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A Reactive Distillation Process To Produce 5-Hydroxy-2-methyl-1,3-dioxane from Mixed Glycerol Acetal Isomers

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Supporting Information

ABSTRACT: The four cyclic glycerol acetal isomers can be readily produced via the acid-catalyzed reaction of glycerol with acetaldehyde or a related acetal species. In the presence of the acid catalyst used in acetal formation, the isomers interconvert to form an equilibrated mixture that contains similar quantities of the four products. Vacuum distillation can separate the four acetals into their purified forms, with the *cis*-5-hydroxy-2-methyl-1,3-dioxane (**1**) as the most volatile. When the distillation is carried out in the presence of an acid catalyst to promote interconversion, **1** is obtained as a nearly pure distillate stream. This is further adapted to a continuous reactive distillation which produced 90−96% **1**. Thus a novel process is presented to convert glycerol to the desired acetal (**1**), which can be further converted to products such as 1,3-propanediol and dihydroxyacetone.

INTRODUCTION

The global rise in biodiesel production has led to the availability of low-cost byproduct glycerol (formed in ∼10 wt % yield from biodiesel).[1] An innovative approach to utilizing glycerol is to transform it into cyclic glycerol acetals (GA) or ketals via reaction with aldehydes or ketones. These acetals and ketals have proven to be effective fuel additives.[2−5] In a 2008 patent, Miller et al.[6] proposed a continuous process to synthesize these compounds along with the formation of biodiesel to obtain a composition useful as a fuel. In addition, acetals and ketals can be used as surfactants[7] and can serve as intermediates for the production of value-added chemicals from glycerol.[8]

Two synthesis routes have been examined to make acetal products from glycerol: direct condensation of glycerol with aldehydes or ketones,[8−12] or the replacement of the alcohol functionality in an existing acetal with glycerol (transacetalization).[8,13] The acetal or ketal products formed via either pathway are 2-substituted-5-hydroxy-1,3-dioxane and 2-substituted-4-hydroxymethyl-1,3-dioxolane compounds, which when formed from asymmetric ketones or aldehydes are produced as both cis- and trans-conformational isomers for a total of four products.

The six-membered dioxane isomers are of particular interest because they are precursors for the production of valuable chemicals such as 1,3-dihydroxyacetone and 1,3-propanediol.[8] If desired, a five-membered dioxolane compound (2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane) can be synthesized with high selectivity (>99%) by reacting acetone with glycerol;[8,9] this selectivity to the five-membered dioxolane is unique to acetone. On the other hand, with other acetal forming reagents, the dioxane compounds are always produced along with their five-membered dioxolane counterparts in quantities determined by the equilibrium constants of the interconversion isomerization reactions. Although lab-scale separation of the isomers was carried out in the 1960s using gas chromatography,[14] large scale production of pure acetal isomers is still a challenge.

In this paper, the synthesis of cyclic GA isomers via glycerol transacetalization with 1,1-diethoxyethane (DEE), a surrogate for acetaldehyde, using Amberlyst-15 cationic exchange resin as the catalyst is described (Scheme 1). The equilibrium composition of the GA isomer mixture formed in transacetalization is characterized, and the use of reactive distillation to produce the pure dioxane isomer **1** is presented. These findings lay the groundwork for a process to make isomer **1** as the sole product of glycerol condensation with acetaldehyde or DEE.

EXPERIMENTAL SECTION

General. Amberlyst-15 cationic exchange resin (16−50 mesh, Sigma-Aldrich), used as the catalyst, was pretreated at 90 °C in a vacuum oven for 2 h prior to use.

