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Supporting information for: Flow chemistry enhances catalytic alcohol-to-alkene dehydration

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General experimental

Reagents

Used as received: 1-Hexanol (99 %, Thermo Scientific), 1-Hexene (99 %, Thermo Scientific), Dihexyl ether (98 %, Thermo Scientific), (2-Methyl-1-butanol (98 %, Thermo Scientific), 2-Methyl-1-butene (98%, Thermo Scientific), 1-Pentanol (99 %, Thermo Scientific), 1-Pentanol, Ethylacetate (99%,Fisher Chemicals) , Diethyl ether (99%,Fisher Chemicals) ,Paraffin oil (Sigma-Aldrich).

Catalysts

Used as received: Hafnium triflate (98% hafnium(IV) trifluoromethanesulfonate, Thermo Scientific), iron triflate (90 % iron(III) trifluoromethanesulfonate, Thermo Scientific), triflic acid (99% trifluoromethane sulfonic acid, Thermo Scientific), sulfuric acid (95 %, Fisher Chemicals), boron trifluoride diethyl etherate (Fluka Analytical), methyltrioxorhenium (98% methyltrioxorhenium(VII) (MTO), Thermo Scientific), triphenylphosphine (99%, Acros Organics), gadolinium triflate (98% gadolinium(III) trifluoromethanesulfonate, Aldrich), γ -Alumina (Sasol SA: 150m³ / g), aluminium chloride (Sigma Aldrich), which was sublimed under vacuum before use.

Autoclave and flow system

Autoclave: Parr Hastelloy autoclave (100 mL) with PTFE insert and magnetic stirrer bar.

Flow Machine: Vapourtec E-Series fitted with Vapourtec PTFE tubing and fittings.

Autoclave used for batch reactions and as the CSTR in the flow setup: Parr Hastelloy autoclave (100 mL).

Analysis

1-Hexanol dehydration to a mixture of hexenes

Gas chromatography

Method used for analysis of hexenes produced in preliminary catalyst screening reactions (Figure 1)

Shimadzu GC-2014 using He carrier gas and FID detector. Column: Agilent J&W DB-WAXETR (PEG stationary phase, 60 m, 0.320 mm, 1.00 μm). 1-Pentanol was used as the internal standard.

Method: Starting oven temperature 55°C, heat to 60°C at 1°C min⁻¹, then heated to 250°C at 30°C min⁻¹, hold for 5 minutes.

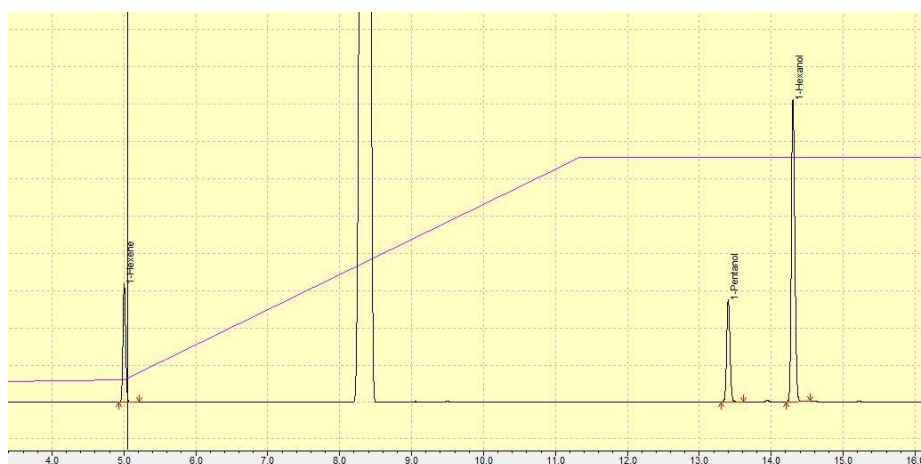


Figure S1. GC chromatograph of hexanol and 1-hexene.

Chromatographs of hexenes produced in reactions

1. On WAXETR

To test for the thermodynamic distribution of hexenes, hex-1-ene (0.3 mL) diluted in ethyl acetate (30 mL) isomerised using nickel phosphite catalyst (73 mg). Samples taken every 10 minutes and quenched with H₂SO₄ (1M in methanol) then injected into GC-FID. The integrations stopped changing after 2 hours at the thermodynamic distribution. The ratio of hex-1-ene : hex-2-ene : hex-3-ene was the same as what is seen in the distribution of hexene isomers from the dehydration of hexanol in the catalytic reactions.

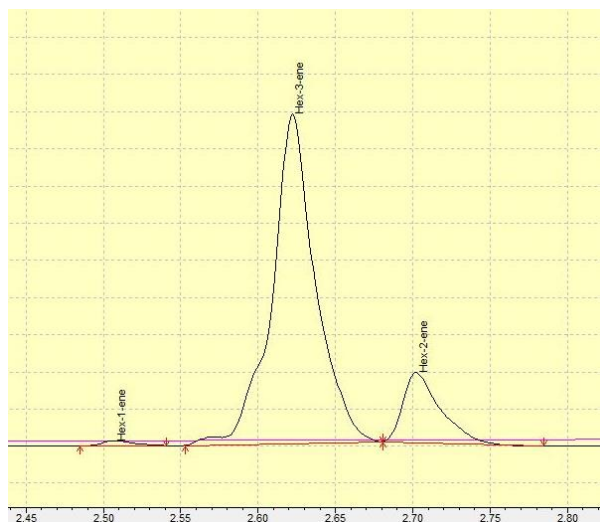


Figure S2. GC chromatograph of hexene isomers as produced in dehydration: 83% hex-3-ene, 15% hex-2-ene and 1% hex-1-ene.

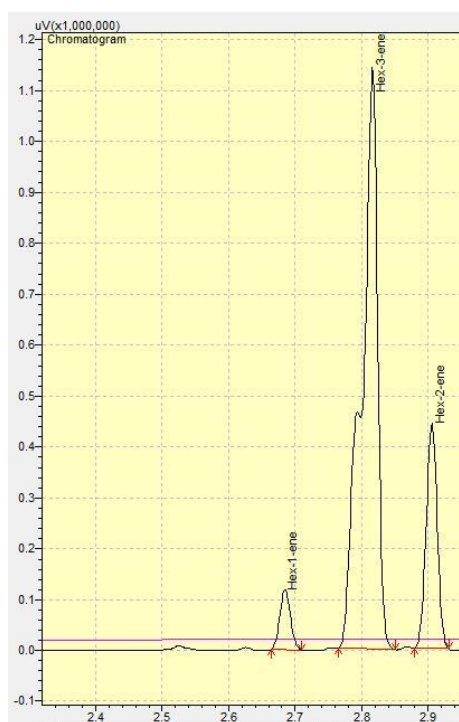


Figure S3. GC chromatograph of hexene isomers from isomerisation of 1-hexene. From an independent experiment run to give the thermodynamic distribution of hexene isomers as a comparison from isomerisation of hex-1-ene using $[\text{Ni}\{\text{P}(\text{OEt})_3\}_4] / \text{H}^+$ as the catalyst.

