrangement of the epoxy bond of the alkyl glycidyl ether, which gives alkoxy ketone in a one-pot synthesis.

KEY WORDS: Addition reactions, alkoxy ketone, glyceryl ether, glyceryl ether derivatives, glycidyl ether, isodiglycerin dialkyl ether, isodiglycerin monoalkyl ether, phase-transfer catalytic Williamson ether synthesis, triglycerin monoalkyl ether.

Alkyl glycidyl ethers are compounds that have a chemically stable ether bond and a highly reactive epoxy bond separated by a methylene ($-CH_2-$) unit. The reactive epoxy ring is readily opened into corresponding alkyl glycerol derivatives by the attack of various nucleophilic reagents such as water, alcohols, acids, amines or thiols.

These alkyl glycerol derivatives are obtained by the ring opening reaction by the previously mentioned nucleophilic reagents; alkyl glyceryl ethers are of special interest due to their pharmaceutical and physical properties (1).

Thus, alkyl glycidyl ether is an industrially important intermediate with a broad application in industry. Generally, alkyl glycidyl ethers have been produced by either of the following two processes: (i) an epihalohydrin is added to an alcohol in the presence of an acid catalyst, such as sulfuric acid, $BF_3 \cdot OEt_2$ or tin tetrachloride, to give a halohydrin ether, followed by ring closure by a dehydrohalogenation reaction with an alkali to obtain the corresponding alkyl glycidyl ether; or (ii) a metal alcoholate is prepared and reacted with the epihalohydrin in an epoxy ring opening reaction, and subsequent epoxy ring closure by the dehydrohalogenation reaction proceeds in one step to give the corresponding alkyl glycidyl ether.

However, these known processes have inherent drawbacks and are not satisfactory to be applied industrially.

In the first process, as is stated in detail in the literature (2), aside from halohydrin ether, an adduct of the produced halohydrin ether is secondarily produced by addition of one or more epihalohydrins. In the second process, it is necessary to prepare a metal alcoholate. But it is generally accepted that, to produce metal alcoholates of higher alcohols by the use of alkali metal hydroxides, polar solvents of a specific type with high dielectric constants must be used (3).

To provide a simple process in which glycidyl ethers can be produced at a high yield from alcohols and epihalohydrins, and which is also suitable for industrial applications, we reported a process for producing the alkyl glycidyl ether by reacting the alcohol with the epihalohydrin in an aqueous alkaline solution under the phase-transfer catalytic Williamson ether synthesis with a catalytic amount of a quaternary ammonium salt as a phase-transfer catalyst (PTC) (1).

Our method for producing the alkyl glycidyl ether was much more useful for its preparation from a polyunsaturated alcohol, such as a terpene alcohol (4), as compared to the conventional method with an alkali metal hydride (5). For example, in the case of farnesyl or phytyl alcohol as the terpene alcohol, the corresponding terpene alkyl glycidyl ether could be obtained at a 85≈90% yield by our method. However, with the alkali metal hydride method, only 30≈45% was obtained (5). Some reactions of the alkyl glycidyl ether and their usefulness as synthetic building blocks will be reviewed in the next section.

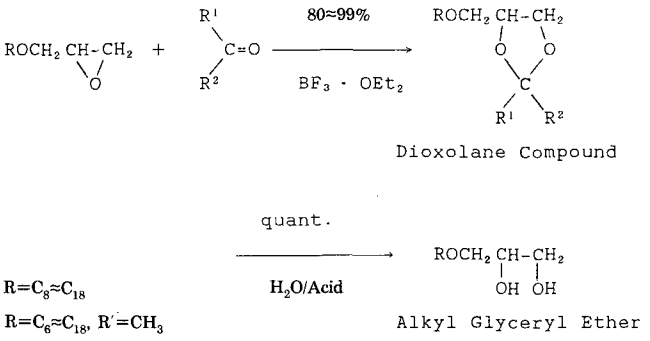
EXPERIMENTAL PROCEDURES

Addition reaction of carbonyl compounds. A 4-alkoxymethyl-1,3-dioxolane compound is the key intermediate for the alkyl glyceryl ether, i.e., the 4-alkoxymethyl-1,3-dioxolane yields an alkyl glyceryl ether quantitatively by acidic hydrolysis. A typical method for the preparation of that dioxolane compound is the dehydrohalogenation reaction between an alkyl halide and the alkali metal alcoholate of the 4-hydroxymethyl-1,3-dioxolane.