GC Analysis. 1-Butanol and 1-propanol were used as the internal standard and solvent, respectively, for the analysis. To prepare samples, 0.16 mL of *n*-butanol and 0.2 mL of reaction sample were added to a 10 mL volumetric flask and the flask was filled with 1-propanol and mixed to form the injected sample. The analysis was carried out on a Perkin-Elmer Sigma 2000 gas chromatograph equipped with a flame ionization detector. A DB-Wax capillary column (15 m × 0.53 mm ×1.0 μm) with on-column injection was used for analysis with the following temperature program: hold at 40 °C for 3 min, ramp to 220 at 30 °C/min, and hold for 1 min. Ultrahigh purity helium was used as the carrier gas at a flow rate of 30 mL/min. Injector and detector chamber temperatures were set at 60 and 300 °C, respectively.

Gas Chromatographic−Mass Spectroscopic Analysis. Structures of the reaction products were identified using gas chromatography−mass spectroscopy. A 1 μL sample was separated in a DB-wax capillary column with a temperature program similar to that described above; electron impact (EI) mass spectra were monitored from 20 to 300 m/z. The MS source was set at 230 °C.

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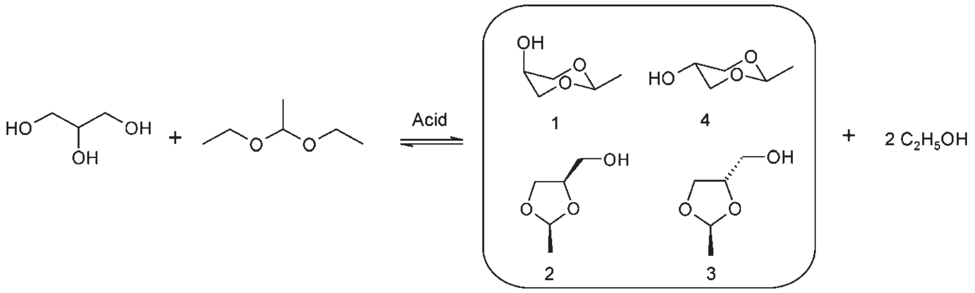
Scheme 1. Formation of cyclic glycerol acetals via transacetalization with DEE



Synthesis of GA Isomers. Cyclic GA isomers were synthesized at 45 °C by mixing glycerol (3.1 kg, 33.9 mol), DEE (4.0 kg, 33.9 mol), and Amberlyst-15 cationic exchange resin (120 g) and stirring for 4 h. 1,1-Diethoxyethane was used instead of acetaldehyde because it is less volatile and less toxic, and is thus more easily handled in the laboratory. After reaction, the mixture was filtered to eliminate the catalyst and then concentrated in a rotary evaporator at 70 °C under a pressure of 25 mmHg to remove unreacted DEE, product ethanol, and any volatile byproducts or impurities. No GA isomer was removed from the mixture under these conditions. The final product obtained contained the four GA isomers and only trace amounts (less than 1 wt % total) of unreacted glycerol and byproducts.

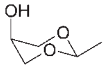
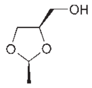
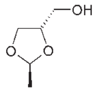
Distillation of GA Isomers. A glass batch vacuum distillation column was constructed to separate the four GA isomers. The column (height = 3.6 m, i.d. = 50 mm) was packed with 0.6 cm 316 Stainless Steel PRO-PAK distillation packing (Scientific Development Co.). The column reboiler, consisting of a 2-L round-bottom flask, was heated with a 750 W electric heating mantle. Vapor temperature was measured at the top of the column.

Three vacuum distillation experiments using various conditions were carried out in this study. To initiate each experiment, a measured quantity of GA isomers and boiling chips were placed in the reboiler. The column was then evacuated to the desired pressure, and the reboiler contents were heated slowly (2 to 3 °C/min initially) to generate GA vapor. When steady state was achieved throughout the column at total reflux (as indicated by steady temperatures in the reboiler and throughout the column), the top product was withdrawn slowly by controlling the power to the reboiler.

