Electronic Supplementary Information (ESI)

Reusability Studies with Lewis and Brønsted Acid Catalysts for Dehydration of the Primary Alcohol 1-Hexanol under Energy-Saving Conditions

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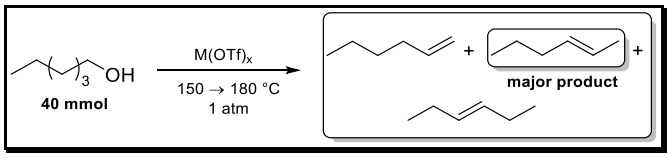
Experimental reagents

Chemicals were commercially bought without any further purification. Reactions were performed under atmospheric pressure or reduced pressure if noted.

Substrates: 1-Hexanol (Alfa Aesar, 99%) was purchased from commercial sources.

Catalysts: $Cu(OTf)_2$ (TCI, > 98 %), $Hf(OTf)_4$ (THERMOS SCIENTIFIC, 98 %) and TfOH (FLUOROCHEM, 99 %) were also commercially purchased.

Dehydration of 1-hexanol using metal triflates at 180 °C oil bath temperature:



1-hexanol (5 mL, 40 mmol) was presented with a catalyst (2 mol%) in a 25 mL round flask and connected to a micro distillation bridge. After heating it for 1.5 hour at 150 °C the temperature was further heated to 180 °C. The reaction was done for 6 – 22 h. After the distillation was finished, two phases were obtained. Through a separation of the organic phase from the water phase the crude product was obtained. The crude yield was then determined. The hexene purity was determined through ^{1}H-NMR spectra.

Table 1. Dehydration of 1-hexanol by 2 mol% metal triflates.

Entry	Metal triflate	Weight / mg	Catalyst loading / mol%	Reaction time / h	Hexene Yield / %
1	Cu(II)	288	2	22	65
2	Cu(II)	1440	10	6	73
3	Hf(IV)	621	2	6	76

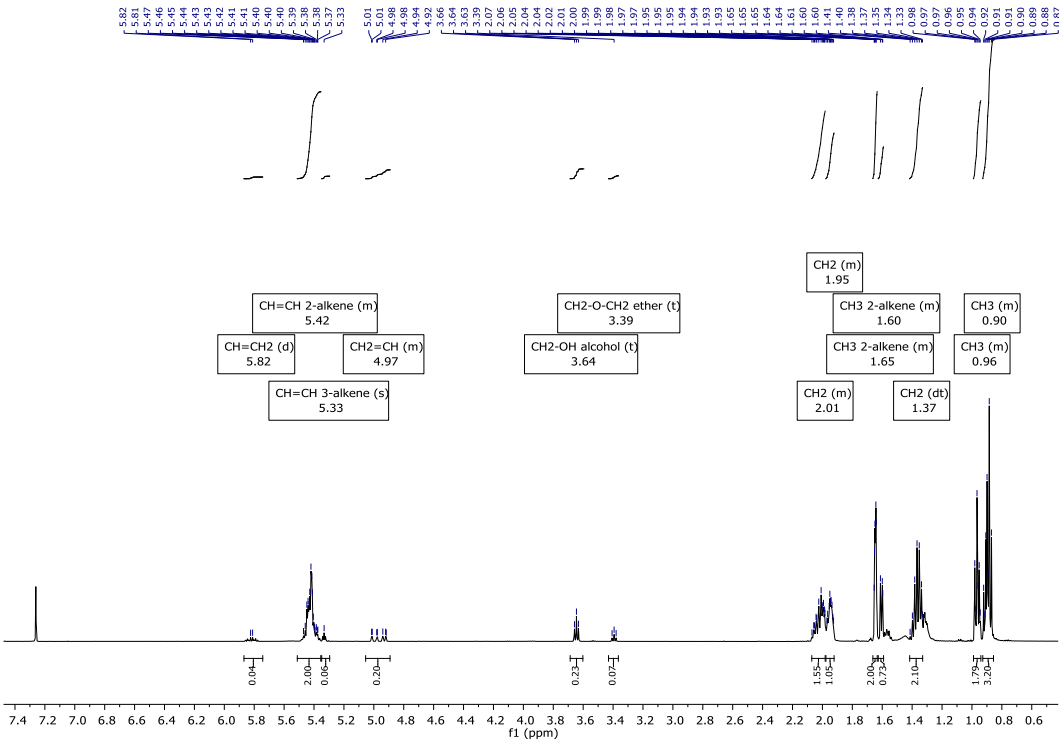


Figure 1. ^{1}H-NMR spectrum of the dehydration of 1-hexanol by $Hf(OTf)_4$ in $CDCl_3$.