2. On DB5

Method used for analysis of hexene isomers and for analysis of hexenes, dihexyl ether and hexanol to produce time profiles of $\text{Hf}(\text{OTf})_4$ and HOTf (Figure 2a and 2b in main paper):

Shimadzu GC-2014 using He carrier gas and FID detector. Column: Agilent DB5 (30 m, 0.25 mm, 0.25 μm).

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Method: Starting oven temperature 40°C, heat to 45°C at 1.5°C min⁻¹, then heat to 320°C at 30°C min⁻¹, hold for 3 minutes.

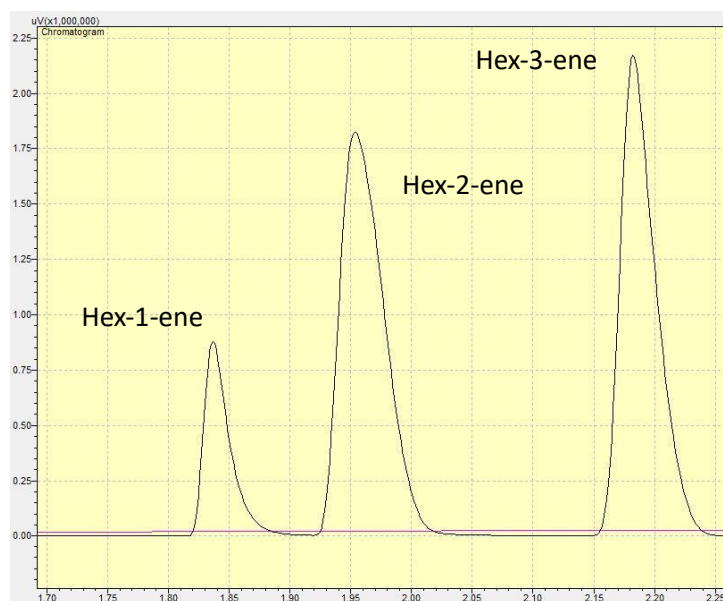


Figure S4. GC chromatograph of hexene isomers.

2-Methyl-butanol dehydration to 2-methyl-1-butene

Gas chromatography

Shimadzu GC-2014 using He carrier gas and FID detector. Column: Agilent J&W DB-WAXETR (PEG stationary phase, 60 m, 0.320 mm, 1.00 µm). 1-Pentanol was used as the internal standard.

Method: Starting oven temperature 55°C, heat to 60°C at 1°C min⁻¹, then heated to 250°C at 30°C min⁻¹, hold for 5 minutes.

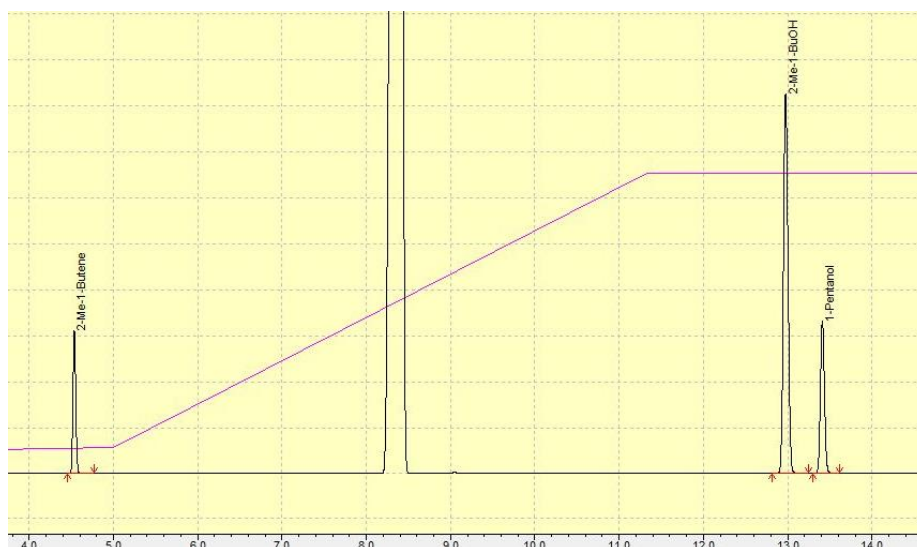


Figure S5. GC chromatograph of 2-methylbutanol and 2-methylbutene.

Catalytic reactions using batch conditions

General method

Hf(OTf)₄ (0.154 g, 0.199 mmol, 0.5 mol%), was added to a clean oven-dried fitted PTFE insert inside a glove box. The insert was sealed within a 100 cm³ Parr stainless steel autoclave which was then transferred to a N₂/vacuum manifold. Hexanol (5mL, 39.83 mmol) was injected into the autoclave through an inlet against a flow of nitrogen. The autoclave was sealed and placed into a pre-heated (180 °C) aluminium heating block. After the reaction run time (4 h), the autoclave was cooled to room temperature in an ice-water bath. The autoclave was vented to remove any gas generated during the reaction. A liquid sample was removed, filtered through a short plug of alumina (acidic) and analysed by GC (100 µL of sample, 1.7 cm³ EtOAc pentanol internal standard solution – sample refiltered through a glass filter paper to remove insoluble salts).