In the first distillation, 896 g (800 mL) of a GA mixture containing 35% GA isomer **1**, 18% **2**, 15% **3**, and 32% **4** were placed in the reboiler. To avoid isomer interconversion, the solution was maintained at a weakly basic state by adding 50 g of sodium carbonate to the mixture. This initial distillation was carried out at a pressure of 20.5 ± 1.0 mmHg (except for Sample 1, where the pressure was temporarily reduced to 9.0 mmHg). Twelve 60-mL distillate samples were collected over the course of this distillation; the average distillate rate was maintained at approximately 2 mL/min.

In the second run, 100 g of Amberlyst-15 cationic exchange resin were added to the reboiler pot with 1344 g (1200 mL) of a mixture of 32 wt % GA isomer **1**, 26 wt % **2**, 20 wt % **3**, and 22 wt % **4**. For this batch reactive distillation, the column pressure was maintained at 1.2 ± 0.2 mmHg. During the distillation, 16 distillate samples were collected with an average volume of 50 mL; the average distillate rate was maintained at 1−2 mL/min.

Table 1. Structure and IUPAC name of GA isomers

	Structure	IUPAC Name	Designation
a)		cis-5-hydroxy-2-methyl-1,3-dioxane	**1**
b)		cis-4-hydroxymethyl-2-methyl-1,3-dioxolane	**2**
c)		trans-4-hydroxymethyl-2-methyl-1,3-dioxolane	**3**
d)		trans-5-hydroxy-2-methyl-1,3-dioxane	**4**

The third distillation experiment was carried out by charging 504 g (450 mL) of a mixture of 36 wt % GA isomer **1**, 16 wt % **2**, 14 wt % **3**, and 34 wt % **4** along with 50 g of Amberlyst-15 cationic exchange resin to the reboiler pot of the glass column. For this experiment, the column pressure was maintained at 2.9 ± 0.2 mmHg. Once the distillate product started to condense at the top of the column, a continuous feed of the same GA isomer mixture was introduced to the column reboiler to maintain its liquid level constant. The feed rate was adjusted to match the distillate rate from the column, which was approximately 1.8 mL/min. During the distillation, 16 distillate samples were collected with an average volume of 58 mL.

In all experiments performed in the column, liquid reflux took place via condensation along the column wall; no external reflux was returned to the column from the distillate product stream.

■ RESULTS AND DISCUSSION

GA Synthesis and Analysis. The transacetalization of glycerol with DEE to produce GA isomers produced a combined yield >95% of theoretical. GC-MS analysis of the product mixture showed the presence of four different structures corresponding[12,15] to the four GA isomers (Table 1).

GA Isomerization Equilibrium. In the presence of a concentration of an acid catalyst above a certain threshold,[8,14] the four GA isomers interconvert and reach an equilibrated composition. To demonstrate this equilibration, three samples obtained from the distillation experiments below with widely differing isomer compositions ((**1**) from 0% to 84%, (**2**) from 2% to 54%, (**3**) from 2% to 41%, and (**4**) from 0% to 63%) were stirred for 5 h at 25 °C in the presence of 5 wt % (relative to GA) Amberlyst-15 cationic exchange resin. Identical isomer compositions were observed in the products from the three samples: isomers **1**, **2**, **3**, and **4** were 37 ± 1%, 17 ± 1%, 13 ± 1%, and 33 ± 1%, respectively. The molar percentages of six-membered isomers (**1** + **4**) and five-membered isomers (**2** + **3**) are approximately 70% and 30%, respectively, at equilibrium.

Rapid isomerization requires vigorous agitation (to ensure mass transfer between solid catalyst and solution) and elevated temperature. For example, Sample 1 took 12 h to reach equilibrium at 0 °C but only 1 h at 80 °C. Increasing temperature also shifts the equilibrium composition (see Figure S-1 in the Supporting Information). For Sample 1, increasing temperature from 0 to 80 °C decreased the sum of (cis- + trans-) six-membered isomers (**1** + **4**) from 78% to 54%. However, the total quantity of cis- (**1** + **2**) and trans- (**3** + **4**) isomers remained essentially constant over all temperatures at 55 ± 2% and 45 ± 2%, respectively.