1-hexene:

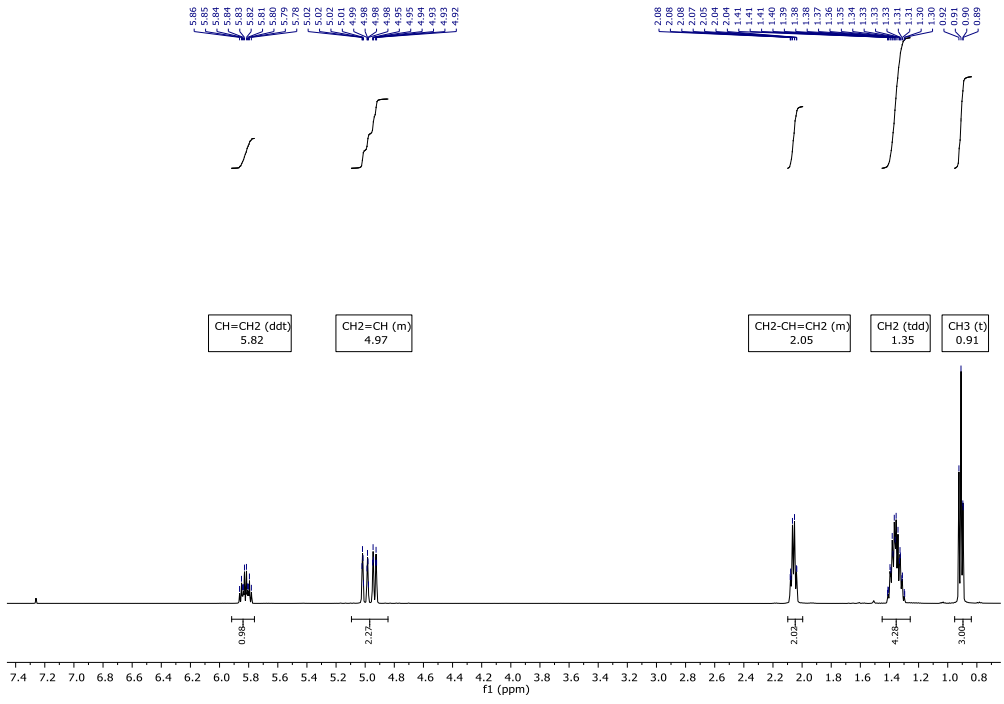


Figure 2. ^{1}H-NMR spectrum of 1-hexene in $CDCl_3$.

^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 5.84 (ddt, J = 16.9, 10.1, 6.7 Hz, 1H, C*H*=CH_2), 5.09 – 4.87 (m, 2H, CH=C*H*$_2$), 2.10 – 2.00 (m, 2H, C*H*$_2$), 1.45 – 1.26 (m, 4H, C*H*$_2$), 0.91 (t, J = 7.1 Hz, 3H, C*H*$_3$).

2-hexene:

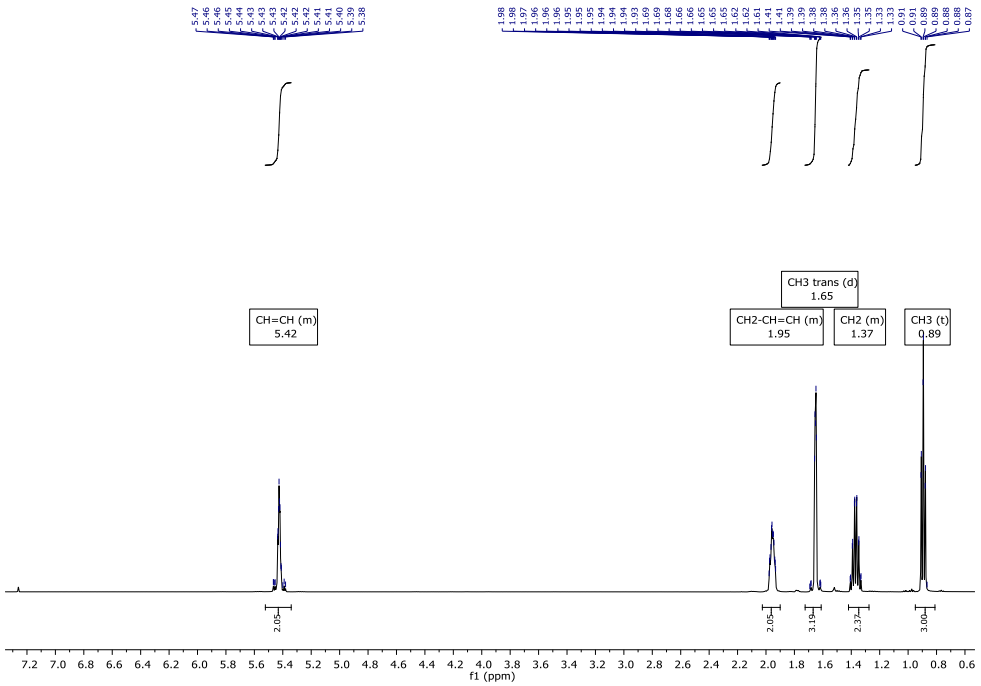


Figure 3. ^{1}H-NMR spectrum of *trans* 2-hexene in $CDCl_3$.