Because this method is much more expensive and tedious, a simple method was needed. Surprisingly, we discovered a simple method for the preparation of the 4-alkoxymethyl-1,3-dioxolane by means of an addition reaction of alkyl glycidyl ether with carbonyl compounds (see Scheme 1).

To catalyze the preparation of the 4-alkoxymethyl-1,3-dioxolane, proton acids and Lewis acids may be used. Preferably, a Lewis acid, such as $BF_3 \cdot OEt_2$, was used.

Generally, the alkyl glycidyl ether may be reacted with 1–30 moles of a carbonyl compound, preferably acetone, per mole of the alkyl glycidyl ether in the presence of 0.01–0.1 mole of an acid catalyst at a temperature of



SCHEME 1

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20–40°C. In practice, however, the yield was better, and the reaction proceeded more smoothly when an excess amount of the carbonyl compound was used. Accordingly, 7–15 moles of the carbonyl compounds per mole of the alkyl glycidyl ether were used. This reaction was exothermic, and it was preferable to gradually add the alkyl glycidyl ether to the carbonyl compounds, together with the acid catalyst, while adjusting the temperature to be within the range of 20–40°C (by the application of a proper cooling operation). The excess amount of carbonyl compounds could then be recovered and reused.

In recent years some destructible surfactants containing a 1,3-dioxolane skeleton, which are obtained by the reaction of epoxy compounds with carbonyl compounds in the presence of acid catalysts, have been reported (6).

Addition reaction of acid anhydrides. Another typical method, hitherto known for the preparation of the alkyl glyceryl ether, is the addition reaction of a carboxylic acid to the alkyl glycidyl ether to obtain a γ-mono ester of α-monoalkyl glyceryl ether, followed by hydrolysis under alkaline conditions. However, this method produces a great amount of self-polymerization by-products of the alkyl glycidyl ether.

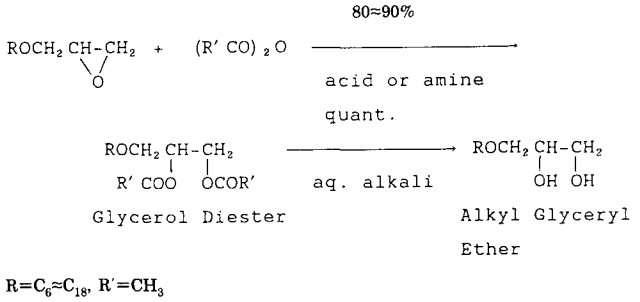
We discovered a simple method for the preparation of the alkyl glyceryl ether *via* a glycerol diester compound, obtained by the addition of an acid anhydride to the alkyl glycidyl ether [shown in Scheme 2 (1)].

As a catalyst for the addition reaction of the acid anhydride to the alkyl glycidyl ether, either an acid or a base can be used. As acid catalysts, Lewis acids were preferred, whereas tertiary amines were preferred as base catalysts.

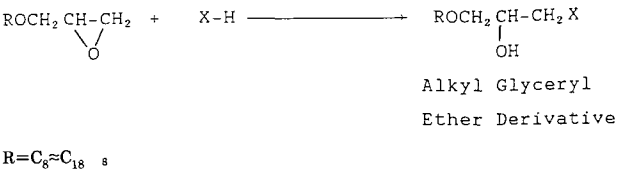
To produce the alkyl glyceryl ether diester from the alkyl glycidyl ether, generally the alkyl glycidyl ether may be reacted with 1–30 moles of an acid anhydride, preferably acetic acid anhydride, per mole of the alkylglycidyl ether, in the presence of 0.01–0.1 mole of an acid catalyst per mole of the alkyl glycidyl ether at a temperature of 20≈50°C, or of a base catalyst at a temperature of 100≈120°C.

In practice, however, the yield was better and the reaction proceeded more smoothly when an excess amount of the acid anhydride was used, i.e., 8–16 moles per mole of the alkyl glycidyl ether.

Addition reaction of XH compounds. The oxirane group in the alkyl glycidyl ether reacts readily with nucleophilic reagents, as previously mentioned. Typical reactions of epoxidated fatty compounds with monoalcohols or polyols lead to a wide range of alkoxy alcohols (fatty ether alcohols) (7).



