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Acid-Catalyzed Etherification of Glycerol with Long-Alkyl-Chain Alcohols

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Surfactants are of great interest to the chemical industry owing to their numerous applications. In 2003 the worldwide production volume was estimated at 12 million tonnes, making surfactants one of organic chemistry's most important markets. The synthesis of biobased surfactants has emerged as a challenging task mainly boosted by the predicted exhaustion of fossil carbon reserves and growing concerns about global warming. In this context, the rational design of catalytic processes for the direct and selective etherification of glycerol (a co-product of the vegetable oil industry) with long-alkyl-chain alcohols is the subject of numerous investigations because the resulting amphiphilic alkylglycerylethers (1) exhibit a greater stability than the corresponding monoglycerides in the presence of water, and (2) can be used as green solvents for catalysis.[1]

To date, the catalytic etherification of glycerol has been achieved starting from activated alcohols (e.g., tertiobutanol[2] or benzyl alcohol[3]) catalyzed over different solid acids (e.g., cation exchange resins, zeolites, or sulfonated silica). In all of these processes the corresponding glycerol ethers have been produced in fair to good yields, but unfortunately they are inefficient when starting from a fatty alcohol such as 1-dodecanol.[3a] Indeed, the catalytic etherification of glycerol with less-activated alcohols, such as aliphatic alcohols, is thermodynamically much more difficult. Fajula and co-workers reported the catalytic etherification of glycerol with ethanol over various solid acid catalysts in 2009.[4] A maximum yield of 40% of monoethoxy glyceryl ethers was obtained at 433 K by using sulfonated polystyrene resins and zeolites with a Si/Al ratio of ca. 25. Although this work was a significant step towards new catalytic routes for the selective etherification of glycerol with aliphatic alcohols, it was hampered by the formation of very large amounts of diethylether. In the same year Weckhuysen and co-workers investigated the acid-catalyzed etherification of various polyols, including glycerol, with fatty alkenes such as 1-octene and 1-dodecene.[5] Although good yields were obtained from propylene glycol and ethylene glycol, very low yields were obtained when starting from 1-octene and glycerol ($<10\%$). In addition, there was no reaction between glycerol and 1-dodecene, showing that the etherification of glycerol with a long alkyl chain is a very difficult task.

So far the only catalytic route allowing the successful synthesis of monododecyl glyceryl ethers was reported by Lemaire and co-workers, who investigated the reductive etherification of glycerol with long-alkyl-chain aldehydes under hydrogen.[6] Although a 75% yield of monododecyl glyceryl ethers was obtained in the presence of Pd/C as catalyst and camphorsulfonic acid as a co-catalyst, the process is limited by the price and the availability of decylaldehyde. The direct catalytic etherification of glycerol with long-alkyl-chain alcohols would be much more economical and environmentally friendly. So far, all attempts to catalytically etherify glycerol with long-alkyl-chain alcohols reported in the literature have failed.

To achieve the successful coupling of glycerol with fatty alcohols several issues need to be addressed: (1) The large difference in polarity between glycerol and fatty alcohols renders the reaction medium biphasic. Therefore, the catalyst has to be active at the glycerol/fatty alcohol interface in order to overcome mass-transfer limitations. (2) The formation of unsymmetrical ethers is thermodynamically unfavorable. (3) The very high reactivity of glycerol (owing to the presence of a secondary hydroxyl group) in acidic conditions may lead to the formation of a wide range of undesired products, especially in a biphasic system where the contact with fatty alcohol is expected to be poor.

Herein, we investigate the catalytic activity of various homogeneous and heterogeneous catalysts towards the etherification of glycerol with long-alkyl-chain alcohols. Under optimized conditions dodecylbenzene sulfonic acid, a so-called surfactant-combined-catalyst, allowed a better contact between the glycerol and fatty alcohol phases, resulting in a significant improvement of the yield of monododecyl glyceryl ethers. To the best of our knowledge, this is the first successful example of the direct etherification of glycerol with fatty alcohols, opening a new route for the synthesis of biobased surfactants.