The higher concentration of cis-isomers at equilibrium has been attributed[16] to intramolecular hydrogen bond formation. Isomer **1** is stabilized by a relatively strong intramolecular hydrogen bond, with the corresponding bond of isomer **4** weaker and bonds of isomers **2** and **3** weakest and nearly identical. Therefore, the cis-isomers are slightly favored.

Distillation of GA Isomers. In the first distillation experiment to separate the four GA isomers, 90% of the initial charge to the still pot was recovered in samples that constitute the distillate product (Table 2). The material remaining in the still pot consisted primarily of isomer **4** and trace amounts of glycerol;

Table 2. Summary of GA isomers recovered in the initial distillation

	Initial GA charge		Product recovery in distillate		
Isomer	Mass (g)	Composition (wt %)	Mass (g)	Percent of total	Percent recovered in distillate (%)
1	311	35	288	36	93
2	166	18	152	19	92
3	132	15	120	15	91
4	287	32	246	30	86
Total	896	100	806	100	90

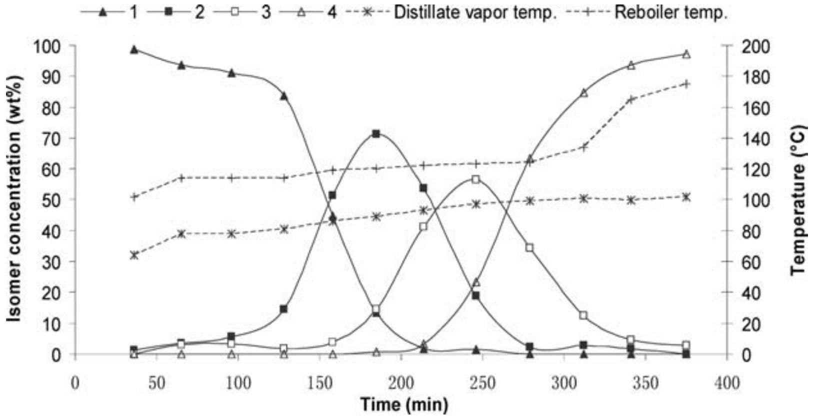


Figure 1. Distillation of GA isomer mixture. Column pressure = 2.5 ± 1.0 mmHg, except for Sample 1, where pressure was temporarily reduced to 9.0 mmHg.

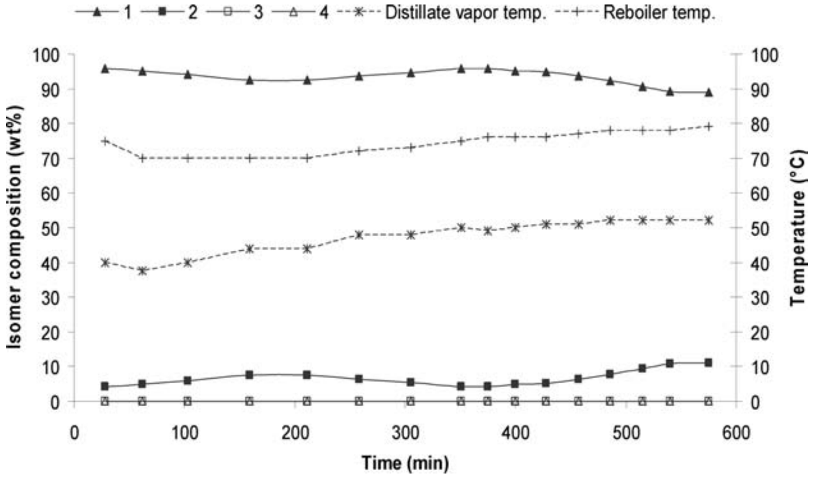


Figure 2. Batch reactive distillation of GA isomers. Column pressure = 1.2 ± 0.2 mmHg.

inclusion of this material gave essentially complete (100 ± 2%) closure of the material balance for the experiment.