SCHEME 2



SCHEME 3

In an analogous method, the alkyl glycidyl ether reacted readily with some nucleophilic agents to give an alkyl glyceryl ether derivative (Scheme 3) (2).

As stated in detail in the literature (8), the alcohol (XH=R′OH) is added at the α-position of the epoxy bond of a glycidyl skeleton to give 1,3-di-*O*-alkyl glyceryl ether derivatives in the presence of alkaline catalysts.

This addition reaction of the alkyl glycidyl ether with an alcohol was effected by reacting 1 mole of the alkyl glycidyl ether and 1–10 moles of the alcohol, preferably 3–5 moles, in the presence of 0.01–0.1 mole of an alkali catalyst, such as NaOMe, under conditions between 80 and 100°C.

Analogous to this method, many other nucleophilic reagents, such as amines, acids, amides, thiols and sodium hydrogensulfite, can be added to the alkyl glycidyl ether.

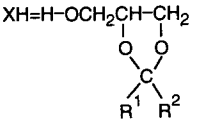
Some of the addition products of amines (XH=R′R′NH) or alcohols (XH=R′OH) to the alkyl glycidyl ether were used as follows: N-acyl-N-2-hydroxy-ethyl amide compounds as skin moisturizing agents for medical and cosmetic uses (9); NH-2-hydroxyalkyl-amino compounds as nonionic surface-active agents (10); amino and R:terpene alkyl compounds as nootropic agents for the treatment of dementia (5); and dioxolane compounds (see Scheme 4) as an intermediate for an α-monoalkyl ether of diglycerin, $ROCH_2CH(OH)CH_2O\text{-}CH_2CH(OH)CH_2OH$, which was obtained by the acidic hydrolysis of the previous dioxolane compounds.

The α-monoalkyl ether of diglycerin is useful as an emulsifier, cleaner, etc. and is preferably used as a component of cosmetic compositions (11).

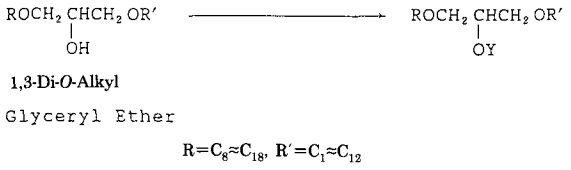
CHEMICAL MODIFICATION OF 1,3-DI-*O*-ALKYL GLYCERYL ETHER

1,3-Di-*O*-alkyl glyceryl ether compounds could be modified to generate new functions (Scheme 5).

Alkylene oxides, such as ethylene oxide or propylene oxide, can add to the reactive hydroxy group of 1,3-di-*O*-alkyl glyceryl ether to give 1,3-di-*O*-alkyl-2-*O*-polyoxyalkylene glycerin with Y = $(CH_2CH_2O)_nH$ or $(CH_2CH(CH_3)O)_nH$, which functions as an nonionic surface-active agent (12).



SCHEME 4



SCHEME 5

A novel glyceryl ether-type phospholipid, $Y=P(O)(O^-)OCH_2CH_2N^+Me_3$, can be derived from 1,3-di-*O*-alkyl glyceryl ether by the reaction of 1,3-di-*O*-alkyl glyceryl ether with 2-chloro-2-oxa-1,4,5-dioxaphospholan and subsequent reaction with trimethylamine in MeCN. The obtained glyceryl ether-type phospholipid derivative exhibited anti-inflammatory, analgesic and antimicrobial activities (13).

PREPARATION OF DIGLYCERIN ISOMER DIALKYL ETHER

In our further studies on the development of the synthetic uses of alkyl glycidyl ethers, we found some new approaches to the syntheses of novel polyol alkyl ethers, such as the diglycerin isomer dialkyl ether, $RO\text{-}CH_2CH[OCH_2CH(OH)\text{-}CH_2OH]\text{-}CH_2OR'$ with $Y=CH_2\text{-}CH(OH)CH_2OH$ (hereinafter referred to as "isodiglycerin dialkyl ether") (Scheme 6) (14).

The isodiglycerin dialkyl ether was readily prepared at a high yield and high purity from the alkyl glycidyl ether, either by process A or process B (as shown in Scheme 6).