Batch Reactor validation

Mass transfer

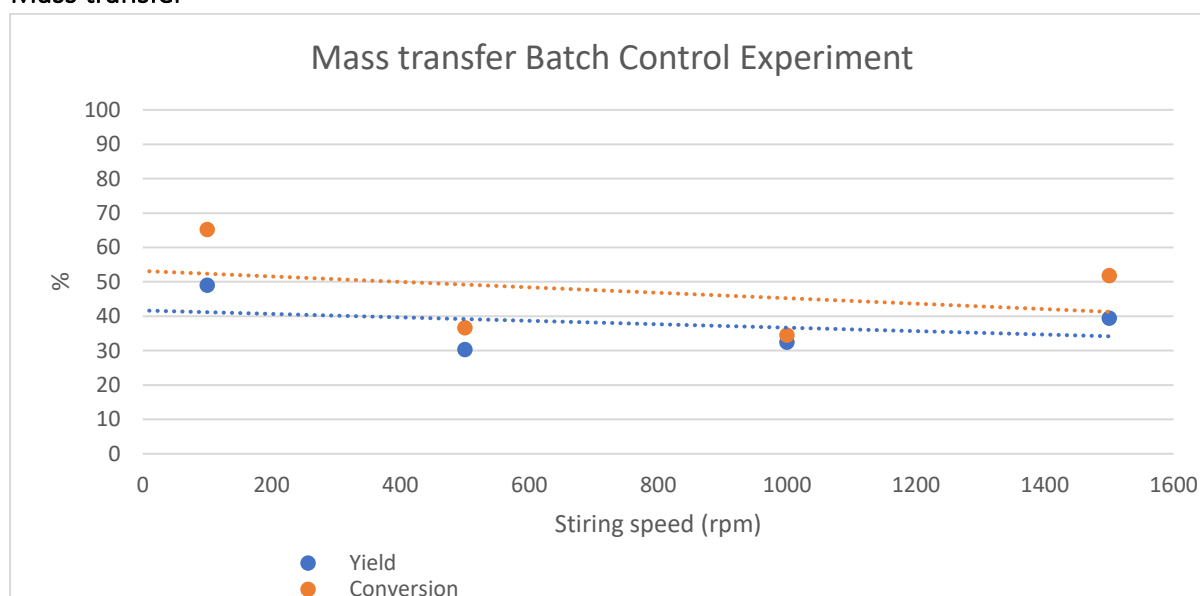


Figure S6. Effect of stir speeds on yield and conversion of hexanol to hexene. Reaction conditions: Hf(OTf)₄ (0.5 mol%), 4h, 180°C, Hexanol (5 mL)

No significant effect on yield and conversion due to stir rate.

Blanks

The reactor was assessed to see if the reactor walls catalysed the dehydration of hexanol to hexene using the reaction conditions: 4 hours, 500 rpm, hexanol (5 mL). It was found that they had little no influence on yield and conversion of hexanol to hexene. (table xx)

Table S1. Blank reactions

Yield (%)	Conversion (%)
0	2.2
0	2.4

Batch Results

Conversion of alcohol can reach 92% after 16 hours, however, yield of alkene stops at 50%. We believe this is due to further reactions of alkene forming polymer species as it is being formed.

ToN = moles alkene / moles of catalyst

ToN after 4 hours: 76

Table S2. ToN after 4 hours

Catalyst	Substrate	mol %	ToN	ToF (h ⁻¹)
Hf(OTf) ₄	1-Hexanol	0.5	76	19
	2-Methyl-1-butanol	0.5	37	9
Fe(OTf) ₃	1-Hexanol	2.5	114	28
		0.5	12	3
HOTf	1-Hexanol	5	9	2
		0.5	9	2
H ₂ SO ₄	1-Hexanol	5	16	4
		0.5	4	1
No catalyst	1-Hexanol	0	N/A	N/A

Dihexyl ether reactions

Hf(OTf)₄ (0.077 g, 0.199 mmol, 0.5 mol%), was added to a clean oven-dried fitted PTFE insert inside a glove box. The insert was sealed within a 100 cm³ Parr stainless steel autoclave which was then transferred to a N₂/vacuum manifold. Dihexyl ether (2.4 mL, 19.91 mmol) was injected into the autoclave through an inlet against a flow of nitrogen. The autoclave was sealed and placed into a pre-heated (180 °C) in aluminium heating block. After the reaction run time (4 h), the autoclave was cooled to room temperature in an ice-water bath. The autoclave was vented to remove any gas generated during the reaction. A liquid sample was removed, filtered through a short plug of alumina (acidic) and analysed by GC (100 µL of sample, 1.7 cm³ Et₂O pentanol internal standard solution – sample refiltered through a glass filter paper to remove insoluble salts).

A stock solution of HOTf was made in toluene (0.1 mL HOTf in 12.5 mL toluene) 1 mL of stock (0.199 mmol, 0.5 mol% HOTf), was added to a clean oven-dried fitted PTFE insert inside a glove box. The insert was sealed within a 100 cm³ Parr stainless steel autoclave which was then transferred to a N₂/vacuum manifold. Dihexyl ether (2.4 mL, 19.91 mmol) was injected into the autoclave through an inlet against a flow of nitrogen. The autoclave was sealed and placed into a pre-heated (180 °C) in aluminium heating block. After the reaction run time (4 h), the autoclave was cooled to room temperature in an ice-water bath. The autoclave was vented to remove any gas generated during the reaction. A liquid sample was removed, filtered through a short plug of alumina (acidic) and analysed by GC (100 µL of sample, 1.7 cm³ Et₂O pentanol internal standard solution – sample refiltered through a glass filter paper to remove insoluble salts).

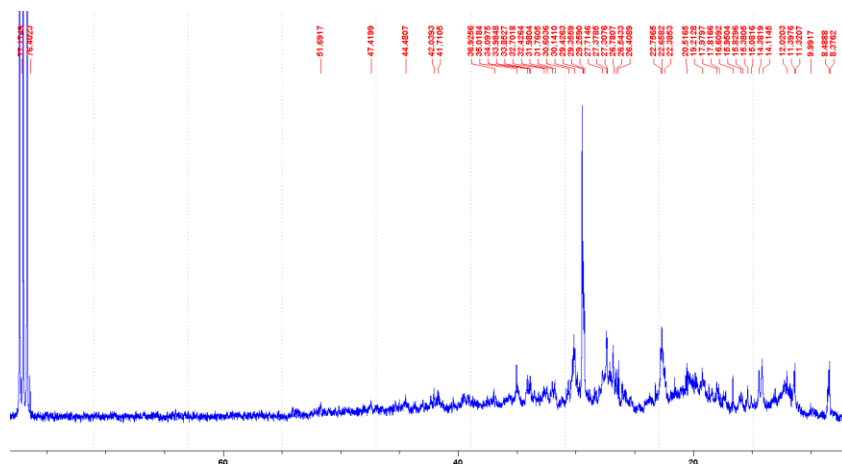


Figure S10. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum from 2-methyl-1-butanol dehydration.