In a first set of experiments an equimolar mixture of glycerol (99% purity) and 1-dodecanol was heated at 130 °C for 24 h in the presence of 10 wt% Amberlyst 70 (A70, corresponding to 1.1 mol% H^+). During the reaction water was continuously removed by distillation. Amberlyst 70 was chosen as a reference solid acid catalyst because of its strong acidity, high thermal stability (up to 190 °C), and high proton exchange capacity ($2.5\ \mathrm{mmol\,g^{-1}}$). The results are summarized in Table 1. Under these standard conditions, only glycerol was converted (57%, entry 1) while 1-dodecanol did not react. Glycerol was only converted to di- (20% yield, mixture of isomers) and triglycerol (5% yield, mixture of isomers) and the carbon mass balance (69%) also clearly showed the conversion of glycerol to unidentified products (presumably acrolein and soluble polymers). An increase of (1) the glycerol/1-dodecanol molar ratio

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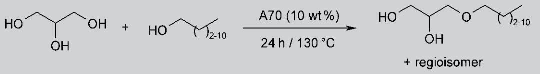
Table 1. Catalytic etherification of glycerol with 1-dodecanol over A70



Entry	Alcohol	Glycerol/alcohol molar ratio	Total glycerol conv. [%]	Alcohol conv. [%]	Monoethers yield [%]	Diglycerol yield [%]	Triglycerol yield [%]	Glycerol carbon mass balance [%]	Alkyl alcohol carbon mass balance [%]
1	1-dodecanol	1	57	0	0	20	5	69	100
2	1-dodecanol	4	36	5	5	22	3	90	100
3[b]	1-dodecanol	4	78	7	7	22	9	64[c]	100
4[d]	1-dodecanol	4	96	10	10	5	4	43[c]	100
5	1-butanol	4	17	26	26	4	0	94	100
6	1-pentanol	4	13	22	22	4	0	96	100
7[e]	1-pentanol	4	36	66	45	12	0	91	79
8	1-hexanol	4	11	13	13	4	0	100	100
9	1-octanol	4	36	5	5	6	0	100	100

[a] Glycerol and 1-dodecanol were heated at 130 °C for 24 h in the presence of 10 wt% A70. Conversions and yields were determined by gas chromatography using dodecane as internal standard. [b] Reaction performed at 145 °C. [c] Tetra-, penta- and hexaglycerol were also detected as minor products. Insoluble black materials were also produced in a larger extent. [d] Reaction performed at 160 °C. [e] Results collected after 96 h.

from 1 to 4 (entry 2), and/or (2) the reaction temperature from 130 °C to 145°C and 160 °C only resulted in the formation of monododecyl glyceryl ethers in very low yields (entries 3 and 4. When increasing the reaction temperature the carbon mass balance was lowered and an insoluble black material was formed. These results confirm that the etherification of glycerol with 1-dodecanol is a highly complex reaction and that, in a biphasic glycerol/1-dodecanol system, the A70 solid catalyst interacts only with glycerol.

To find a suitable method for the catalytic etherification of glycerol with long-alkyl chain alcohols, we next investigated the influence of the chain length on the yield of monoalkyl glyceryl ethers (Figure 1). Mixtures of glycerol with either 1-butanol, 1-pentanol, 1-hexanol, 1-octanol, or 1-dodecanol (molar ratio 4:1) were heated at 130 °C for 24 h in the presence of 10 wt% A70. The reaction medium was monophasic in the cases of butanol and pentanol, and as expected corresponding monobutyl glyceryl and monopentyl glyceryl ethers were obtained in yields of 26% and 22% (Table 1, entries 5 and 6). Diglycerol was produced as minor side product, in 4% yield. After 96 h, monopentyl glyceryl ethers were obtained with an unprecedented maximum yield of 45% (entry 7). Unfortunately the yield of monopentyl glyceryl ether dropped with prolonged reaction time due to (1) subsequent etherification to dipentyl glyceryl ethers, and (2) oligomerization of monopentyl glyceryl ethers.