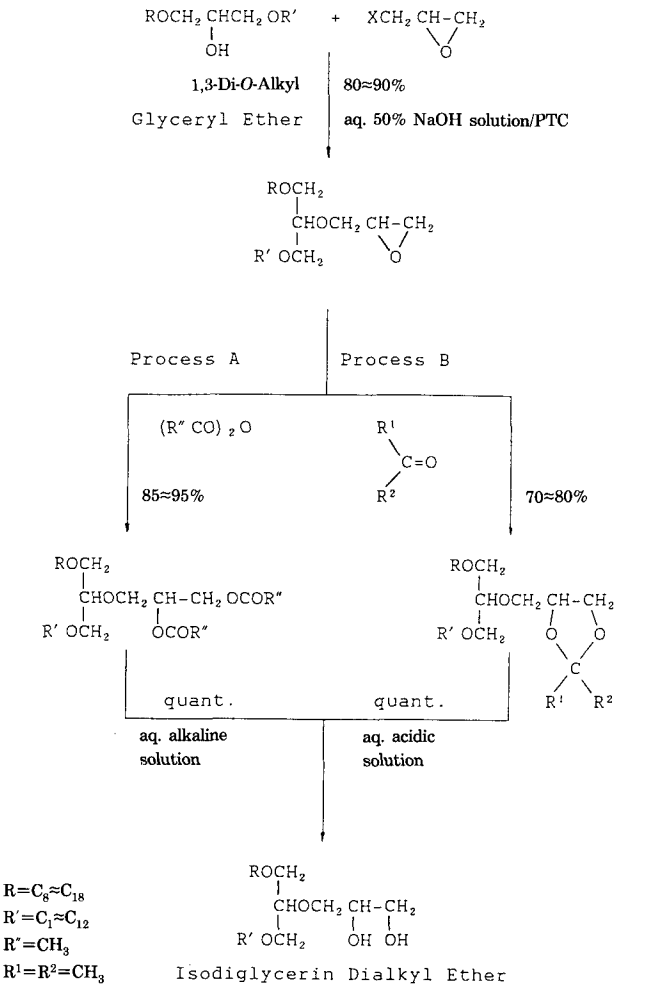
In process A, the alkyl glycidyl ether (1 mole) in the presence of an alkaline catalyst, such as NaOMe (0.01–0.1 mole per mole of the alkyl glycidyl ether), was added to the alcohol (3–5 moles) according to a known method (8) to form the 1,3-di-*O*-alkyl glyceryl ether at a 85≈95% yield.

The obtained 1,3-di-*O*-alkyl glyceryl ether (1 mole) was reacted with the epihalohydrin, such as epichlorohydrin (2–3 moles), while using quaternary ammonium salts (0.05 mole), such as tetrabutyl ammonium bromide, as the PTC and 50% aqueous NaOH solution (4–6 moles) to give the corresponding glycidyl ether, 1,3-di-*O*-alkyl-2-*O*-2′,3′-epoxypropylglycerin. The obtained 1 mole of the glycidyl ether was added to the acid anhydride (such as acetic acid anhydride, 8–16 moles), in the presence of 0.01–0.1 mole of a Lewis acid catalyst, for example, as $BF_3 \cdot OEt_2$, or a base catalyst, such as tertiary amine, to give the corresponding glyceryl ether diester-type compound.

The reaction proceeded smoothly and gave higher yields when the acid anhydride was used in excess. The unused excess of acid anhydride could be recovered and reused.

The reaction with Lewis acid was exothermic, and it was beneficial to keep the reaction temperature below 60°C. On the other hand, when tertiary amine was used as the catalyst, no generation of heat took place. It was necessary to keep the reaction temperature between 90–120°C by the application of heat.

The hydrolysis reaction of the obtained diester compound in the subsequent step can be performed by any of the known techniques. It was preferable to heat 1 mole of the diester compound with 2–5 moles of aqueous alkaline, preferably aqueous NaOH solution at a temperature between 80–100°C.



SCHEME 6

Upon hydrolysis of the obtained diester compound under conditions as indicated in the previous paragraphs, the intended isodiglycerin dialkyl ether compound was quantitatively obtained.

In process B we added to 7–15 moles of a carbonyl compound, such as acetone, 1 mole of the alkyl glycidyl ether as prepared in process A, in the presence of 0.01–0.1 mole of Lewis acid, such as $BF_3 \cdot OEt_2$, at a temperatue between 20–40°C. This reaction was exothermic. The alkyl glycidyl ether was added to the carbonyl compound coexisting with the acid catalyst, during which a suitable operation, such as cooling, was applied to the reaction mixture. Under the reaction conditions as indicated above, the dioxolane compound could be ordinarily obtained at yields of 70≈80%.

