

A Solvent-Free Method for Making Dioxolane and Dioxane from the Biorenewables Glycerol and Furfural Catalyzed by Oxorhenium(V) Oxazoline

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Low catalyst loading of a cationic oxorhenium(V) oxazoline complex, [2-(2'-hydroxyphenyl)-2-oxazolinato(-2)]oxorhenium(v), condenses diols and aldehydes to give 1,3-dioxolanes in excellent yields under neat conditions and reasonably mild temperatures. The reaction is applicable to biomass-derived furfural and glycerol. The resulting cyclic acetals may find use as value-added chemicals and/or oxygenate fuel additives. Differences in the stereoselectivity of the reaction for epoxides versus diols provide insight into the reaction mechanism.

Biomass is an abundant and renewable resource. Its conversion to liquid fuels and value-added chemical feedstock is an active area of research that has intensified in the past few years due to the need to replace petroleum.¹ The molecular components of lignocellulosic biomass besides lignin are five- and six-carbon sugars,² and it has been shown that liquid fuels can be prepared via aqueous hydroreforming followed by aldol condensation.³ Recent results have shown improved furfural production above the moderate yields from lignocellulosic biomass that have been historically observed.⁴ Glycerol is the main byproduct from biodiesel production, and it has been identified by the U.S. Department of Energy as a target molecule for research and development.⁵ Therefore, we reasoned that coupling furfural with glycerol to

produce the 1,3-dioxolane (2-(furan-2-yl)-1,3-dioxolan-4-yl)methanol⁶ is appealing, especially if it can be done under solvent-free and catalytic conditions. 1,3-Dioxolanes have been reported to possess a high octane content as fuel additives and as potential substitutes for MTBE.⁷ In the pharmaceutical and fragrance industries, 1,3-dioxolanes are used as intermediates as well as final products.⁸ They have also found applications in polymer and steroid chemistry.^{9–11}

Cyclic acetals are commonly used as protective groups in organic synthesis because of their stability against all types of nucleophiles, bases, and many oxidants.¹² 1,3-Dioxanes and 1,3-dioxolanes are generally prepared from carbonyl compounds with 1,3- or 1,2-alkanediol in the presence of a Brønsted or a Lewis acid catalyst. A typical procedure employs *p*-toluenesulfonic acid in refluxing toluene and requires the continuous removal of water (Dean–Stark apparatus). Methyltrioxorhenium (MTO) has been reported to catalyze 1,3-dioxolane production from epoxides and aldehydes.¹³ However, MTO shows severe inhibition by water and does not catalyze the reaction with diols. We describe herein an efficient method for transforming furfural and diols into 1,3-dioxolane catalyzed by [2-(2'-hydroxyphenyl)-2-oxazolinato(-2)]oxorhenium(V) tetrakis(pentafluorophenyl)borate (Scheme 1). Our reaction is solvent-free, effective for the reaction of furfural with glycerol, is not inhibited by water, and requires reasonably mild temperatures (ambient to 100 °C).

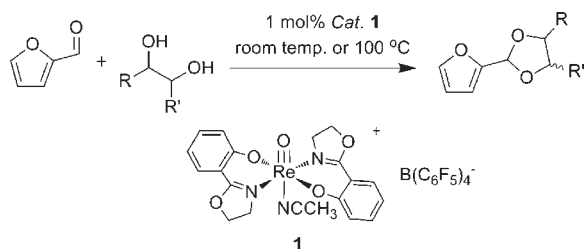
A 1 mol % catalyst loading of **1**¹⁴ and a 5-fold excess of furfural with respect to diol under neat conditions and ambient temperature affords good conversion to the corresponding 1,3-dioxolane. The time of reaction, however, is

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Scheme 1. 1,3-Dioxolane Formation from Furfural and Diols Catalyzed by Oxorhenium(V) **1**