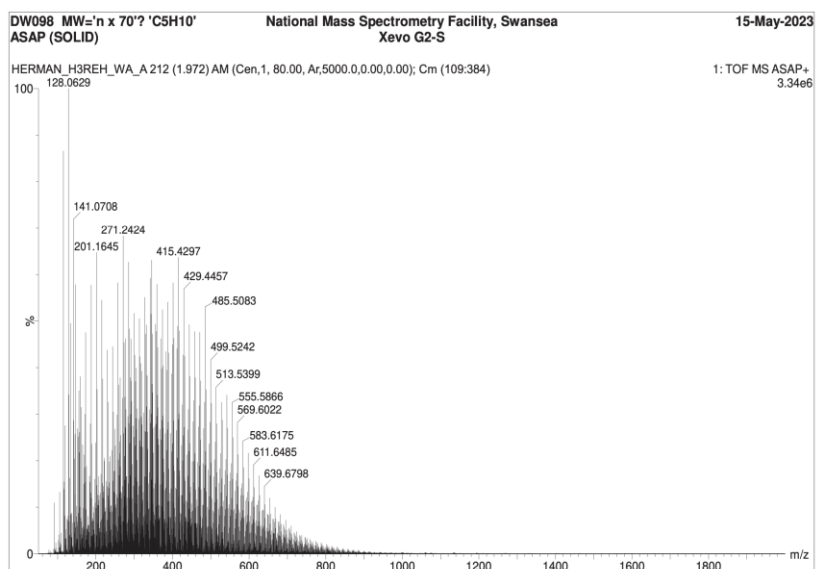


Figure S11. ASAP mass spectrum from 2-methyl-1-butanol dehydration.

Isobutanol Dehydration

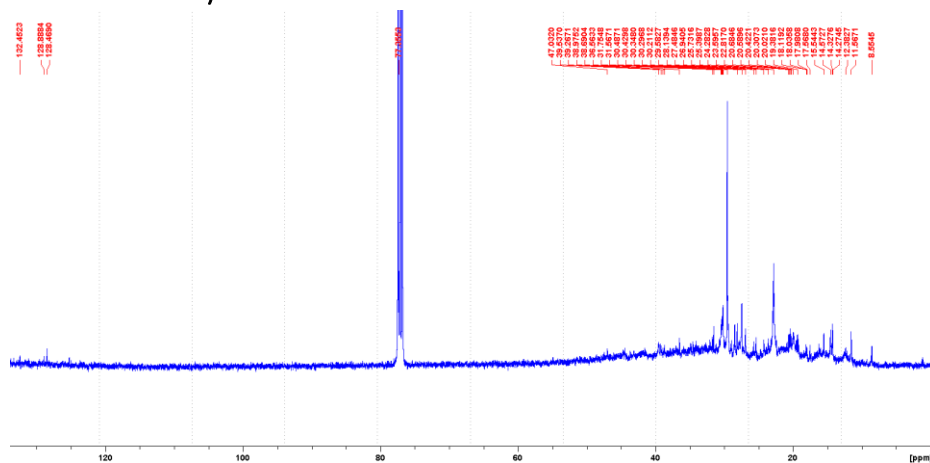


Figure S12. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum from isobutanol dehydration.

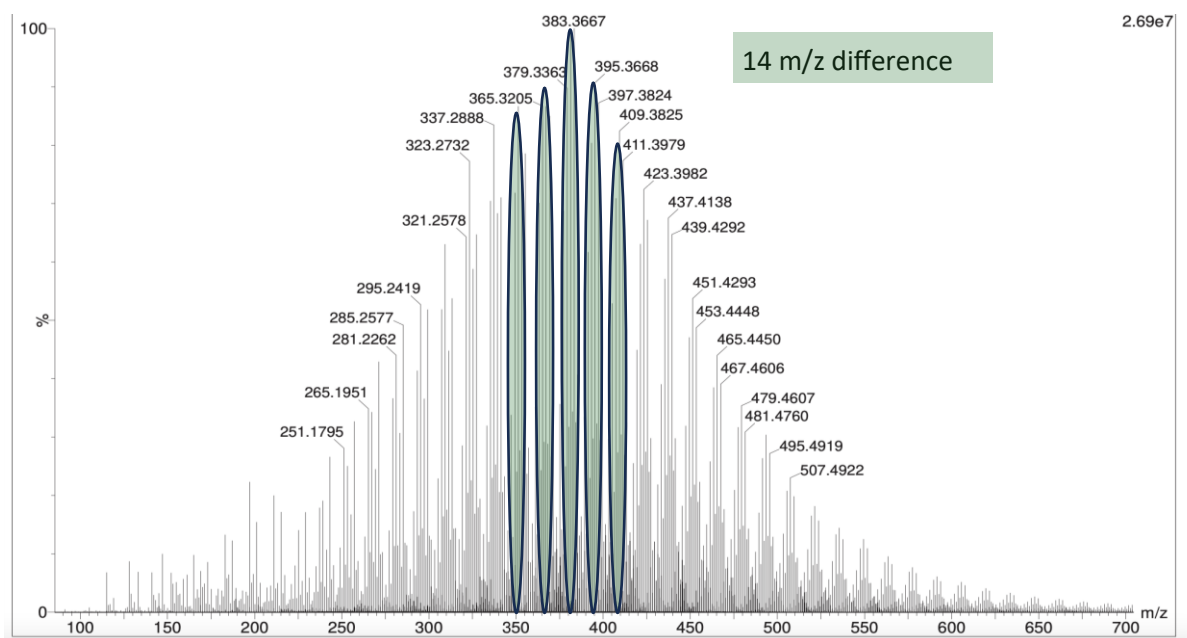


Figure S13. ASAP mass spectrum from isobutanol dehydration (4 h reaction).

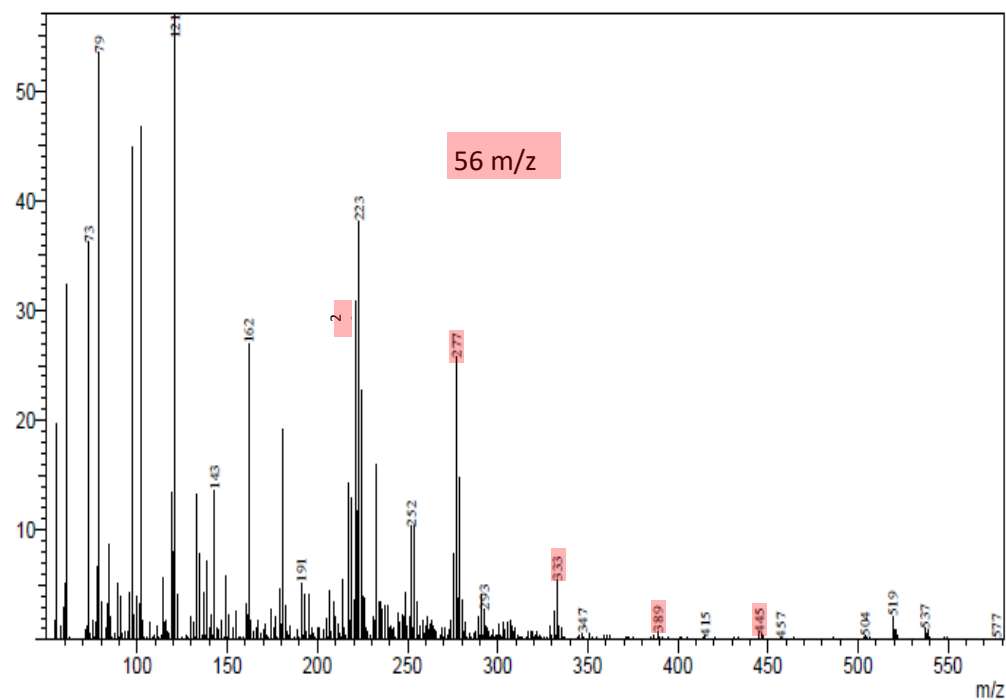


Figure S14. ASAP mass spectrum from isobutanol dehydration (1 h reaction).