Figure 1 gives the reboiler liquid temperature, vapor temperature at the top of the column, and composition (via GC) of the distillate samples taken during the distillation. The results clearly show the order of decreasing volatility of the GA isomers as **1**, **2**, **3**, and finally **4**. As the more volatile isomers are removed from the still pot, liquid and vapor temperature gradually increase.

In this run, the six-membered isomers **1** and **4** separated reasonably well from the five-membered isomers **2** and **3**. As shown, the first three samples collected during the distillation contained high concentrations (>90%) of isomer **1**, with the first one composed of 99% **1**. Likewise, the last two samples contained >90% of isomer **4**, with the final sample composed of 97% **4**. However, the total recovery of six-membered dioxane species (**1** + **4**) as highly concentrated products (> 90 wt %) was 330 g, only 55% of the amount of those isomers initially present. Other samples were mixtures of four isomers.

Batch Reactive Distillation of GA To Produce Isomer 1. In the above distillation of GA isomers, the maximum quantity of six-membered isomers achievable is determined by the feed composition, since no reaction can occur. However, if interconversion of GA isomers is facilitated in combination with distillation, removal of the most volatile isomer **1** from the isomer mixture will result in interconversion toward re-equilibration, thus producing more isomer **1**. As long as the isomer interconversion rate is faster than the distillation rate, the charge in the still pot will approach its equilibrium composition and provide a stable isomer **1** source such that isomer **1** is the sole product recovered in the distillate.

Table 3. Summary of GA isomers recovered in batch reactive distillation

	Initial GA charge		Product recovered in distillate		
Isomer	Mass (g)	Composition (wt %)	Mass (g)	Percent of total	Percent recovered in distillate (%)
1	430	32	836	93	194
2	349	26	59	7	17
3	269	20	0	0	0
4	296	22	0	0	0
Total	1344	100	895	100	67

To demonstrate this, a batch reactive distillation experiment was carried out. As shown in Figure 2 and Table 3, this experiment produced a high concentration of isomer **1** (from 89% to 96%) in all samples; the total quantity of distillate produced (895 g) contained 93 wt % isomer **1**. The other species in the distillate was isomer **2**; no trans-isomers (**3** or **4**) were collected. Two-thirds of the initial charge to the still pot was distilled, suggesting that continuous interconversion of GA isomers and recovery of isomer **1** are possible.

Continuous Reactive Distillation To Produce Isomer 1. A continuous reactive distillation experiment to produce isomer **1** was therefore carried out. This experiment (Figure 3) produced a high concentration of isomer **1** (90%−96%) continuously during operation of the column. The reboiler temperature and distillate vapor temperature were essentially constant during operation, indicating that the reboiler composition was constant and that the column was operating at steady state. The total quantity of distillate obtained was 1028 g, more than twice the amount of the initial charge to the reboiler, demonstrating that continuous production of isomer **1** from the GA acetal mixture is feasible. Based on these results, it is fully expected that an appropriately designed commercial-scale column with sufficient separation capacity would provide essentially pure isomer **1** (Figure 4).

Glycerol and aldehyde or acetal would be introduced to Reactor 1 to produce mixed GA isomers. With DEE or other acetal as the aldehyde/acetal component, reaction with glycerol proceeds to completion and thus a simple stirred tank or packed bed reactor suffices as Reactor 1. With acetaldehyde as the aldehyde, the reaction is thermodynamically limited and Reactor 1 is most advantageously a reactive distillation column. Following Reactor 1, the mixed GA isomers are heated to remove product ethanol, water, and unreacted acetaldehyde. The mixture of GA isomers is then introduced to the reboiler of a continuous reactive distillation column containing an acid catalyst. Isomer **1** would be produced as a continuous distillate stream from the column.