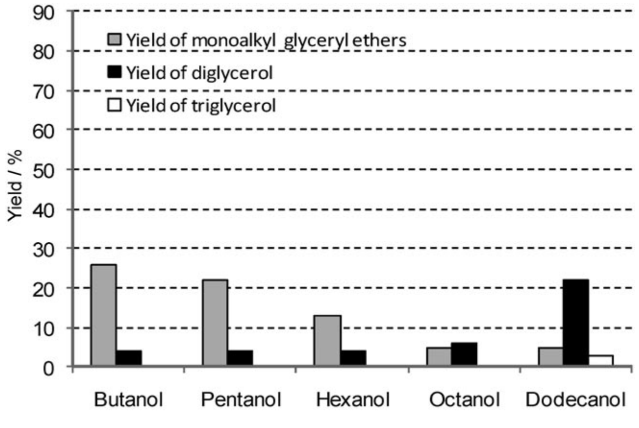


Figure 1. Catalytic etherification of glycerol with various alkyl alcohols over A70 (10 wt%). Results are given after 24 h of reaction at 130 °C and using a glycerol/alkyl alcohol molar ratio of 4.

When starting from 1-hexanol the reaction medium became turbid. The conversion rate of 1-hexanol was two times lower than that of 1-butanol and 1-pentanol (Figure 1). After 24 h, 13% 1-hexanol was consumed compared to 25% when starting from 1-butanol and 1-pentanol, indicating that the catalyst activity dropped significantly with an increase of the alkyl alcohol chain length (Table 1, entry 8). The yield of monoalkyl glyceryl ethers was also lowered: after 24 h a monohexyl glyceryl ethers yield of 13% was achieved, showing that contact between the glycerol and 1-hexanol phases become more difficult. However, the yield of diglycerol still remained low (4%). The reaction medium was biphasic when starting from 1-octanol and 1-dodecanol. Conversion of the alkyl alcohol was very low while the glycerol conversion was increased (Table 1, entries 2 and 9). Indeed, after 24 h the conversion of 1-octanol and 1-dodecanol and the yield to the corresponding monoalkyl glyceryl ethers remained below 5% while di- and triglycerol were produced in higher yields (22% yield for 1-dodecanol). Clearly, in a biphasic system the A70 catalyst interacts more strongly with the glycerol phase than with the alkyl alcohol phase, at the expense of the yield of monoalkyl glyceryl ethers. Notably, no monoalkyl glyceryl ethers were formed when using other well-known solid acid catalysts such as a sulfonated mesoporous silica (SBA-SO_3H), K-10 montmorillonite, and H-ZSM-5 zeolite (Si/Al ratio = 1000), or homogeneous acid catalysts such as *para*-toluene sulfonic acid (*p*TSA) and triflic acid, further demonstrating the complexity of this reaction (see Supporting Information Table S1).

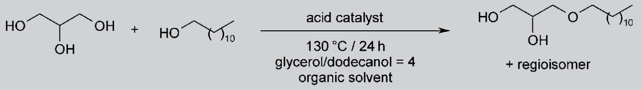
On the basis of this study one may conclude that monoalkyl glyceryl ethers can be selectively produced over A70 from glycerol and alkyl alcohols with a chain length shorter than six carbon atoms. Contrary to what was observed by Fajula and co-workers when using ethanol,[4] the starting alkyl alcohols in this work were selectively converted to the corresponding monoalkyl glyceryl ethers while dialkyl ethers where not formed, facilitating the isolation of the corresponding monoglyceryl alkyl ethers. This result stems from (1) dilution of the alkyl alcohol in the glycerol phase (in the case of monophasic system), and (2) the high affinity of the A70 resin for the glycerol phase.