Table S3. Substrate Comparison

Temperature (°C)	Time (h)	Hexanol to Hexene			2-Methylbutanol to 2-methyl butene		
		Yield (%)	Conversion (%)	Selectivity (%)	Yield (%)	Conversion (%)	Selectivity (%)
180	1	5.4	85.0	6.3	15.8	54.8	29.0

Reaction conditions: 180 °C, 1 hour, Hf(OTf)₄ (0.5 mol%), 500 rpm, 100 mL Autoclave

Results show a branched alcohol is easier to dehydrate but the alkene is more reactive.

CSTR reaction

CSTR Setup

Flow Machine: Vapourtec E-Series fitted with Vapourtec PTFE tubing and fittings.

Autoclave used for batch reactions and as the CSTR in the flow setup: Parr Hastelloy autoclave (100 mL).

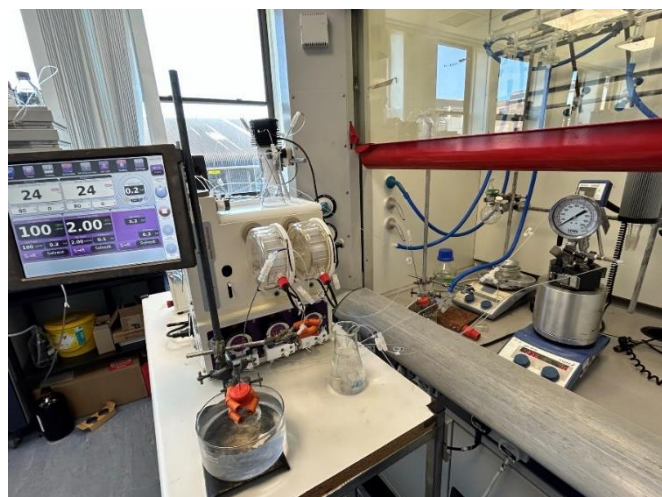
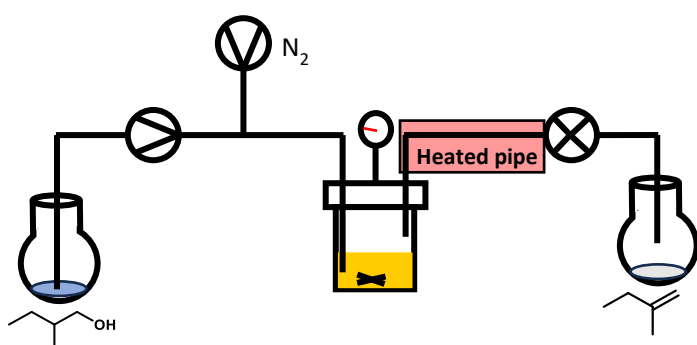


Figure S15. CSTR set up.

CSTR Method

[Hf(OTf)₄] (0.5476 g, 0.706 mmol), and paraffin oil (5 mL) were added to a clean oven-dried PTFE insert inside a glove box. The insert was sealed within a 100 cm³ Parr Hastelloy autoclave which was then placed in the preheated aluminium block (180°C) and hooked up to the Vapourtec E series via vapourtec tubing and fittings as shown above with a stir rate of 500 rpm. The tubing was purged with N₂ (100 mL min⁻¹). The valves on the autoclaves were opened and system was pressurized to 1.4 barg using N₂. Once the autoclave was up to temperature and pressure the flow of 2-methylbutanol (0.1 mL min⁻¹) was started. T₀ was determined from when the alcohol entered the reactor. Samples were taken directly from the eluent at 20-minute intervals. The sample was analysed using GC-FID (25 μL of sample, 0.4 cm³ EtOAc/pentanol internal standard solution).

CSTR Validation

The CSTR was evaluated through a series of control experiments design to asses: mass transfer, concentration gradients and if the reactor walls would catalyse the reaction. To assess mass transfer the yield and conversion were measured at multiple different stirring rates (Figure S15). It was determined that there was no significant variation in conversion and yield with stir rate therefore the reaction was not under mass transfer control. The concentration gradients were assessed in a similar way but by measuring the effect of stirring rate on the activity of the catalyst. This again showed no effect meaning the reactor was free from concentration gradients (Figure S17). The reactor walls were tested by adding no catalyst, here we found no meaningful yield or conversion was produced by the reactor walls (Figure S16).¹

Mass transfer

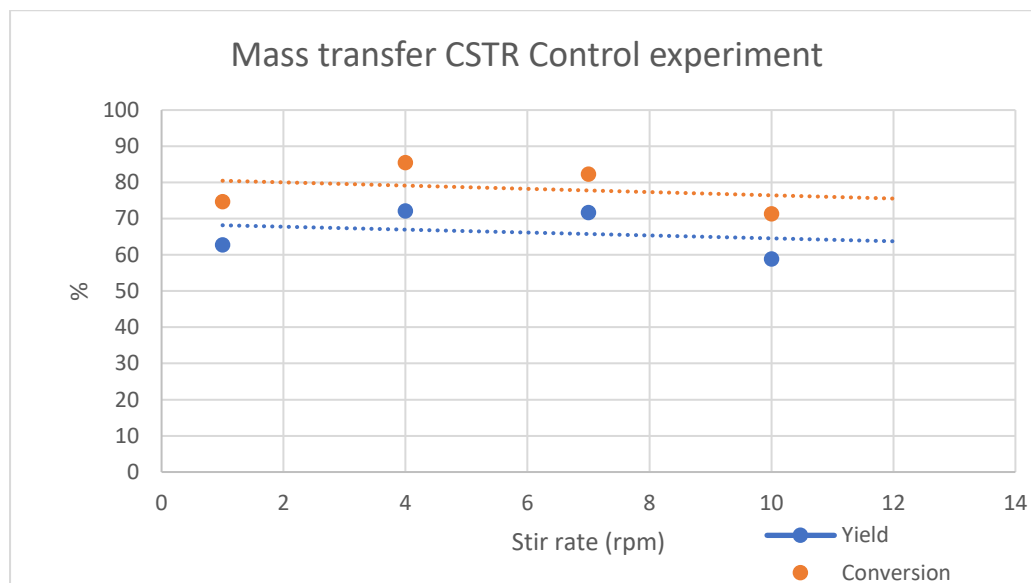


Figure S16. Effect of stir speeds on yield and conversion of 2-Methylbutanol to 2-methylbutene. Reaction Conditions: 180°C, $\text{Hf}(\text{OTf})_4$ (0.35 g), Paraffin oil (5 mL), 2-Me-BuOH flow rate 0.1 mLmin⁻¹ Flow rate N₂ 2 mLmin⁻¹, Pressure 3.1 bar.

