The Oxidation of Glycerol via Asymmetric Hydrogenation of Acetone

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December, 2006
Abstract
We have investigated catalytic dehydrogenation of glycerol with the goal of converting it to a more valuable product. We chose to use Noyori’s catalyst to change glycerol to glyceraldehyde. We observed that the reaction rate is slow with few turnovers; this demonstrates a new possible line of research for using glycerol to make other interesting chemicals. By using Ru(TsDPEN)(η⁶-cymene), Noyori’s catalyst, the chemistry can be shown to work before the catalyst decomposes.

Introduction
With more bio-diesel being used today than in the past the amount of glycerol produced each year has been increasing. Glycerol is produced in surplus. We studied a method to produce glyceraldehyde from glycerol. Our strategy employs Noyori’s catalyst; it uses the glycerol as a hydrogen source for the reaction and transfers the hydrogen to a ketone. Based on the known hydrogen transfer chemistry of Ru(TsDPEN)(η⁶-cymene), Noyori’s catalyst, we envisioned a process based on the two steps in schemes 1 and 2.

Scheme 1: Noyori’s catalyst, 1, dehydrogenates glycerol to form glyceraldehydes

Scheme 2: Noyori’s catalyst transfers the hydrogen to acetone to form 2-propanol

In step one, two hydrogen atoms are removed from the glycerol molecule and one of two products are produced glyceraldehyde as shown in scheme 1 or dihydroxyacetone. In step two, the two hydrogen atoms are transferred from Noyori’s catalyst to acetone producing 2-propanol as shown in scheme 2.

The goal of our research was to find how well the Noyori catalyst would run this reaction and which product it would produce. Noyori’s catalyst was chosen for its high reported yield and high entioselectivity in other hydrogen transfer catalyses. Using this catalyst we hoped to make enantiopure glyceraldehyde from glycerol.
Results

The research I did this semester focused on the oxidation of glycerol via transfer hydrogenation. At the beginning of my research these reactions were completely unexplored. Therefore, initially we prepared Ru(TsDPEN)(η⁶-cymene), Noyori’s catalyst, and investigated its solubility. Glycerol and our target, glyceraldehydes, are not soluble in acetone. Though all the reactants and products were soluble in water, the Ru(TsDPEN)(η⁶-cymene) was converted to a non-catalytically active form. The solution to the solubility issue was dimethylsulfoxide (DMSO). This solvent dissolved the reactants and products and did not cause decomposition of the catalyst.

Additionally, considerable amount of effort was devoted to developing a viable analytic method to study the reaction. At first we thought that we could use the HPLC to separate and detect the glycerol, glyceraldehydes, and dihydroxyacetone. This proved not to be the case, because the glycerol was not undetectable by our HPLC. Gas chromatography was not investigated due to the very high melting and boiling points of glyceraldehyde and dihydroxyacetone. One of the methods that we found to verify that either glyceraldehyde or dihydroxyacetone were produced was a Tollen’s test. With this test we were able to show that a reducing sugar was present in the reaction mixture after the reaction had run for six hours.

Reactions were performed on an NMR-scale in DMSO-d₆ with 5 mol % catalyst to glycerol and acetone. By ¹H NMR spectroscopy, isopropanol was detected: δ 1.03 (d, CH(CH₃)₂OH) and at 3.78 (sep, CH(CH₃)₂OH). However, the resonances due to glycerol obscure the spectra and it was not possible to confirm the presence of glyceraldehydes or dihydroxyacetone. Additionally, these experiments indicate that the reaction of Noyori’s catalyst, compound 1, and glycerol give the Ru(H) intermediate, compound 2. This is supported by detection of characteristic resonance in the ¹H NMR spectrum at -5.6 ppm.

With NMR at this scale I could only tell that the reaction produced isopropanol. The NMR also showed that the reaction had not gone to completion because there was still a high concentration of glycerol and acetone.

A positive to the Tollen’s test showed that there was an glyceraldehyde or dihydroxyacetone present in the reaction solution being tested. Tollen’s test does not give a positive to glycerol, acetone, nor 2-propanol. Tollen’s test did give positive results for both glyceraldehydes and dihydroxyacetone.

Discussion

Our research indicates that the Noyori catalyst catalyzes the transfer dehydrogenation of glycerol. Unfortunately, the research also shows the catalyst is deactivated after only a few turnovers. The cause of the catalyst deactivation is currently unknown.

Based on our NMR scale reactions we attempted to scale up to try and identify glyceraldehydes. Unfortunately scaling up did not aid us. This is due to inability to separate the compounds on a large scale and the lack of characteristic peaks for the products in ¹H NMR spectra.

The solubility was solved though that made the NMR tube reactions possible. Dimethylsulfoxide (DMSO) was used to help the solubility of glycerol into acetone, this allowed for a homogenous mixture of the reactants and the catalyst.
Another issue that prevented the determination of which product was the low number of turnovers for the catalyst, this kept the concentration of the products too low to be detected over the reactants. Further experiments with a higher percent of catalyst to glycerol are necessary.

Though the compound was never isolated, there is evidence that the reaction was occurring. The use of the Tollens test shows the presence of either an aldehyde or an α-hydroxyketone, like dihydroxyacetone. The NMR shows the progression of the reaction through the 2-propanol peaks at δ 1.03 (d). The reaction is slow and heat is required for it to proceed. This particular catalyst has a low turnover rate for this system, but testing other variations of this catalyst would help make a determination of why.

Outlook

Testing smaller arene groups on the ruthenium would give a good idea of the steric effect in this system, and if it is the cause of the reaction to proceeding slowly. The sterics caused by the arene group effect both the rate and the selectivity of the catalyst, for this reason trying an arene with smaller ligands off of it could increase the rate of the reaction and maintain the selectivity.