To overcome mass transfer problems particular attention has to be paid to the design of the catalyst. Ideally, a catalyst would have to exhibit some sulfonic sites and also be able to operate at the glycerol/1-dodecanol interface. Kobayashi and co-workers have extensively studied the performances of dodecylbenzene sulfonic acid (DBSA) for catalysis in a biphasic water/oil mixture.[7] A recent Review related to micellar catalysis in organic reactions is available.[8] In these works, DBSA acts not only as acid catalyst but also as emulsifier. We have recently reported that these surfactant-combined-catalysts can be successfully employed when using glycerol, opening a new strategy for our purpose.[9] Hence, we investigated the etherification of glycerol with 1-dodecanol at 130 °C in the presence of DBSA. Using 2 mol% of DBSA, the reaction medium was still biphasic. DBSA strongly interacts with the 1-dodecanol phase in these conditions, leading to a significant enhancement of the 1-dodecanol conversion, to 72% (Table 2, entry 1). On the other hand, the glycerol conversion was lowered (26%). Importantly, compared to other acid catalysts tested the higher affinity of DBSA for the 1-dodecanol phase unavoidably induces the formation of didodecyl ether (62% yield). Nevertheless, utilization of this Brønsted-acid surfactant-combined-catalyst contributed to increase the monododecyl glyceryl ethers up to 10%.

To further improve the contact between the glycerol and 1-dodecanol phases, we increased the amount of DBSA until a monophasic system was obtained. Up to 20 mol% of DBSA was necessary to observe a monophasic system (Table 2, entry 2). This relatively large amount of DBSA is consistent with existing literature related to catalysis in biphasic water/oil mixtures. Interestingly, the formation of monododecyl glyceryl ethers was favored when using 20 mol% of DBSA: a yield of 25% was achieved within 3 h. The emulsification of the reaction medium also resulted in a decrease of the production of side product (di-dodecylether), from 62% to 19%. As mentioned above, the monododecyl glyceryl ethers yields dropped with prolonged reaction time due to oligomerization and/or subsequent etherification with 1-dodecanol. This also applies to 1-octanol, as in the presence of 20 mol% of DBSA the corresponding monooctyl glyceryl ethers were isolated with a maximum yield of 24% yield (compared to 5% over A70), offering the first route for the etherification of glycerol with long-alkyl-chain alcohols.[10]

Even though DBSA is a very cheap acid catalyst, the utilization of 20 mol% of DBSA is a drawback. Therefore, with the aim of decreasing the catalytic amount of DBSA to at most 10 mol%, while maintaining good interaction between the glycerol and 1-dodecanol phases we studied the possible use of an organic solvent. The choice of the organic solvent was limited because the solvent should be able to dissolve glycerol as well 1-dodecanol in reasonable amounts. We focused on the use of dimethylsulfoxide (DMSO), diglyme, 1,4-dioxane, and sulfolane. Unless noted otherwise all reactions were performed in an autoclave (autogeneous pressure) at 130 °C starting from a glycerol/1-dodecanol molar ratio of 4, in the presence of 10 mol% of H^+ and stopped after 24 h. To highlight the effect of DBSA on the catalytic etherification of glycerol with 1-dodecanol, we first used A70 as a reference acid catalyst. In DMSO, diglyme, and 1,4-dioxane, 1-dodecanol mostly remained unaltered and only glycerol was converted (20%, 65%, and 73%, respectively; Table 2, entries 4–6). Surprisingly, neither di- nor triglycerol were detected in DMSO and diglyme, and glycerol was only converted to unidentified products. In 1,4-dioxane, the formation of about 10% diglycerol was detected (entry 6). The reaction was very slow in sulfolane: 60 h were necessary (versus 24 h without organic solvent) for a glycerol conversion of 38% (entry 7). This may be attributed to dilution of the reaction medium. However, the reaction selectivity was higher since the corresponding monododecyl glyceryl ethers were produced with 10% yield. Notably, the yield of di-dodecylether remained lower than 10%, indicating that in sulfolane the A70 catalyst still reacts with difficulty with 1-dodecanol. When the reaction temperature was raised from 130 °C to 160 °C in sulfolane, the contact between glycerol and 1-dodecanol was improved and the yield of monododecyl glyceryl ethers increased