^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 5.52 – 5.34 (m, 2H, C*H*=C*H*), 2.03 – 1.90 (m, 2H, CH_2-CH=CH), 1.65 (d, *J* = 3.36 Hz, 3H, CH=CH-CH_3), 1.42 – 1.28 (m, 2H, CH_2), 0.89 (t, *J* = 7.3, 1.1 Hz, 3H, CH_3).

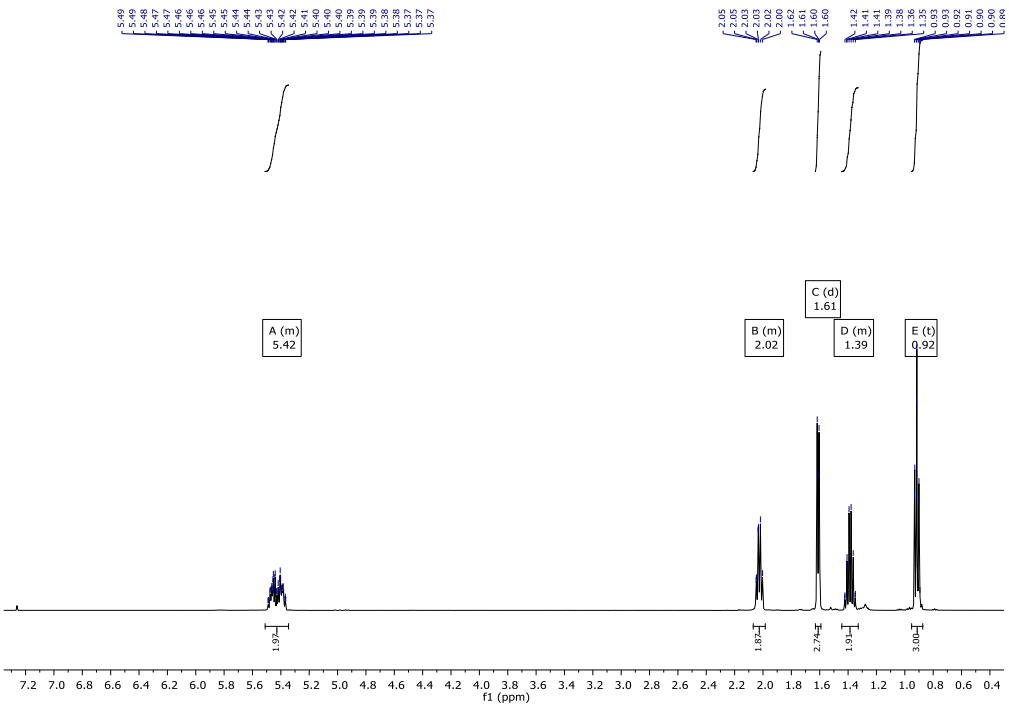


Figure 4. ^{1}H-NMR spectrum of *cis* 2-hexene.

^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 5.51 – 5.35 (m, 2H, C*H*=C*H*), 2.07 – 1.98 (m, 2H, CH_2-CH=CH), 1.61 (d, J = 6.72 Hz, 3H, CH=CH-CH_3), 1.44 – 1.33 (m, 2H, CH_2), 0.92 (t, *J* = 7.4, 3H, CH_3).

3-hexene:

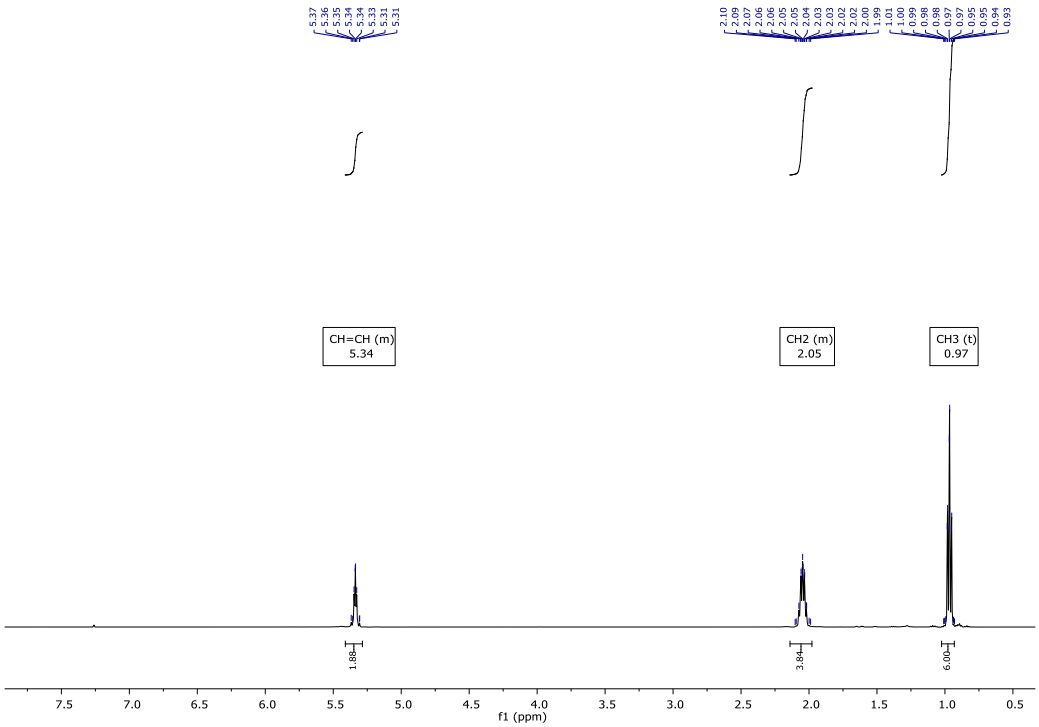


Figure 5. ^{1}H-NMR spectrum of 3-hexene.

^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 5.41 – 5.29 (m, 2H, C*H*=C*H*), 2.14 – 1.98 (m, 4H, CH_2), 0.97 (t, *J* = 7.6, 6H, CH_3).

di-*n*-hexyl ether:

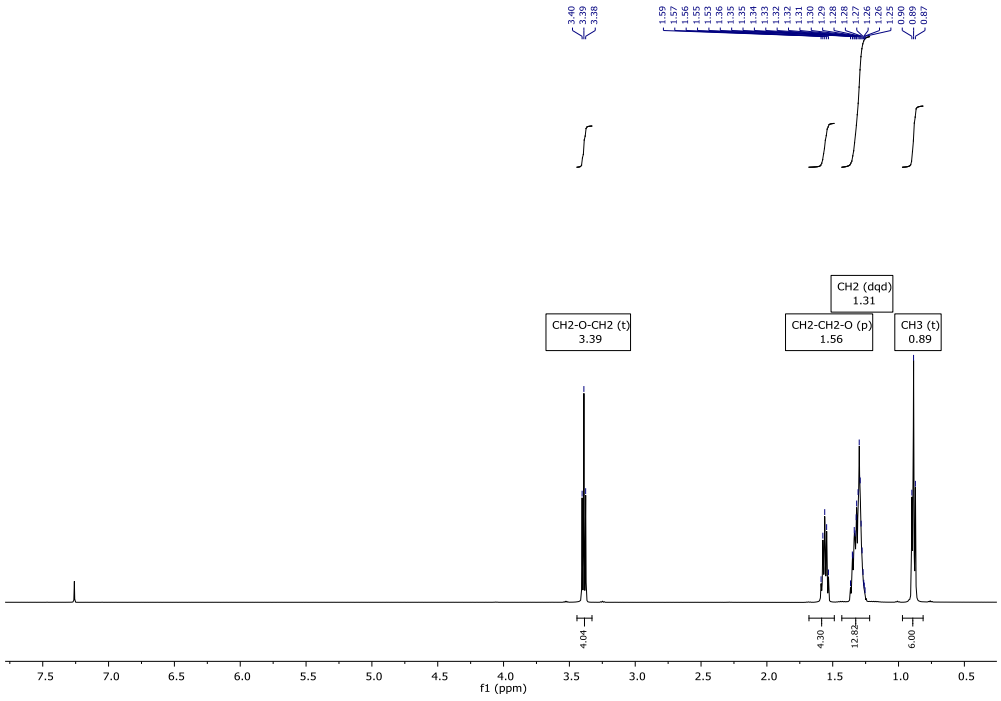


Figure 6. ^{1}H-NMR spectrum di-*n*-hexyl ether.

^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 3.39 (t, *J* = 6.7 Hz, 4H, C*H*$_2$-O-C*H*$_2$), 1.55 (q, *J* = 7.0 Hz, 4H, C*H*$_2$-CH$_2$-O-CH$_2$-C*H*$_2$), 1.31 (dddd, *J* = 15.2, 10.9, 7.1, 2.7 Hz, 12H, C*H*$_2$), 0.89 (t, *J* = 6.7 Hz, 3H, C*H*$_3$).