There are other reactions that should be done to see the effect that the products have on the catalyst, using dihydroxyacetone and the diacetal of glyceraldehyde instead of glycerol. The glyceraldehyde reactions should be done in two reactions with acetone used with one reaction and 2-propanol used in the other. The same reactions should be done with dihydroxyacetone for comparison. These reactions would give a better understanding of the reaction system. Reactions with large percent of catalyst to glycerol should also be done, to see if with the limit turnover enough product can be made to be detected.

Experimental Details

All of the reactions were done under nitrogen using Schlenk methods unless otherwise stated. RuCl$_3$ was obtained from Pressure Chemical. α-Phellandrene, glycerol, glyceraldehyde, N-(4-toluenesulfonyl)-1,2-diphenylethylenediamine (TsDPEN) and dihydroxyacetone were purchased from Aldrich. The DMSO and acetone was purchased from Chemstores. The acetone was freshly distilled from CaSO$_4$ before each run and the DMSO and glycerol were degassed by sparging N$_2$. The catalyst was prepared in two steps following literature procedures as described below.

\[
\{\text{RuCl}_2(\eta^6-\text{p-cymene})\}_2
\]

\[
2\text{RuCl}_3 + 2\text{C}_{10}\text{H}_{16} \rightarrow \{\text{RuCl}_2(\eta^6-\text{p-cymene})\}_2
\]

This starting material was produced following the prep by M.A. Bennett, T.N. Huang, T.W. Matheson, and A.K. Smith in Organometallic Compounds. This reaction can be performed under normal atmosphere, but ours was performed under nitrogen. In a 150 mL round bottom flask 2.0 g hydrated ruthenium trichloride (RuCl$_3$·3H$_2$O) (7.7 mmole) from pressure chemical was added to 100 mL of absolute ethanol and started stirring. This mixture then had 10 mL of α-phellandrene, and is heated to reflux for 4 hours. After less than an hour the solution turned reddish brown. The solution is
cooled. Crystals are formed upon cooling and they are isolated by filtration followed by vacuum drying. There is some product still in solution that can be obtained by recrystallization. The yield was 1.5428 g (2.52 mmole, 65.4%). This compound as stated by the prep is air stable. The \(^1\)H NMR peaks in CDCl\(_3\) with a TMS internal standard as given are \(\delta 1.26\) (doublet, CH\(_3\)), 2.13 (singlet, CH\(_3\)), 2.88 (septet, CH\(_2\)CH\(_3\)), and 4.60 – 4.72 (doublet of doublets, CH\(_3\)).

**Noyori Catalyst**

\[
\{\text{RuCl}_2(\eta^6\text{p-cymene})\}_2 + (R,R)-\text{TsDPEN} \rightarrow
\]

The compound was made following the procedure that the Noyori group published in Angew. Chem. Int. Ed. Engl. in 1997. To 7 mL CH\(_2\)Cl\(_2\), 0.3062 g \{RuCl\(_2(\eta^6\text{p-cymene})\}_2\} (0.5 mmole), 0.3664 g (R,R)-TsDPEN (1.0 mmole), and 0.400 g KOH are added. This mixture is then stirred at room temperature for 5 min, after which 7 mL of water is added and the solution will turn a dark purple. The organic layer is separated from the water layer and dried over CaH\(_2\) and filtered from the CaH\(_2\), then the solvent is removed invacuo.

\(^1\)H NMR on a 400 MHz in [D\(_8\)]toluene \(\delta 1.20, 1.25\) (d, CH(C\(_6\)H\(_5\))\(_2\) from p-cymene), 2.05 (s, CH\(_3\) from p-cymene), 2.22 (s, CH\(_3\) from p-Ts), 2.53 (m, CH(CH\(_3\))\(_2\) from p-cymene), 4.08 (d, HCNH), 4.89 (s, HCN-p-Ts), 5.11, 5.27, 5.28, 5.39 (d, CH\(_{\text{aromatic}}\) from p-cymene), 6.87, 7.67 (d, CH\(_{\text{aromatic}}\) in p-Ts), 7.2-7.7 (m, p-TsNCH(C\(_6\)H\(_5\))CH(C\(_6\)H\(_5\))NH).

**Tollen’s solution**

In a beaker or flask place 7.5 mL of 0.1 M silver nitrate, add ammonium hydroxide drop wise till solution turns cloudy then clear again. Then add 4 mL of 0.8 M potassium hydroxide, add ammonium hydroxide until solution turns clear again.

**Representative NMR scale catalyst**

In an NMR tube, in a glove box transfer 0.0309 g (0.05mmol) of Noyori’s catalyst, and 0.0644 g of glycerol (0.70 mmol). Acetone (0.015 mL, 0.0406 g, 0.70 mmol) is added to the NMR tube. DMSO-d\(_6\) was added to dissolve the reagents. An NMR is then taken as quickly as possible and once an hour for 6 hours. After 6 hours NMR is taken once a day. Higher catalyst loading gives more production of 2-propanol. After heating the solution changes from purple to yellow. After 4 hours, the solution starts to turn brown. In two days, signs of catalyst decomposition are evident by the sharpening of glycerol resonances in the \(^1\)H NMR spectra of the reaction mixture. Glycerol’s downfield peak at \(\delta 4.36\) becomes sharper and more defined. The progression of the reaction was monitored via the 2-propanol doublet at \(\delta 1.03\).
Acknowledgements

I greatly appreciate the financial support provided by Mr. and Mrs. Plagens. I would also like to thank Aaron Sadow for the opportunity to do this research and to Ben Baird, James Dunne and Jiachun Crystal Su for all of their help, advice, and encouragement.

Reference