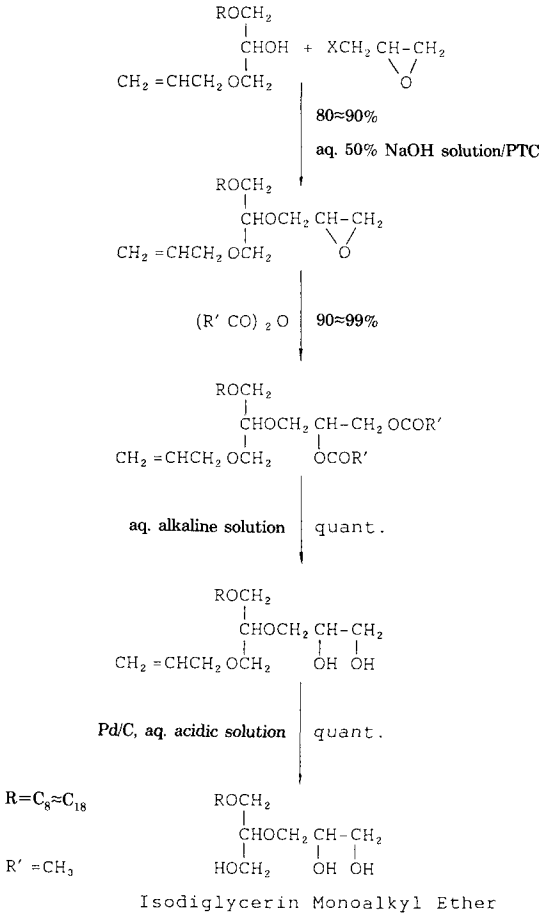
The obtained dioxolane compound was then hydrolyzed under acidic conditions by any known method to give the intended isodiglycerin dialkyl ether compound as prepared by process A. Typically, it was convenient to heat the dioxolane compound in water with an acid catalyst, such as sulfuric, hydrochloric phosphoric or acetic acid. The amount of the acid catalyst was usually in the range of 0.1–0.5N. Preferably, the water was admixed with water-soluble organic solvents, such as methanol, ethanol or

isopropanol. The hydrolysis was effected at a temperature between 70–100°C. The resulting isodiglycerin dialkyl ether compounds are useful as emulsifiers, emolients, humectants or thickners (14). More interesting applications of these isodiglycerin dialkyl ether compounds were discovered in our laboratory as follows.

An aqueous or aqueous alcoholic solution containing 1.0≈2.0 wt% of isodiglycerin dialkyl ether showed coloration that changed according to the surfactant concentration (15). For instance, 2.0 wt% of an aqueous solution containing the surfactant showed a purple color. With dilution to 1.0 wt%, the color of the solution gradually changed to blue, green, yellow and red. Furthermore, the color of these solutions, when observed in reflected light, differed from that observed in transmitted light. On the basis of phase diagram studies and scanning electron micrograph determinations, the structure of these colored solutions was concluded to be a dispersion of multilamellar liquid crystals that contained large amounts of water within the interlayers. It was thus considered that the coloration had arisen from the interference of light reflected at the interface of lamellar layers whose thickness was comparable to that of the wavelength of visible light.

Another application example was the enhancement of percutaneous absorption of active materials. For example, the isodiglycerin dialkyl ether compound enhanced the percutaneous absorption of a wide range of drugs, such as insulin, indomethacin, mefenamic acid, methyl salicylate, naphthiomate and aspirin (16).

A further-modified isodiglycerin dialkyl ether compound, $ROCH_2$-$CH(OCH_2CH(OH)CH_2NR'R^2)$-$CH_2OR'$ ($Y=CH_2$-$CH(OH)CH_2NR'R^2$ in Scheme 5), which can be derived as the reaction product of the above glycidyl ether with alkyl amines, was useful for prophylaxis of a wide range of viral diseases by stimulating the production of interferon in the host (17).



SCHEME 7

PREPARATION OF ISODIGLYCERIN MONOALKYL ETHER

In our extensive studies of the preparation of novel polyolether compounds, starting from the alkyl glycidyl ether, we discovered another type of novel isodiglycerin monoalkyl ether compound (Scheme 7).