In this process, glycerol and acetaldehyde are inexpensive chemical substances that are readily available. The challenges of using acetaldehyde directly is the formation of water, which must be separated from the acetals, and the fact that the reaction is

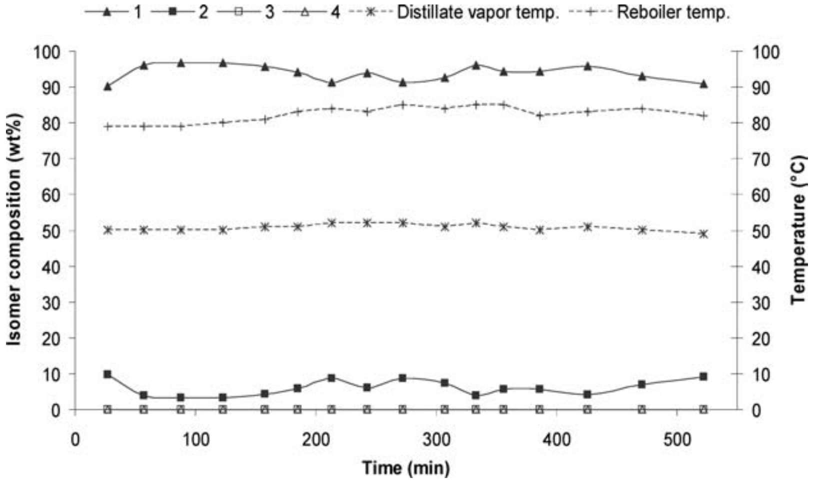


Figure 3. Continuous reactive distillation of GA isomers. Column pressure = 2.9 ± 0.2 mmHg.

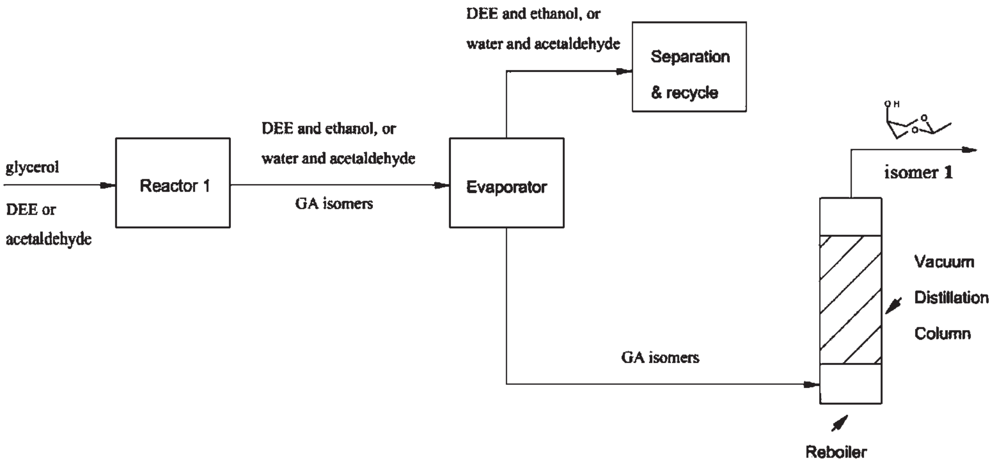


Figure 4. Process concept for continuous production of cis-5-hydroxy-2-methyl-1,3-dioxane (isomer **1**) from glycerol.

thermodynamically limited. If DEE is used, it must be formed from ethanol and acetaldehyde by reactive distillation or another process to overcome the thermodynamic limitation of its formation;[17] however, once formed DEE reacts to completion with glycerol.

CONCLUSIONS

Four isomers are formed in the acetalization of glycerol with acetaldehyde. Distillation of the isomers shows that isomer **1** (*cis*-5-hydroxy-2-methyl-1,3-dioxane) is the most volatile and is distilled preferentially such that nearly pure isomer **1** is initially produced. When an acid catalyst is added to the mixture of isomers such that interconversion can occur during distillation, nearly pure isomer **1** is produced in quantitative yield from glycerol. This process is further transformed into a continuous reactive distillation.

ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Equilibrium distribution of GA isomers at different temperatures. This material is available free of charge via the Internet at http://pubs.acs.org.

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