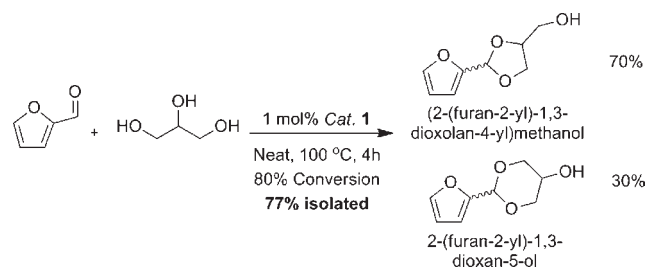
long, requiring approximately 24 h (entry 1, Table 1). While 1,2-hexanediol is completely miscible with furfural, not all diols are at room temperature. This poses a significant drawback to running the reaction at ambient temperatures. For example, *cis*-1,2-cyclohexanediol is not miscible with furfural. This problem can be solved by adding a solvent such as THF. The use of a solvent, however, results in only 50% conversion of the diol to 1,3-dioxolane after 48 h (entry 2, Table 1), which compounds the problem of slow kinetics. We found that an attractive solution to these problems is to conduct the reaction under neat conditions (solvent-free) at 100 °C. At this moderately elevated temperature, all diols tested so far are completely miscible with furfural and the reactions reach completion ($\geq 90\%$ yield) within a few hours (entries 3 and 4, Table 1). Catalyst **1** is also effective for epoxides under neat conditions (entries 5 and 6, Table 1). In addition to furfural, our catalytic process works well for a variety of conventional aldehydes and ketones with di- and even tetra-substituted epoxides. A summary table is provided in the Supporting Information. At the end of the reaction, the catalyst remains viable. Reaction ensues upon the addition of a diol. However, the kinetic lifecycle of the catalyst was not fully evaluated. Even though several Lewis, solid heteropolyacid, and zeolite catalysts¹⁵ are suitable for the synthesis of 1,3-dioxolane, they invariably require the use of solvent and the removal of water.¹⁶ A strength of our methodology is the ability to form acetals in the absence of a solvent. Moreover, our rhenium catalyst allows the use of epoxides as a substrate for acetal formation, leading to an indirect formation of acetals from olefins.

Glycerol is currently produced in large amounts from the hydrolysis or methanolysis of triglycerides (vegetable oils) in the process of making biodiesel. The latest figures show that ca. 6 billion L of biodiesel can be produced annually worldwide.¹⁷ Since 1 mol of glycerol is produced for every 3 mol of methyl esters (i.e., 10% by weight of the total product), 363 million kilos of new glycerol would be added to the market. As a result, several catalytic processes have been described and reviewed in the literature for the conversion of glycerol into value-added chemicals.¹⁸ Our catalyst's

Table 1. Yields of 1,3-Dioxolanes from the Reaction of Furfural with Diols and Epoxides^a

| Entry | Substrate | Conditions | t/ h | % Yield ^b (isolated) |
|-------|-----------|------------------------|------|---------------------------------|
| 1 | | Room temp. neat | 24 | 70 |
| 2 | | Room temp. THF solvent | 48 | 50 |
| 3 | | 100 °C neat | 5 | 91 |
| 4 | | 100 °C neat | 5 | 90 (81) |
| 5 | | Room temp. neat | 24 | 100 |
| 6 | | Room temp. neat | 24 | 100 |

^a Typical reaction conditions: 0.040 mmol of **1**, 4.0 mmol of substrate (epoxide or diol), and 20.0 mmol of furfural. ^b NMR yields, isolated in parentheses.

Scheme 2. Catalytic Conversion of Glycerol and Furfural to Cyclic Acetals, 1,3-Dioxolane and 1,3-Dioxane

tolerance of water and its effectiveness with diols under neat conditions have prompted us to investigate its ability to catalyze 1,3-dioxane and 1,3-dioxolane formation from glycerol and furfural (Scheme 2). We found glycerol to be immiscible with furfural at ambient temperatures. Catalyst **1** is soluble in furfural and remains soluble in the aldehyde layer upon the addition of glycerol. Upon heating to 100 °C, the biphasic mixture of glycerol and furfural containing 1 mol % **1** became a homogeneous single-phase solution. The reaction ensued to afford the two regioisomers 2-(furan-2-yl)-1,3-dioxan-5-ol and (2-(furan-2-yl)-1,3-dioxolan-4-yl)methanol with an overall 80% conversion in only 4 h. Each of the products gave two stereoisomers in nearly equal amounts. Excess furfural was readily removed under a vacuum. The organic products in the resulting crude oil were extracted with diethyl ether. The precipitate including **1** was filtered. Removal of the diethyl ether solvent gave an oil, a mixture of the products (Scheme 2). This mixture can be purified further through a silica plug eluted with 1:2 hexanes/Et₂O followed by Et₂O alone. The two (2-(furan-2-yl)-1,3-dioxolan-4-yl)methanol diastereomers were separated successfully as pure compounds. However, the 2-(furan-2-yl)-1,3-dioxan-5-ol product was obtained as a diastereomeric mixture, which is a liquid at room temperature. The pooling of all the cyclic acetal products gave a total isolated yield of 77%.