This approach succeeded by the addition reaction of an allyl alcohol to the alkyl glycidyl ether and the deallylation reaction *via* isomerization of the allyl ether group to a vinyl ether group, catalyzed by palladium/active charcoal (Pd/C) in the acidic condition (18). Other unit reactions were similar as for the previously mentioned isodiglycerin dialkyl ether compounds (shown in Scheme 6).

The starting 1-*O*-allyl-3-*O*-alkyl glycerin was effected by reacting 1 mole of the alkyl glycidyl ether with 7–15 moles of allyl alcohol in the presence of 0.01–0.1 mole of catalytic alkali, such as NaOMe, at a temperature between 70–90°C. The obtained 1-*O*-allyl-3-*O*-alkyl glycerin (1 mole) was then reacted with an epihalohydrin, such as epichlorohydrin (3–5 moles), by Williamson ether synthesis under the PTC condition with quaternary ammonium salts (0.05–0.3 mole), such as tetrabutyl ammonium hydrogensulfate, and 50% aqueous NaOH solution (2–3 moles) at a reaction temperature between 40–60°C to give the corresponding glycidyl ether, 1-*O*-ally-2-*O*-2′,3′-epoxypropyl-3-*O*-alkyl glycerin.

The obtained 1 mole of alkyl glycidyl ether was reacted with 8–16 moles of the acid anhydride, such as acetic acid anhydride, in the presence of 0.01–0.1 mole of tertiary amine, such as triethyl amine, as catalyst at a temperature between 90–120°C to give the addition product, 1-*O*-allyl-2-*O*-2′,3′-di-*O*-acetylpropyl-3-*O*-alkyl glycerin (glyceryl ether diester compound) in almost quantitative yield.

The thus obtained glyceryl ether diester compound could be hydrolyzed by any of the known methods. A typical example is as follows: 1 mole of the glyceryl ether diester compound was added gradually to aqueous alkaline, such as aqueous NaOH solution (2–5 mole), with the co-existence of a water-soluble solvent including lower alkyl alcohols, such as methanol, ethanol or isopropanol, at a temperature between 70–90°C. Upon hydrolysis of the diester compound under conditions as indicated previously, 1-*O*-allyl-2-*O*-2′,3′-dihydroxy propyl-3-*O*-alkyl glycerin (isodiglycerin dialkyl ether compound) is obtained in substantial amounts.

The deallylation reaction of the obtained isodiglycerin dialkyl ether compound containing a 1-*O*-allyl group can be done as follows: 1 mole of the ether compound and aqueous methanol or ethanol solution were refluxed at a temperature between 70–90°C in the presence of 20–30 g of Pd/C and 20–30 g of protonic acid, such as *p*-toluene sulfonic acid. The deallylation reaction proceeded gradually

and was completed after 10 h to give the intended isodiglycerin monoalkyl ether in almost substantial yield.

Thus obtained isodiglycerin monoalkyl ether compounds were useful in the same applications as the previously mentioned isodiglycerin dialkyl ether compounds (19,20).

PREPARATION OF TRIGLYCERIN MONOALKYL ETHER

We were also interested in the preparation of an alkyl ether of a linear oligomer of glycerin, such as triglycerin or tetraglycerin. At first we tried to prepare a linear triglycerin monoalkyl ether compound (21). In this approach, the key compound was the commercially available 4-hydroxymethyl-1,3-dioxolane (glycerin ketal). The preparative strategy for the triglycerin monoalkyl ether compound is summarized in Scheme 8.