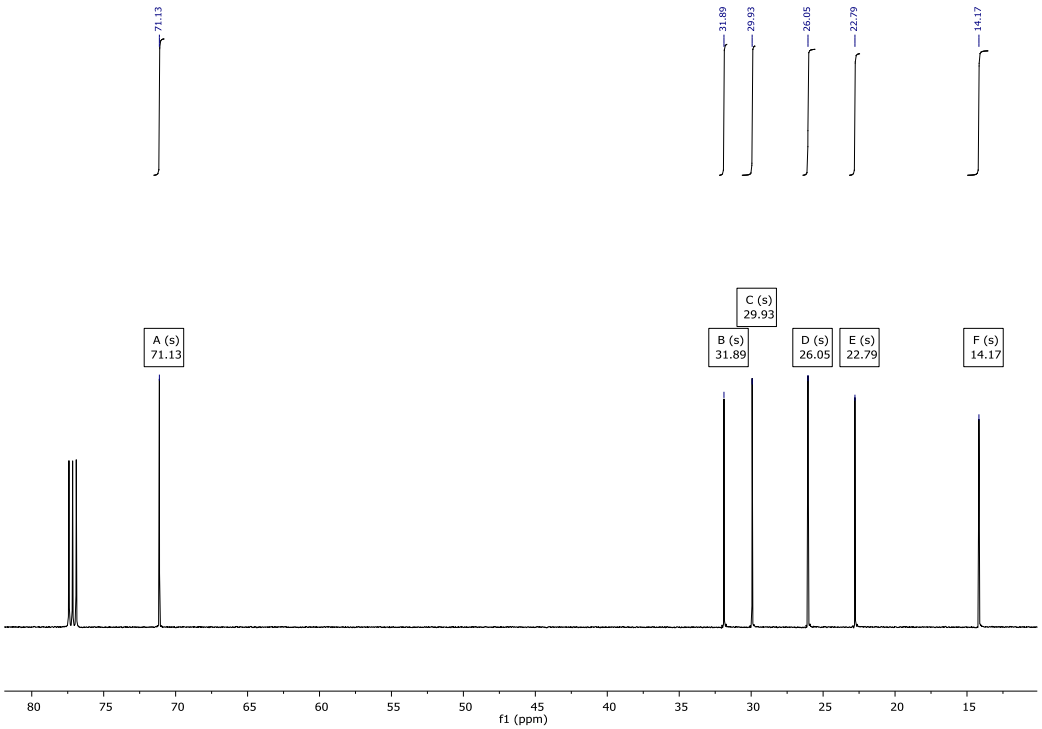


Figure 7. ^{13}C-NMR spectrum of di-*n*-hexyl ether.

^{13}C-NMR (500 MHz, $CDCl_3$): δ (ppm) = 71.13, 31.89, 29.93, 26.05, 22.79, 14.17.

1-hexene:

^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 5.84 (ddt, J = 16.9, 10.1, 6.7 Hz, 1H, C*H*=CH$_2$), 5.09 – 4.87 (m, 2H, CH=C*H*$_2$), 2.10 – 2.00 (m, 2H, C*H*$_2$), 1.45 – 1.26 (m, 4H, C*H*$_2$), 0.91 (t, J = 7.1 Hz, 3H, C*H*$_3$).

trans 2-hexene:

^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 5.52 – 5.34 (m, 2H, C*H*=C*H*), 2.03 – 1.90 (m, 2H, C*H*$_2$-CH=CH), 1.65 (d, *J* = 3.36 Hz, 3H, CH=CH-C*H*$_3$), 1.42 – 1.28 (m, 2H, C*H*$_2$), 0.89 (t, *J* = 7.3, 1.1 Hz, 3H, C*H*$_3$).

cis 2-hexene:

^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 5.51 – 5.35 (m, 2H, C*H*=C*H*), 2.07 – 1.98 (m, 2H, C*H*$_2$-CH=CH), 1.61 (d, J = 6.72 Hz, 3H, CH=CH-C*H*$_3$), 1.44 – 1.33 (m, 2H, C*H*$_2$), 0.92 (t, *J* = 7.4, 3H, C*H*$_3$).

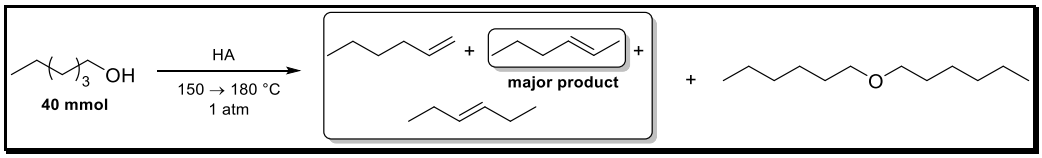
3-hexene:

^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 5.41 – 5.29 (m, 2H, C*H*=C*H*), 2.14 – 1.98 (m, 4H, C*H*$_2$), 0.97 (t, *J* = 7.6, 6H, C*H*$_3$).

di-*n*-hexyl ether:

^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 3.39 (t, *J* = 6.7 Hz, 4H, C*H*$_2$-O-C*H*$_2$), 1.55 (q, *J* = 7.0 Hz, 4H, C*H*$_2$-CH$_2$-O-CH$_2$-C*H*$_2$), 1.31 (dddd, *J* = 15.2, 10.9, 7.1, 2.7 Hz, 12H, C*H*$_2$), 0.89 (t, *J* = 6.7 Hz, 3H, C*H*$_3$).

