An efficient synthesis of glyceryl ethers: catalyst-free hydrolysis of glycidyl ethers in water media

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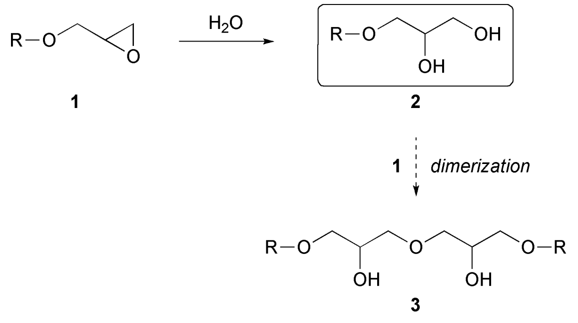
Hydrolysis of hydrophobic glycidyl ethers in pressurized water media afforded the corresponding glyceryl ethers in good to excellent selectivity within several minutes without catalyst.

Glyceryl ether and its derivatives are well known as a group of ether lipids and are of great interest due to their pharmaceutical and physical properties.[1] In particular, alkyl glyceryl ethers are utilized as nonionic surfactants and have been widely applied to cosmetics, personal care and household products.[2] In general, alkyl glyceryl ethers are obtained from corresponding alkyl glycidyl ethers, and various synthetic methods have been proposed.[3] For example, Urata *et al.* reported that alkyl glycidyl ethers were converted into corresponding dioxolanes or 1-*O*-alkyl-2,3-di-*O*-acetylglycerols and subsequent hydrolysis was carried out to provide alkyl glyceryl ethers in high yield and high selectivity.[4] Although these methods were useful, it was necessary to make great efforts for purification and a lot of waste materials were generated for industrial production. To solve such problems, direct hydrolysis of glycidyl ethers with water molecules has been suggested (Scheme 1).[5] However, a dimerization reaction occurred preferentially because of the low solubility of glycidyl ethers in water. Therefore, a decrease in yield and selectivity of glyceryl ethers often resulted without appropriate organic solvents.



Scheme 1

Table 1 Hydrolysis of glycidyl ethers under hydrothermal conditions[a]

Entry	Substrate	Water/**1** (mol/mol)	Reaction time/min	Conversion (% of **1**[b])	Selectivity (% of **2**[b])
1	**1a**	2	120	>99	66
2		8	10	>99	89
3		20	5	>99	95
4	**1b**	2	540	>99	70
5		6	140	>99	82
6		20	120	>99	91

[a] All reactions were carried out at 200 °C, 1.5 MPa. [b] Determined by GC analysis.

Recently, Jamison's group revealed that the cascade epoxide-opening reaction was promoted by hot water to obtain polyether marine natural products selectively.[6] Furthermore, Qu *et al.* reported that hydrolysis of epoxides and aziridines proceeded in hot water, and they proposed hot water acted as a moderate acid catalyst, reactant and solvent.[7] These results suggested that epoxy compounds were able to be hydrolyzed in several hours by the use of a large excess of water. In this paper, we report our experiments on the direct hydrolysis of glycidyl ethers in pressurized water media at high temperature. By adopting this method, hydrophobic glycidyl ethers were able to be converted selectively into corresponding glyceryl ethers without catalyst within several minutes.

Our initial examination was focused on the possibility of selective hydrolysis of glycidyl ethers **1** under hydrothermal conditions. Different equivalents of water were added to an autoclave reactor with butyl glycidyl ether **1a** (R = butyl) as a representative substrate. Although **1a** was completely consumed in 120 min with 2 molar equivalents of water (200 °C, 1.5 MPa), butyl glyceryl ether **2a** was obtained in only 66% selectivity (entry 1 in Table 1) and the dimerization product **3a** was formed as the main by-product. The excessive amount of water played an important role in hydrolysis of glycidyl ethers both in reactivity and selectivity. With 8 and 20 molar equivalents of water, the reaction proceeded immediately within 10 min to give **2a** in 89 and 95% selectivity, respectively (entries 2 and 3). Subsequently, we carried out the reactions with the more hydrophobic substrate **1b** (R = 2-ethylhexyl). In contrast to previous examinations, the consumption of **1b** was sluggish and **2b** was obtained in 91% selectivity after 120 min at 200 °C, even if 20 molar equivalents of water were applied to the reaction (entry 6).

To accomplish further improvement of reactivity and selectivity, we next examined the influence of reaction temperature against hydrolysis of **1b**. For this purpose, we designed a

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Table 2 Hydrolysis of glycidyl ethers with tubular reactor [a]

Entry	Substrate	R	Water/**1** (mol/mol)	Temp/ °C	Pressure/MPa	Residence time/min	Conversion (% of **1**[b])	Selectivity (% of **2**[b])
7	**1b**	2-ethylhexyl	10	250	5.0	7.2	88	92
8			40	250	5.0	5.2	>99	96
9			80	250	5.0	3.9	>99	98
10[c]	**1c**	isodecyl (isomer mixture)	100	250	5.0	1.3	41	>99
11[c]			100	270	6.5	1.3	83	>99
12[c]			100	270	6.5	2.5	>99	>99
13	**1d**	hexyl	80	250	5.0	4.0	>99	98
14	**1e**	3,5,5-trimethylhexyl	80	250	5.0	4.0	98	90
15	**1f**	phenyl	80	250	5.0	4.0	>99	99

[a] Reaction tube: 1 mm i.d., 1700 mm. [b] Determined by GC analysis. [c] These reactions were carried out with 1 mm i.d., 10 000 mm tube.

