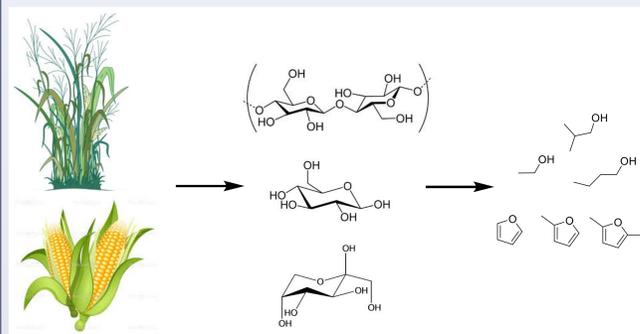




## Introduction

Biomass has the potential to replace petroleum feedstock for many chemical products, yet the fundamental chemistry for converting biomass derived chemicals into useful chemical products is lacking.

Due to advancements in research and industry, carbohydrates from biomass can be converted into alcohols, furans, and other small organic molecules on a large scale. Ethanol production is well established; currently providing nearly 10% of US fuel (1). Biobutanol is undergoing commercialization (2). A variety of furans can easily be produced at industrial scale, but so far their market has remained small (3).

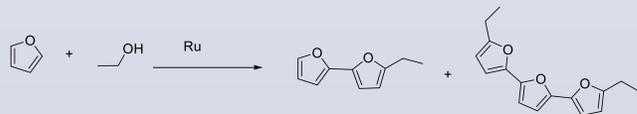


Alcohols and furans are strong candidates as fuel replacements, but several problems limit their direct application. The short chain alcohol ethanol is hygroscopic and significantly lower in energy density than petrol. This causes fuel transport challenges and limits its potential use as a drop in fuel to roughly 10-15% blends with more hydrophobic, energy dense compounds. Simple furans such as furan and dimethyl furan have known toxicity problems, including carcinogenicity and genotoxicity (4).

By developing the basic chemistry of furans and furan alkylation, new furan derived chemical architectures of inherently lower toxicity are sought that would still be useful as fuels. This will enable the use of the potentially abundant furan feedstocks from biomass.

## Background and Proposed Reaction

Dixneuf et al discovered that furans can be alkylated using ruthenium catalysts in alcohols to generate mixtures of products (5):



Based on this precedent, the following reaction is proposed. Butanol is shown but various alcohols could be employed:



By removing the hydroxyl groups from the, the fuel value of these carbon sources is increased. Depending on product volatility, which will depend on the alcohol chosen, fuel applications may be for petrol or diesel.

By extending the chain length, toxicity may be ameliorated by reducing enzyme binding and nucleic acid interactions by the furans.

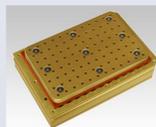
## Objectives

- Investigate the basic chemistry of aromatic heterocycle alkylation by alcohols. Discover and optimize homogeneous transition metal catalysts for this purpose.
- Apply the borrowing hydrogen methodology to activate alcohols towards nucleophilic attack by furans, using H<sub>2</sub>O as a leaving group and a final hydrogenation step to generate reduced products.
- Analyze the utility of furan-alcohol coupling products for use as gasoline and diesel substitutes or oxygenates.
- In collaboration perform ecological and mammalian toxicological tests on chemical products to build an understanding of how these molecules might perturb metabolic systems and affect living organisms.

## Methods

### Parallel Reaction Experimentation

Using vials, 24 well plates, or 96 well plates, reaction conditions are chosen using precedent from previous experiments in combination with expectations derived from proposed reaction mechanisms. The most common variables examined are temperature, solvent, reaction stoichiometry, and transition metal catalyst.



### GC-MS Analysis

GC-MS (gas chromatography-mass spectroscopy) is used to identify volatile products produced in the reactions examined by the parallel experimentation technique. Since fuels, especially petrol require a good degree of volatility, this analytical method selects for products that have this fuel property.



### Scale Up and NMR analysis

Once reaction conditions and a catalyst are identified that produce a product of interest, the reaction can be scaled up, and the product isolated using chromatography. Then analysis using NMR (nuclear magnetic resonance spectroscopy) enables unambiguous determination of the product structure. This is important in cases where chemical isomers will give similar GC-MS spectra.

### Toxicological Analysis

High content screening mechanistic assays in fish cell lines will be conducted that allow simultaneous evaluation of multiple modes of toxicity. Fish cell lines include FHM and Rtgill-W1, established by the Vulpe lab.