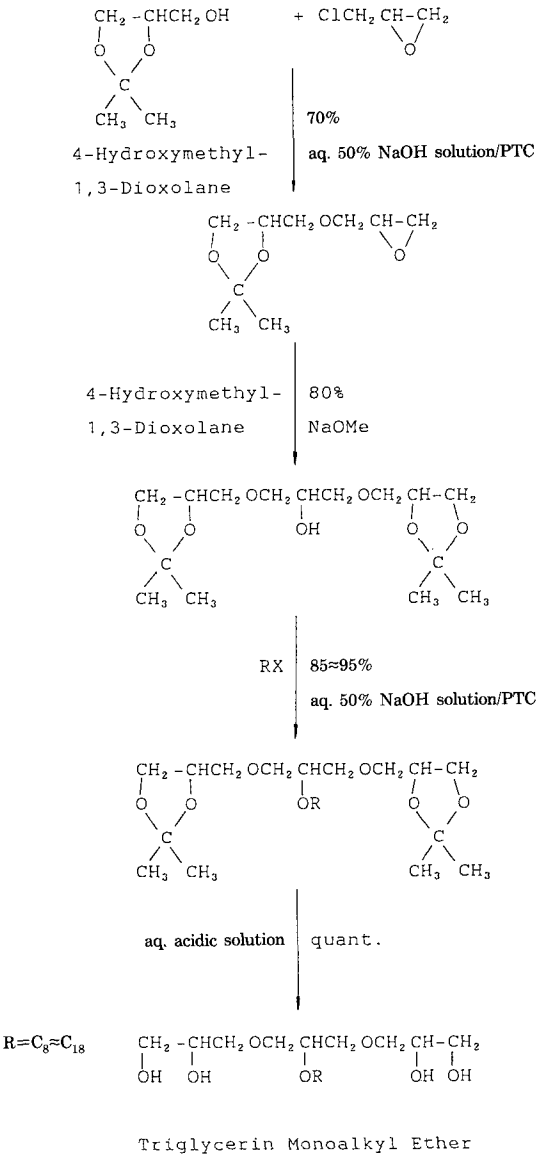
The glycidyl ether of 4-hydroxymethyl-1,3-dioxolane was obtained at a high yield by the PTC Williamson ether synthesis, as previously mentioned: Epichlorohydrin (1.5≈2.5 moles) was added to 1.0 mole of the 4-hydroxymethyl-1,3-dioxolane in the presence of 0.05–0.1 mole of a quaternary ammonium salt, such as tetrabutyl ammonium bromide, and the co-existence of both aqueous NaOH solution (3–5 moles) and 1000 mL *n*-hexane at a temperature between 40–50°C, to give the corresponding glycidyl ether of 4-hydroxymethyl-1,3-dioxolane as a colorless liquid at *ca.* 70% yield. Then, to 4-hydroxymethyl-1,3-dioxolane (3–6 moles) the obtained glycidyl ether of 4-hydroxymethyl-1,3-dioxolane (1 mole) was added in the presence of NaOMe (0.05–0.2 mole) at a temperature between 90–100°C to obtain the intermediary 1,3-*bis*-*O*-(2,3-*O*-isopropylideneglycerol) glycerin as a colorless liquid. The intermediary 1,3-*bis*-*O*-(2,3-*O*-isopropylideneglycerol)glycerin (briefly, a *bis*-dioxolane compound) is a known compound (22).

The Williamson ether synthesis of the *bis*-dioxolane compound with an alkyl halide and PTC succeeded smoothly to give the corresponding *bis*-dioxolane monoalkyl ether compound.

Subsequent acidic hydrolysis of the obtained *bis*-dioxolane monoalkyl ether compound proceeded quantitatively to give the intended triglycerin monoalkyl ether compound.

A typical Williamson ether synthesis of the *bis*-dioxolane compound with an alkyl halide was as follows. Generally, 1 mole of the *bis*-dioxolane compound may be reacted with an equimolar amount of the alkyl halide in the presence of 50% of aqueous NaOH solution (3–5 moles per mole of the *bis*-dioxolane compound) and 0.05–0.2 mole of the quaternary ammonium salt, such as tetrabutyl ammonium hydrogensulfate, at a temperature between 40–60°C to give the corresponding alkyl ether of the *bis*-dioxolane compound. Furthermore, regarding the reaction solvent, anything may be employed unless it adversely affects the key reaction. Aliphatic hydrocarbons, such as hexane, heptane and octane, are preferred.

Hydrolysis of the monoalkyl ether of the *bis*-dioxolane compound may be carrried out by any of the methods known as hydrolysis methods for dioxolane compounds. It was, however, preferable to conduct the hydrolysis reaction by using 0.05–1.0N of acidic aqueous solution. The hydrolysis reaction may be carried out by adding to water a water-soluble organic solvent, such as a lower alkyl



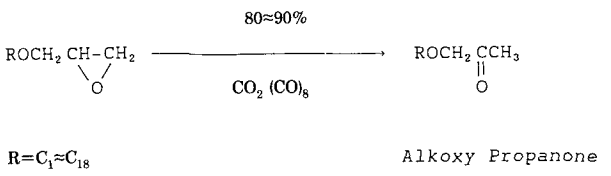
SCHEME 8

alcohol, for example MeOH, EtOH or *iso*-PrOH, at a temperature between 70–100°C. Upon conducting the hydrolysis reaction under these conditions, the intended compound triglycerin monoalkyl ether could be obtained substantially in a stoichiometric amount from the alkyl ether of the *bis*-dioxolane compound.