Table 2. Catalytic etherification of glycerol with 1-dodecanol in the presence of an organic solvent



Entry	Catalyst	Solvent	Glycerol conv. [%]	Dodecanol conv. [%]	Monoether yield [%]	Diglycerol yield [%]	Didodecylether yield [%]
1	DBSA	–	26	72	10	9	62
2	DBSA[c]	–	59	50	25	9	19
3	A70	–	36	5	5	22	0
4	A70	DMSO	20	0	0	0	0
5	A70	diglyme	65	0	0	0	0
6	A70	1,4-dioxane	73	<10	0	10	0
7	A70[b]	sulfolane	38	17	10	11	7
8	A70[c]	Sulfolane	78	28	20	11	8
9	DBSA	sulfolane	72	68	30	14	38

[a] Conversions and yields were determined by gas chromatography using dodecane as internal standard, 0.1 equiv of H^+ was used for catalytic experiments. [b] Results collected after 60 h of stirring at 130 °C. [c] Reaction performed at 160 °C.

from 10% to 20%, while the formation of diglycerol side product remained similar (11%; entries 7–8). However, at 160 °C the carbon mass balance on glycerol is low (40%, see Table 1), indicating the formation of unidentified glycerol-based products. Inspired by the results described above, we investigated the possible use of DBSA in sulfolane. As expected the reaction rate was higher in the presence of DBSA; mostly 70% conversion of glycerol and 1-dodecanol was observed after 24 h (compared to 38% conversion of glycerol after 60 h of reaction over A70; entry 9). Interestingly the use of DBSA increased the yield of monododecyl glyceryl ethers to an unprecedented 30%, further demonstrating the great potential of surfactant-combined-catalyst for the catalytic etherification of glycerol with 1-dodecanol.

In conclusion, we show that over A70 aliphatic alcohols with a chain length shorter than six carbon atoms are selectively converted into the corresponding monoalkyl glyceryl ethers with maximum yields of 45%. When starting from 1-octanol and 1-dodecanol the reaction medium becomes biphasic, inducing mass transfer problems. A surfactant combined-catalyst, DBSA, allows emulsification of the reaction medium, resulting in the formation of monododecyl glyceryl ethers with 30% yield. This work is the first successful example of direct etherification of glycerol with long-chain alcohols such as 1-octanol and 1-dodecanol, thus providing a new and straightforward route for the design of biobased surfactants.

Experimental Section

In a typical procedure, glycerol (21 mmol) and the corresponding alcohols (5.3 mmol) were mixed together and heated for 24 h at 130 °C in the presence of the desired acid catalysts (0.1 equiv H^+). During the reaction water was continuously removed by distillation. The reaction progress was monitored by gas chromatography. Prior to analysis, the sample was silylated as follows: to the sample (30 mg) was added 410 μL of pyridine, 210 μL of hexamethyldisilazane, and 110 μL of trimethylchlorosilane, and the resulting mixture was stirred at room temperature for 10 min. Then, the solution was filtered in order to remove the pyridinium salts before injection.

At the end of the reaction, the crude was directly purified over silica gel using heptane/ethylacetate (70:30) as eluent. As an alternative, products of the reaction could also be first extracted from the glycerol phase by addition of ethyl acetate prior to purification over silica gel. In the case of DBSA, dilution of the reaction medium in ethanol followed by a treatment with a A26 resin was necessary prior to purification over silica gel. This procedure removes the DBSA, which hinders the isolation of the monododecylglyceryl ethers over silica gel.

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Keywords: catalysis · etherification · fatty alcohols · glycerol · renewable resources

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[10] Data on 1-octanol are not reported in Table 2 because of overlapping peaks in the gas chromatogram. We prefer to provide the isolated yields of monooctyl glyceryl ethers. See the Experimental Section for more information on the purification of the glyceryl ethers.

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