Dehydration of 1-hexanol by Brønsted acids

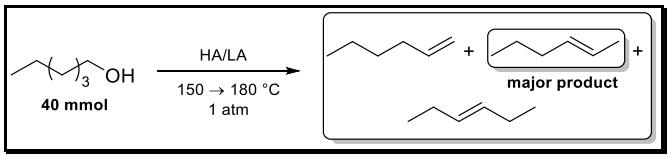


1-hexanol (5mL, 40 mmol) was presented with a BRØNSTED acid (HA) (2-10 mol%) in a 25 mL round flask and connected to a micro distillation bridge. It was first heated for 1.5 hours at 150 °C then to 180 °C. After 6 - 22 h the reaction was terminated. In the case of only ether formation, the crude mixture was filtered using a celite column and then purified using a silica column and cyclohexene as an eluent. After evaporation of the solvent, the yield and purity were determined. When the hexene was formed, the organic phase of the distillation fraction was separated from the aqueous phase and weighted. Afterwards, a ^{1}H-NMR spectrum was measured, and the alkene yield determined.

Table 2. Dehydration of 1-hexanol using Brønsted acids.

entry	Brønsted acid	catalyst loading / mol%	pKa	substrate loading / mmol	substrate loading / mL	reaction time / h	Ether yield / %	alkene yield / %
1	acetic acid	10	4.8	40	5	22	not formed	
2	H_3PO_4	10	2.1	40	5	22	not formed	
3	trifluoracetic acid	10	0.23	40	5	22	not formed	
4	tosylic acid	10	- 2.8	40	5	22	96	not formed
5	H_2SO_4	10	- 3	40	5	22	86	not formed
6	TfOH	10	- 14	40	5	6	5	73
7	TfOH	2	- 14	40	5	6	80	8
8	TfOMe	10	NA	40	5	6	10	62
9	Aquivion®	10	NA	40	5	6	3	55
10	$HNTf_2$	10	- 14	40	5	6	81	12

Dehydration of 1-hexanol for 20 cycles



1-hexanol (5mL, 40 mmol) was presented with a LEWIS or BRØNSTED acid (2-10 mol%) in a 25 mL round flask and connected to a micro distillation bridge. It was first heated for 1.5 hours at 150 °C then to 180 °C. After 6 h the reaction was terminated. The organic phase of the distillation fraction was separated from the aqueous phase, then weighted, and measured by ^{1}H-NMR. After the end of each cycle 5 mL of 1-hexanol was added and the reaction redone. This was repeated for a total of 20 cycles.

Table 3. Alkene yields of the dehydration of 1-hexanol using $Cu(OTf)_2$, $Hf(OTf)_4$ and TfOH..

Cycles	**Alkene yields / %**		
	$Cu(OTf)_2$ (10 mol%)	$Hf(OTf)_4$ (2 mol%)	TfOH (10 mol%)
1	66	79	74
2	75	72	73
3	69	80	78
4	71	86	61
5	61	78	72
6	60	66	73
7	66	76	72
8	67	75	76
9	71	82	73
10	76	76	72
11	69	78	74
12	75	78	76
13	75	77	75
14	76	77	77
15	73	78	76
16	77	78	76
17	74	78	76
18	78	77	78
19	78	77	77
20	74	77	78

Table 4. Total TON of the dehydration of 1-hexanol using $Cu(OTf)_2$, $Hf(OTf)_4$ and TfOH..

Cycles	Total TON		
	$Cu(OTf)_2$ (10 mol%)	$Hf(OTf)_4$ (2 mol%)	TfOH (10 mol%)
1	6.6	39.5	7.4
2	14.1	75.5	14.7
3	21	115.5	22.5
4	28.1	158.5	28.6
5	34.2	197.5	35.8
6	40.2	230.5	43.1
7	46.8	268.5	50.3
8	53.6	306	57.9
9	60.7	347	65.2
10	68.3	385	72.4
11	75.2	424	79.8
12	82.7	463	87.4
13	90.2	501.5	94.9
14	97.8	540	102.6
15	105.1	579	110.2
16	112.8	618	117.8
17	120.2	657	125.4
18	128	695.5	133.2
19	135.8	734	140.9
20	143.2	772.5	148.7

Calculation of costs

Costs were calculated using the formula (1) and (2). Prices for the catalysts and substrate were obtained from sources which mirror industrial costs. In case of $Cu(OTf)_2$ and $Hf(OTf)_4$ costs were determined by starting from metal chloride and TfOH. The syntheses of the metal triflates is described in literature.[1] Operation costs were not included in the calculation of the costs (which, thus, only consider variable costs).