Local models will be developed to determine how small changes in furan-derivative chemical structure can influence their toxicity, to help identify new synthetic target compounds and to determine the toxicity of compounds produced by exploratory efforts in catalysis.

## Results and Analysis

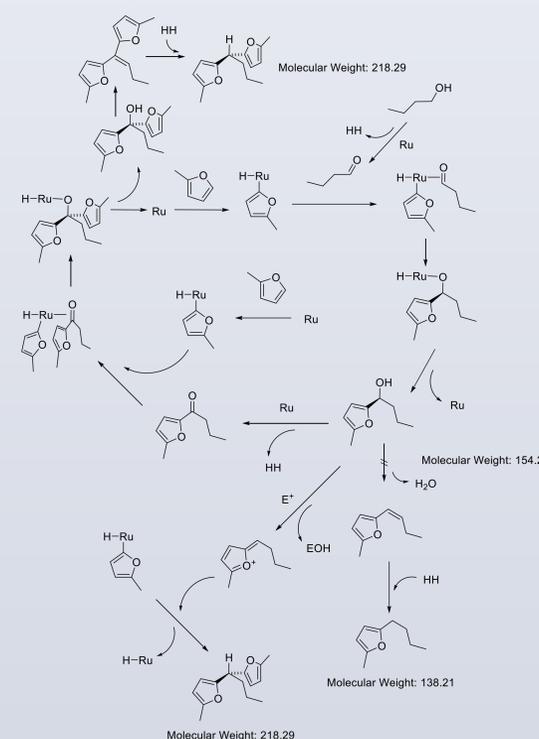
It has been found that ruthenium catalysts are effective for the formation of a variety of products from furans and alcohols. In contrast to the expected reactivity of these substrates, the following reaction is observed using ligandless Ru(II) catalyst:



This product has potential as a diesel oxygenate, and can undergo further hydrogenation/dehydration to generate useful diesel fuel replacement.

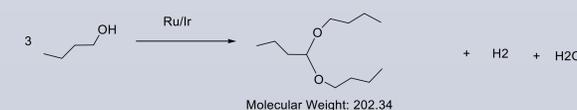
RuI<sub>3</sub>, 3AgBF<sub>4</sub> and [Ru(benzene)Cl<sub>2</sub>]<sub>2</sub>, 2AgBF<sub>4</sub> have selectivity for m=218 product in all conditions where furan and alcohol are both present. Furan byproducts are seen at high furan concentrations and with base additives. A reaction stoichiometry enriched in alcohols is critical for selectivity with these substrates.

The following mechanistic scheme is proposed to explain the observed reaction selectivity:

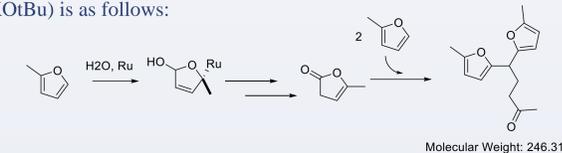


From the intermediate furfuryl alcohol, the dehydration/hydrogenation pathway to the m=138 product is slower than the competing dehydrogenation/alkylation and dehydration/alkylation pathways towards the m=218 product.

A related catalyst system, [Ir(COE)<sub>2</sub>]<sub>4</sub>, gave selectivity for this same product, but in the presence of bisphosphine ligand (diphenylphosphinoferrrocene), underwent reversal of selectivity to generate dibutoxybutane (also seen by Ru(II) catalysis in alcohols):



While this compound could have application in diesel fuels as a high molecular weight oxygenate, it is not a target heterocouple product. The primary side reaction in basic conditions ([Ru(benzene)Cl<sub>2</sub>]<sub>2</sub>, 2AgBF<sub>4</sub>, KOtBu) is as follows:



This product is derived solely from furans. Like the m=218 product from neutral Ru(II) catalysis, it could have fuel value after additional hydrogenation/dehydration steps.

Studies into the toxicity of the identified compounds are just underway, and their results will feedback towards ongoing catalyst design efforts.

## Conclusions

By investigating the basic reactivity of alcohols and furans using alkylation catalysts, an entryway into novel chemistry using these substrates has been achieved.

Further development of this chemistry will broaden human understanding of what chemical products can be achieved using renewable alcohol and furan feedstocks, and what applications they may be used for. Here fuel application has been considered since replacing these high volume chemicals with renewables will have a particularly large impact on reducing carbon emissions.

By designing a research platform where product toxicity is considered in the early stages of research, the eventual products, if commercialized will be much more likely to be safe for humans and the environment.

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## Acknowledgements

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