No significant effect on yield and conversion due to stir rate. Reactor is free of mass transfer issues.

Blanks

Reaction setup was tested with no $\text{Hf}(\text{OTf})_4$ for 100 minutes. The volatiles collected in the collection flask were analysed (5 data points). Average yield of 2-methyl-1-butenes: 1.0%. Average conversion: 0%.

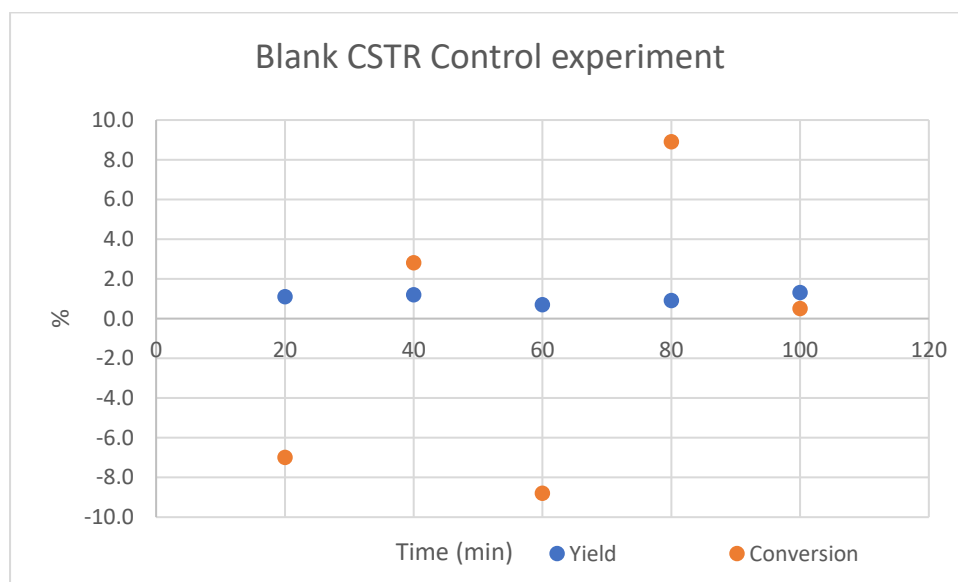


Figure S17. Control experiment: Blank run in CSTR with 2-methylbutanol. Reaction Conditions: 180°C, Paraffin oil (5 mL), 500 rpm, 2-Me-BuOH flow rate 0.1 mLmin⁻¹ Flow rate N₂ 2 mLmin⁻¹, Pressure 3.1 bar.

Interphase gradients

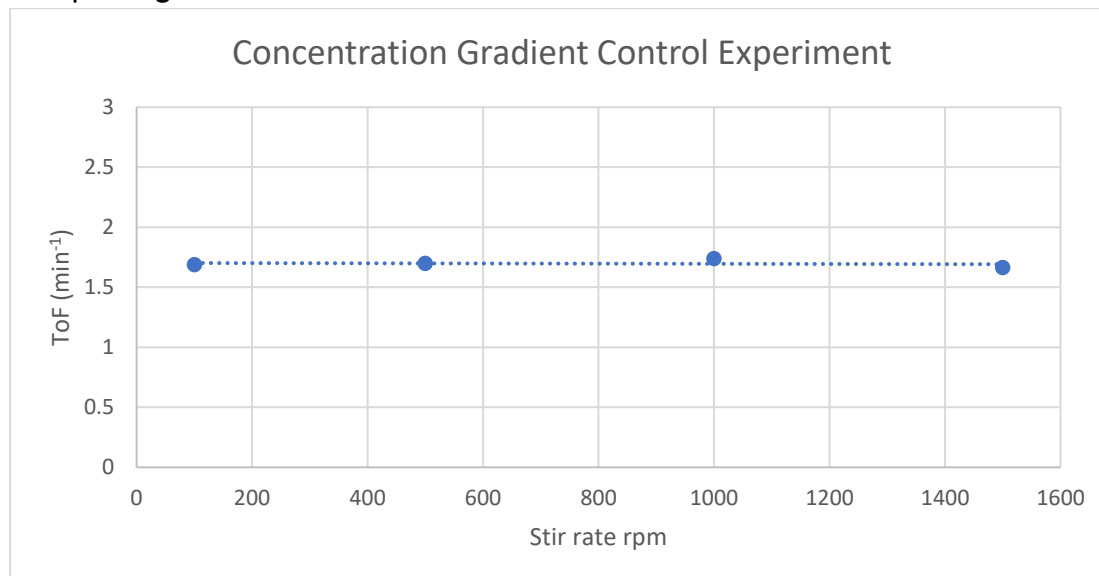


Figure S18. Effect of stirring rate on turn over frequency (ToF). Reaction Conditions: 180°C, Hf(OTf)₄ (0.35 g), Paraffin oil (5 mL), 2-Me-BuOH flow rate 0.1 mLmin⁻¹ Flow rate N₂ 2 mLmin⁻¹, Pressure 3.1 bar.

No significant effect on rate of reaction due to stir rate, therefore reactor is free of concentration gradients.