First, the usage costs were calculated by including the substrate costs (equation 1). Thus, costs per mmol of alkene production were determined and then extrapolated for a kg synthesis for each cycle.

$$costs\ per\ mmol = \left(\frac{cost_{catalyst}}{\sum_i^6 x_i{\cdot}40\ mmol} + \frac{\sum_i^6 cost_{1-hexanol}}{\sum_i^6 x_i{\cdot}40\ mmol} \right) \cdot 9.78\ \cdot 10^3 \quad (1)$$

Second, the usage costs were calculated without including the substrate costs (equation 2). Thus, costs per mmol of alkene production were determined and then extrapolated for a kg synthesis for each cycle allowing to apply Formula 2 instead.

$$costs\ per\ kg = \left(\frac{cost_{catalyst}}{\sum_i^6 x_i{\cdot}40\ mmol} \right) \cdot 9.78 \cdot 10^3 \quad (2)$$

Table 5. Costs of substrate and catalysts.

entry		Costs per kg / $	Loading / mol%	Amound / g	Costs 1 cycle / $
1	1-hexanol	2[2]	100	4.07	$8 \cdot 10^{-3}$
2	$CuCl_2x2H_2O$	1[3]			
3	HfCl4	600[4]			
4	TfOH	1.21[5]	10	0.60	$7.26 \cdot 10^{-4}$
5	$Cu(OTf)_2$	4.42	10	1.44	$6.36\ \cdot 10^{-3}$
5	$Hf(OTf)_4$	604.84	2	0.62	0.375

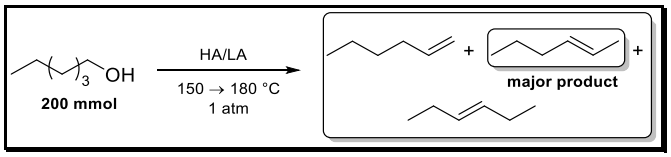
Table 6. Costs per kg produced alkene in the dehydration of 1-hexanol using $Cu(OTf)_2$, $Hf(OTf)_4$ and TfOH without consideration of substrate costs.

Cycles	**Costs per mmol / $**		
	$Cu(OTf)_2$ (10 mol%)	$Hf(OTf)_4$ (2 mol%)	TfOH (10 mol%)
1	1.817	112.151	0.638
2	0.851	58.675	0.321
3	0.571	38.355	0.210
4	0.427	27.949	0.165
5	0.351	22.430	0.132
6	0.298	19.219	0.110
7	0.256	16.499	0.094
8	0.224	14.477	0.082
9	0.198	12.766	0.072
10	0.176	11.506	0.065
11	0.160	10.448	0.059
12	0.145	9.568	0.054
13	0.133	8.833	0.050
14	0.123	8.204	0.046
15	0.114	7.651	0.043
16	0.106	7.168	0.040
17	0.100	6.743	0.038
18	0.094	6.369	0.035
19	0.088	6.035	0.034
20	0.084	5.735	0.032

Table 7. Costs per kg produced alkene in the dehydration of 1-hexanol using $Cu(OTf)_2$, $Hf(OTf)_4$ and TfOH with consideration of substrate costs.

Cycles	**Costs per mmol / $**		
	$Cu(OTf)_2$ (10 mol%)	$Hf(OTf)_4$ (2 mol%)	TfOH (10 mol%)
1	4.784	114.630	3.284
2	3.628	61.269	2.985
3	3.368	40.898	2.821
4	3.214	30.420	2.904
5	3.213	24.909	2.867
6	3.221	21.767	2.835
7	3.185	19.051	2.819
8	3.152	17.037	2.787
9	3.106	15.306	2.775
10	3.047	14.049	2.770
11	3.028	12.988	2.758
12	2.990	12.105	2.742
13	2.958	11.371	2.732
14	2.928	10.742	2.718
15	2.911	10.187	2.708
16	2.886	9.703	2.700
17	2.871	9.276	2.692
18	2.849	8.903	2.681
19	2.830	8.570	2.674
20	2.820	8.269	2.665

FED-BATCH reactions of the dehydration of 1-hexanol



1-hexanol (40 mmol) was presented with $Hf(OTf)_4$ (2 mol%, 0.8 mmol, 0.62 g) or TfOH (10 mol%, 4 mmol, 0.35 mL) in a 50 mL two-necked round flask and connected to a micro distillation bridge by one neck. On the other neck a septum was placed with a tube pierced which was connected to a syringe pump. The reaction was first heated for 1.5 hours at 150 °C then to 180 °C. As soon as the reaction was heated to 180 °C, the syringe pump was activated. Reactions were terminated after a further 20 mL of 1-hexene (160 mmol) was added. The organic phase of the distillation fraction was separated from the aqueous phase, then weighted, and measured by ^{1}H-NMR. Comparison reactions in FED-BATCH

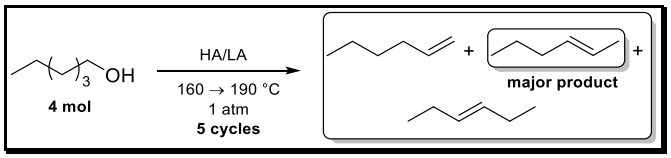
Table 8. Alkene yields of the dehydration of 1-hexanol (200 mmol) in BATCH and FED-BATCH.