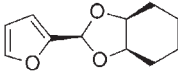
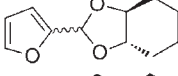
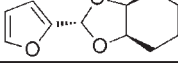
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Table 2. Stereoisomeric Products from the Reaction of Furfural with *cis*-Cyclohexene Oxide, *cis*-1,2-Cyclohexane Diol, and *trans*-1,2-Cyclohexane Diol^a

| |  |  |  |
|---|---|---|---|
|  | 4 | 55 | 0 |
|  | 87 | 0 | 100 |
|  | 9 | 45 | 0 |

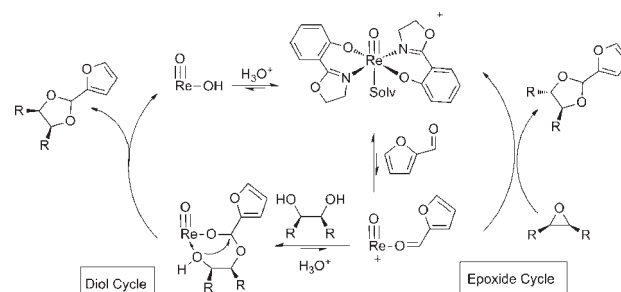
^a 1 mol % **1**, neat, room temperature and 24 h for epoxide, and 100 °C and 5 h for diols.

The tetrakis-pentafluorophenyl borate was used as the anion because it gives a high purity cationic form of the oxorhenium catalyst that is soluble in the furfural/glycerol (or diol) solution. However, it has the disadvantage of a large molecular weight. Under the same conditions, the chloride precursor [2-(2'-hydroxyphenyl)-2-oxazolinato(-2)]oxorhenium(V) chloride, Re(O)(hoz)₂Cl (**2**), gives ca. 70% conversion of furfural and glycerol into 2-(furan-2-yl)-1,3-dioxan-5-ol and (2-(furan-2-yl)-1,3-dioxolan-4-yl)methanol.

With respect to the mechanism, we initially hypothesized that the reaction could be proceeding via the epoxide and the rhenium catalyst serves a dual function, one as a Lewis acid to establish the equilibrium between vicinal diol and epoxide¹⁹ and the second to activate the aldehyde toward attack by the epoxide. However, the reaction with glycerol yielded two regioisomers, 1,3-dioxolane resulting from vicinal diol and a six-membered dioxane ring from the reaction of the 1,3-diol groups of glycerol. It should be noted here that catalyst **1** does not interconvert the 1,3-dioxolane and 1,3-dioxane products. Hence, we probed the stereoselectivity of the reaction for epoxides versus diols.

The stereochemistry of the products was compared for *cis*-cyclohexene oxide to that for *cis*-1,2-cyclohexane diol and *trans*-1,2-cyclohexane diol. All three possible stereoisomers are shown in Table 2. The reaction with cyclohexene oxide gave (3*a*S,7*a*S)-2-(furan-2-yl)hexahydrobenzo[d][1,3]dioxole with inversion in stereochemistry. In contrast, the reactions with *cis*- and *trans*-1,2-cyclohexanediol afforded products with a retention of stereochemistry. A similar series of experiments was conducted with benzaldehyde and stilbene oxide (*cis* and *trans*) and diol (meso- and (*R,R*)-hydrobenzoin).

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Scheme 3. Proposed Mechanism for Oxorhenium(V) Catalyzed 1,3-Dioxolane Formation from Furfural with Epoxide or Diol

The results from these experiments were consistent with those observed for furfural and cyclohexene oxide and cyclohexane diol (see the Supporting Information).

On the basis of these results, we suggest similar but divergent mechanisms for epoxides and diols (Scheme 3). The oxorhenium catalyst activates the aldehyde via coordination. The Re–aldehyde complex undergoes attack by the epoxide or diol. Epoxide affords either a rhenium dioxolane metallacycle, which upon closure results in inversion at carbon, or direct attack of the epoxide onto the aldehyde results in inversion at carbon. Formation of a carbocation intermediate is unlikely since a mixture of isomers is not observed. In the case of diols, the vicinal –OH group attacks the aldehyde carbon to extrude the dioxolane product, leaving behind an oxorhenium hydroxide, which regenerates the catalyst upon protonation.

In summary, we have reported an improved and efficient method for converting vicinal diols and aldehydes to cyclic acetals in high yields using an oxorhenium(V) oxazoline catalyst. The process is solvent-free, thus, green, amenable to the isolation of products, can be run at a low catalyst loading, and is complete in reasonable time. Mechanistic investigations suggest that epoxides and diols react via divergent pathways based on the stereochemical selectivity of their respective reactions. Furthermore, the oxorhenium(V) oxazoline chloride precursor, Re(O)(hoz)₂Cl, is also an effective catalyst for glycerol conversion with furfural. Work is underway in our laboratory to extend these transformations to other biomass-derived compounds and develop tandem conversion of the produced cyclic acetals to other value-added chemicals.

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Supporting Information Available: Experimental detail, characterizations, and NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.