CSTR results

Fine screen

Table S4. Catalyst testing operating conditions for 2-methyl-1-butanol dehydration reactions in the CSTR

Optimised catalytic conditions	For screening activity	For screening selectivity	For producing pure alkene
Paraffin oil	5 mL	5 mL	5 mL
Catalyst	0.705 mmol	0.705 mmol	0.705 mmol
Reactor volume	100 mL	100 mL	100 mL
Stirring rate	500 rpm	500 rpm	500 rpm
N ₂	100 mL min ⁻¹ (gas)	100 mL min ⁻¹ (gas)	100 mL min ⁻¹ (gas)
2-methyl-1-butanol	0.1 mL min ⁻¹ (liquid)	0.1 - 0.2 mL min ⁻¹ (liquid)	0.1 mL min ⁻¹ (liquid)
Pressure	1.4 barg	1.4 barg	3.1 barg
Reactor temperature	180°C	180°C	180°C
Outlet temperature	160°C	160°C	Room temperature

Altering residence time in the reactor by changing the flow rate of alcohol through the system:

Individual results:

Hf(OTf)₄:

Table S5. Hf(OTf)₄ average yield, conversion, selectivity and mass balance for each flow rate tested

Flow rate (mL/min)	Yield (%)	Conversion (%)	Selectivity (%)	Mass balance
0.100	30.7	65.4	46.9	0.838
0.133	22.2	44.1	50.1	0.709
0.166	19.6	38.2	51.6	0.542
0.200	17.5	27.7	62.5	0.642

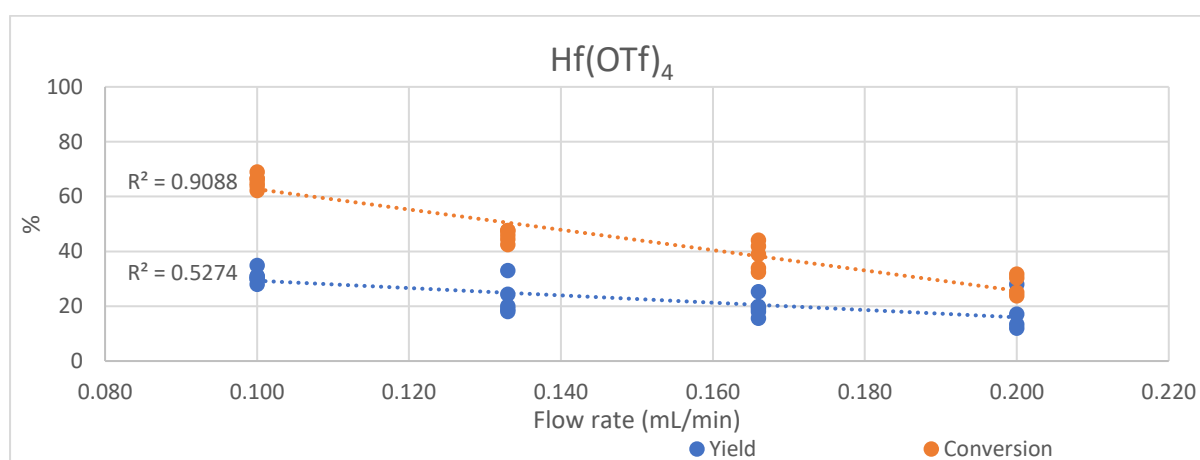


Figure S19. Effect of flow rate on yield and conversion in 2-methyl-1-butanol dehydration reactions using Hf(OTf)₄ as the catalyst.

HOTf:

Table S6. HOTf average yield, conversion, selectivity and mass balance for each flow rate tested

Flow rate (mL/min)	Yield (%)	Conversion (%)	Selectivity (%)	Mass Balance
0.100	25.4	53.1	47.8	0.715
0.133	31.5	51.7	61.0	0.867
0.166	15.5	34.0	43.1	0.867
0.200	2.0	4.3	53.2	1.065

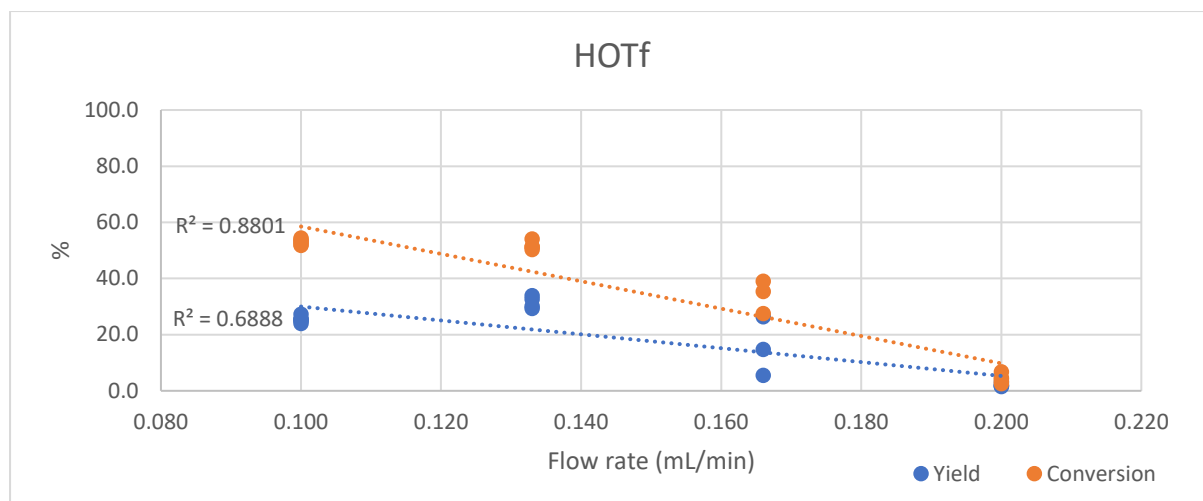


Figure S20. Effect of flow rate on yield and conversion in 2-methyl-1-butanol dehydration reactions using HOTf as the catalyst.

Fe(OTf)₃:

Table S7. Fe(OTf)₃ average yield, conversion, selectivity and mass balance for each flow rate tested

Flow rate (mL/min)	Yield (%)	Conversion (%)	Selectivity (%)	Mass Balance
0.050	22.4	64.9	34.7	0.616
0.100	10.1	30.5	34.8	0.956
0.133	4.4	8.4	67.0	1.066
0.166	1.8	2.7	85.6	1.135

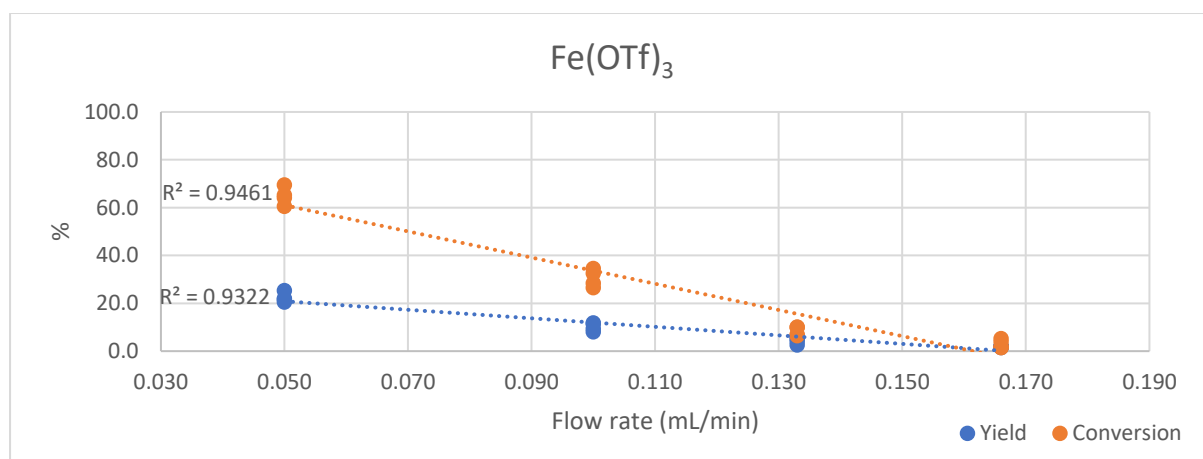


Figure S21. Effect of flow rate on yield and conversion in 2-methyl-1-butanol dehydration reactions using Fe(OTf)₃ as the catalyst.