Entry	flow rate / mL h^{-1}	time / h	Alkene yields	
			$Hf(OTf)_4$	TfOH
1	BATCH	30	72	76
2	0.7	30	49	78
3	0.85	25	53	75
4	1	21.5	54	74
5	1.2	18	58	73

Table 9. Total TON of the dehydration of 1-hexanol (200 mmol) in BATCH and FED-BATCH.

Entry	flow rate / mL h^{-1}	Total TON	
		$Hf(OTf)_4$	TfOH
1	BATCH	180	38
2	0.7	122.5	39
3	0.85	132.5	37.5
4	1	135	37
5	1.2	145	36.5

100-fold scale increase in the dehydration of 1-hexanol



1-hexanol (500 mL, 4 mol) was presented with TfOH (35 mL,40 mmol, 10 mol%) in a 500 mL two-necked round flask and connected to a distillation bridge. It was first heated for 1.5 hours at 160 °C then to 190 °C. After 6 h the reaction was terminated. The organic phase of the distillation fraction was separated from the aqueous phase, then weighted, and measured by ^{1}H-NMR. After the end of each cycle 500 mL of 1-hexanol was added and the reaction redone. This was repeated for a total of 20 cycles.

Table 10. 100-fold scale-up in the dehydration of 1-hexanol.

Cycles	Crude Yield / %	Alkene Yield
1	87	78
2	88	75
3	87	77
4	85	75
5	86	76

Figure 8. Set up for the 100-fold scale increase of the dehydration of 1-hexanol (left) including obtained alkene fractions (brown flasks) and crude mixture (Schott bottle).

Calculation of operational costs for 5 mL scale

$$Energy\ consumption = c_{1-hexanol} \cdot m_{1-hexanol} \cdot \Delta T + W_{stirrer} \cdot t \quad (3)$$

$$Energy\ consumption = 2{,}438\ \frac{J}{K \cdot g} \cdot 4{,}07\ g \cdot 155\ K + 0.1\ kW \cdot 6h + \quad (4)$$

$$Energy\ consumption = 1.5\ kWh \quad (5)$$

Costs = 0.18 $/kWh x Energy consumption (6)

With $c_{1\text{-}hexanol}$ and $m_{1\text{-}hexanol}$ as the specific heat capacity of mass of 1-hexanol, respectively. $W_{stirrer}$ describes the energy consumption of the stirrer (600 W) with the assumption that once the desired temperature is reached, the actual consumption is at 0.1 kW.

Calculation of sustainability metrics

The sustainability metrics were calculated using the following equations from literature[1].

$$E - factor = \frac{mass_{waste}}{mass_{Product}} \cdot 100\% \quad (7)$$

$$PMI = \frac{mass_{total}}{mass_{Product}} \cdot 100\% \quad (8)$$

With $mass_{waste}$, $mass_{Product}$ and m_{total} describing the mass of the waste and product as well as the total mass.

References

1 A. Allahverdiyev, J. Yang and H. Gröger, *Green Chem.*, 2024, **26**, 7869–7878.

2 Alibaba, *https://www.alibaba.com/product-detail/1-Hexanol-CAS-111-27-3_1601008920798.html?spm=a2700.galleryofferlist.normal_offer.d_price.204213a0v9b8Gz*, **Access: 23.09.2024**.

3 Alibaba, *https://www.alibaba.com/product-detail/professional-supplier-copper-chloride-dihydrate-CuCl2_10000019194693.html?spm=a2700.galleryofferlist.normal_offer.d_price.3e7713a00RkjOO*, **Access: 23.09.2024**.

4 Alibaba, *https://www.alibaba.com/product-detail/Factory-supply-hafnium-chloride-hafnium-tetrachloride_1600277046240.html?spm=a2700.galleryofferlist.normal_offer.d_title.22b013a0TPLrot*, **Access: 23.09.2024**.

5 Indiamart, *https://www.indiamart.com/proddetail/triflic-acid-cas-number-1493-13-6-2849952076330.html?pos=1&kwd=triflic%20acid&tags=CC|||8211.142|Price|product|||IVESI|rsf:gd-|-qr_nm:splt-rlx-gd|res:RC3|com-cf:nl|ptrs:na|ktp:N0|mc:289681|mtp:S|qry_typ:P|lang:en|wc:2|cs:8480|v=4*, **Access: 23.09.2024**.