tubular reactor system equipped with plunger pumps and a back pressure regulating valve (Fig. 1).† The substrate and water were injected to the reaction coil respectively and heated at a certain temperature. The molar ratio of water and **1b** was set to 10/1 by adjusting the flowing quantity of each pump. The pressure was set, using the back-pressure regulating valve, to be higher than the saturated aqueous vapor pressure at that temperature. Fig. 2 illustrates the rate of consumption of glycidyl ether **1b** at various reaction temperatures. At 230 °C, the consumption of **1b** was still sluggish. However, the reaction was accelerated tremendously with an increase in temperature and the conversion of **1b** was up to 99% within 10 min at 250 °C or more. And we have found that the selectivity of **2b** could be improved by increasing the amount of water (entries 7–9, in Table 2). The more hydrophobic substrate **1c** (R = isodecyl, isomer mixture) was hydrolyzed selectively within 3 minutes, although a high reaction temperature was required (entries 10–12). In addition, we attempted hydrolysis of other aliphatic and aromatic glycidyl ethers, and corresponding glyceryl ethers were obtained efficiently and selectively (entries 13–15).

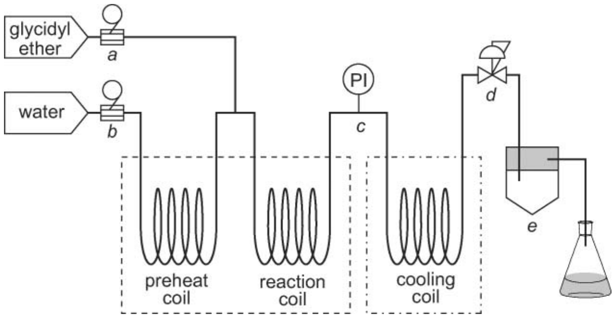

Fig. 1 Schematic diagram of flow reaction system for hydrolysis of glycidyl ethers. (*a*, *b*: plunger pumps, *c*: pressure indicator, *d*: back pressure regulating valve, *e*: water/oil separator).

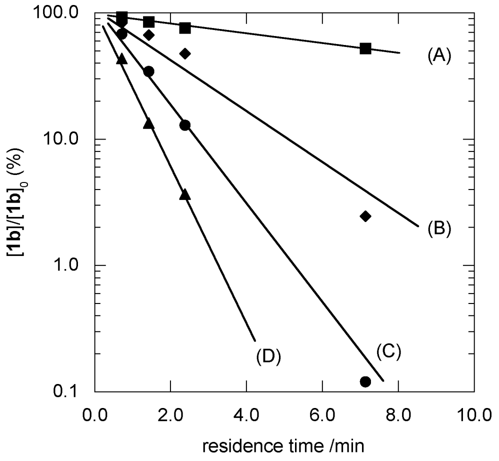

Fig. 2 Consumption rate of **1b** at various temperatures. All reactions were carried out with 10 molar equivalents of water. (A) 230 °C, (B) 250 °C, (C) 270 °C, (D) 285 °C.

According to our experimental results, the hydrolysis reaction of glycidyl ethers did not require any catalysts and the selective addition of water molecule was observed in pressurized water media at high temperature within several minutes. Water under these conditions is called subcritical water and has been widely used for extraction of valuable materials from biomass,[8] for oxidative degradation of hazardous materials[9] and for hydrolysis of triglycerides.[10] However, applications of subcritical water for selective organic synthesis seems to be limited.[11]

Since the critical point of water is 374 °C and 22.1 MPa, there is a wide range of temperatures and pressures between ambient and supercritical water conditions. Water in the subcritical region has unique characteristics, such as dramatically decreased dielectric constant (permittivity) and surface tension with increasing temperature under moderate pressures.[12] For instance, the dielectric constant of water at 250 °C is equal to that of methanol at ambient temperature. Therefore, the solubility of nonpolar organic compounds in water is greatly enhanced with increasing temperature. In the hydrolysis of glycidyl ethers, it is conceivable that the improvement of selectivity and reactivity was able to be achieved owing to the enhancement of the solubility of glycidyl ethers by tuning of temperature and water ratio.

Thus, we have found that glyceryl ethers can be prepared selectively by the direct hydrolysis of corresponding glycidyl ethers in pressurized water media at high temperature. In the case of using glycidyl ethers having middle-to-long alkyl chain as substrates, the products and water were easily separated after cooling to ambient temperature at atmospheric pressure. Since this reaction requires no catalysts and solvents, no impurities (except for those originating from the raw materials) are present in the separated water. Therefore, it is possible to reuse the collected excessive water by a simple separation process. By adopting a water recycling system, we achieved 90% water recovery and confirmed the hydrolysis reaction was continuously executable.

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Notes and references

† The flow reaction system (Fig. 1); deionized water was introduced into the preheated coil from a plunger pump and heated with oil bath. The preheated water from the coil went through a T-connector and the glycidyl ether was introduced at this connector from another plunger pump. The water–glycidyl ether mixture then passed through the reaction coil (1 mm i.d., 1700 mm). At the end of the reaction tube, the overall reaction pressure was checked with an indicator. After passing the cooling coil, the reaction mixture was introduced into a water–oil separator through a back pressure regulating valve. For a typical reaction (Table 2, entry 9), the oil bath was set to a temperature at 250 °C, the water pump was then set to a constant flow of 300 μL min^{-1}, and then water flow was commenced as the oil bath was heated. The back pressure regulator was set for an overall system pressure of 5.0 MPa and the cooling bath was operated at 80 °C. The pump for 2-ethylhexyl glycidyl ether **1b** was set to a constant flow of 43.1 μL min^{-1} (the molar ratio of water/**1b** became 80/1) and introduced into the system. After hydrolysis, the water/oil stream was cooled and depressurized, and collected in a water–oil separator. 2-Ethylhexyl glyceryl ether **2b** was obtained from oil phase.

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