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H₂SO₄:

Table S8. H₂SO₄ average yield, conversion, selectivity and mass balance for each flow rate tested

Flow rate (mL/min)	Yield (%)	Conversion (%)	Selectivity (%)	Mass balance
0.050	0.5	8.9	9.4	1.268
0.100	0.8	2.7	40.9	1.258
0.133	0.5	1.6	44.7	1.136

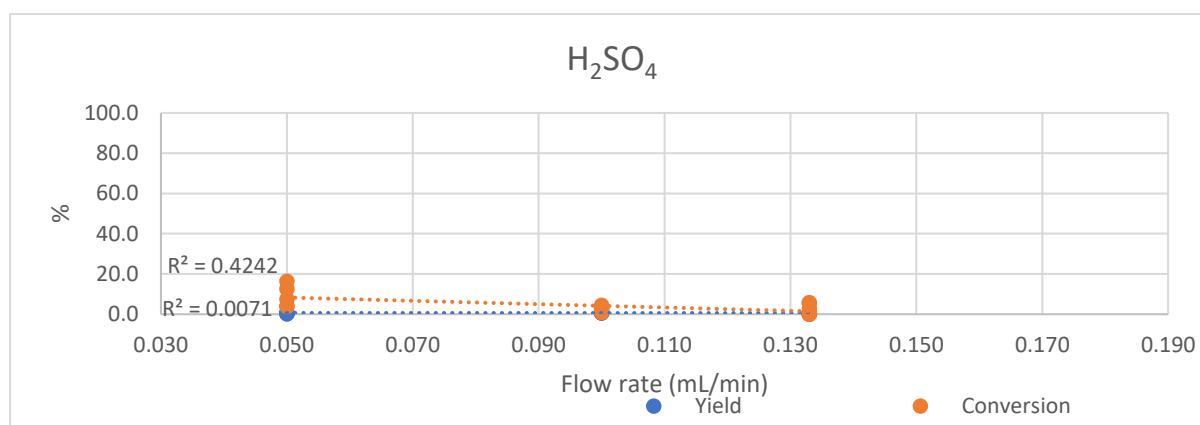


Figure S22. Effect of flow rate on yield and conversion in 2-methyl-1-butanol dehydration reactions using H₂SO₄ as the catalyst.

Activity

Activity can be measured in multiple ways, we opted to measure in two ways the first was by using the equation (equation 1) for CSTR that converts mass balance to turnover frequency using conversion of starting material under the same conditions (see paper).

$$V_t = \frac{F_0 \times x}{n_c} \quad x = \frac{F_0 - F_1}{F_0}$$

V_t: Turnover rate

x : Fractional conversion of reactant ($x = \frac{F_0 - F_1}{F_0}$)

F₀: Molar flowrate of reactant into the reactor

F₁: Molar flow rate of unconverted reactant leaving the reactor

n_c: Moles of catalyst

Equation 1. Mass balance equation for calculating turnover frequency from a CSTR

The second way was by altering the flow rate of the alcohol and therefore the residence time of the alcohol required to generate 30% conversion of starting material. The faster the flow rate the shorter residence time is required. This can be seen in figure S23. Both The results show Hf(OTf)₄ to be the most active followed by HOTf then Fe(OTf)₃. This method of activity testing was not sufficient for H₂SO₄ as it could not generate 30% conversion with our lowest flow rate.

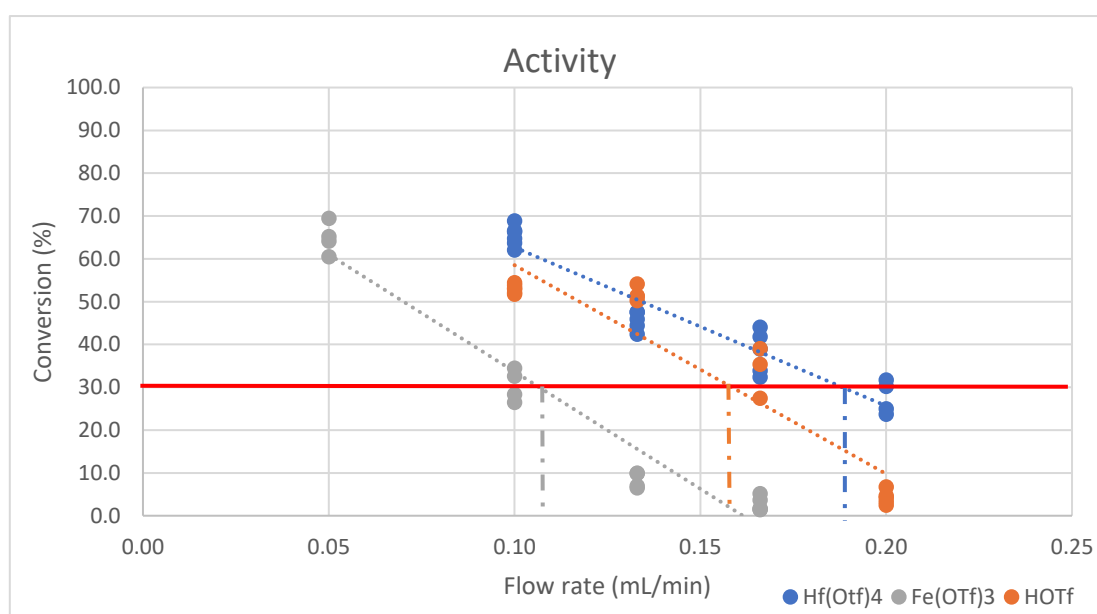


Figure S23. Effect of flow rate on conversion for Hf(OTf)₄, HOTf and Fe(OTf)₃. The flow rate required to generate 30% conversion for each catalyst is shown.

References

1. Catalytica, *A Practical Guide to Catalyst Testing: Basic Guide*, Catalytica, 1987.