These triglycerin monoalkyl ethers, in which R represents a group containing from 8 to 18 carbon atoms, had a well-balanced susceptibility to moisture. Thus, they had a high moisturizing effect and functioned well as humectants in cosmetics (21).

REARRANGEMENT REACTION

Rearrangement of epoxides to carbonyl compounds by acid catalysts has been previously reported (23). However, little is known about the rearrangement of the alkyl glycidyl ether.



SCHEME 9

Surprisingly, we discovered a selective rearrangement of the alkyl glycidyl ether to 1-alkoxy-2-propanone (alkoxy propanone) by group-VIII transition-metal carbonyl complexes (Scheme 9) (24).

The rearrangement of epoxy compounds to carbonyl compounds by group-VIII transition-metal carbonyl complexes has been reported by Pradi *et al.* (25). However, analogous rearrangements for alkyl glycidyl ether were hitherto unknown.

The rearrangement could be carried out in the presence of catalytic amounts of metal carbonyl dinucleus complexes, such as octa-carbonyl complexes of CO, with the co-existence of lower alcohols. Additionally, this rearrangement could be conducted in a one-pot synthesis.

One published (26) method for the preparation of 1-alkoxy-2-propanone is based on the reaction of an alcohol with 2-chloro-1-(chloromethyl) ethyl methoxymethyl ether under alkaline conditions in dioxane and then by acidic hydrolysis (26).

The typical rearrangement reaction of alkyl glycidyl ether by group-VIII transition-metal carbonyl complexes is as follows. A solution of 0.01–0.1 mole of metal carbonyl dinucleus complexes, such as octa-carbonyl complexes of CO, in 30–50 moles of lower-alkyl alcohol, especially MeOH, was placed in a reaction flask in a nitrogen atmosphere at 25–30°C. An evolution of CO gas occurred, and the dark brown solution turned light pink after a few hours. After completion of the CO gas evolution, 1 mole of the alkyl glycidyl ether was added gradually to the above CO carbonyl solution at a temperature between 25–30°C over a period of a few hours. The reaction was exothermic, and the color of the reaction mixture changed to pink, then to dark brown, and finally to dark violet. After removal of the alcohol, distillation of the reaction mixture gave the intended 1-alkoxy-2-propanone at a good yield.

1-Alkoxy-2-propanone was used for the preparation of destructible surfactants that contained a 1,3-dioxolane ring. Subsequent amination and quaternization of such destructible surfactants gave cationic surfactants, which catalyzed the reaction of 1-bromooctane with sodium iodide. Catalysis by these surfactants was superior to that by conventional quaternary ammonium salts (27).

RESULTS AND DISCUSSION

The alkyl glycidyl ether can now be readily prepared at an industrial scale from the reaction of the alcohol with epihalohydrin by the PTC Williamson ether synthesis by using quite inexpensive quaternery ammonium salts under mild conditions (room temperature to 40°C).

The ring-opening reaction of the glycidyl ether with nonpolar carbonyl compounds or acid anhydrides by acidic or alkaline catalysts led to the preparation of 1-*O*-alkyl-2,3-di-*O*-substituted glyceryl ether derivatives, which gave industrially useful 1-*O*-alkyl glyceryl ethers by hydrolysis at high yields both, inexpensively and at high levels of purity.

Another type of epoxy ring opening of the alkyl glycidyl ether occurred regioselectively in the presence of alkaline catalysts to obtain the regioisomerically pure 1,3-disubstituted glyceryl ether that contained a free hydroxy group in the 2-position of the glycerin skeleton.

The modification of the free hydroxy group of 1,3-disubstituted glyceryl ether led to the preparation of various multifunctionalized C3-building blocks that contained selectively functionalized alkyl glyceryl ethers, which were cosmetically, pharmacologically and industrially interesting.

Analogous regioisomerically pure monoacyl- and diacylglycerides that contained free hydroxy group were also investigated concerning their usefulness as synthetic building blocks and led to various kinds of surfactants and pharmacologically active compounds (28). The alkyl glycidyl ethers, as glycerin derivatives, thus present many possibilities for future developments in glycerin chemistry.

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